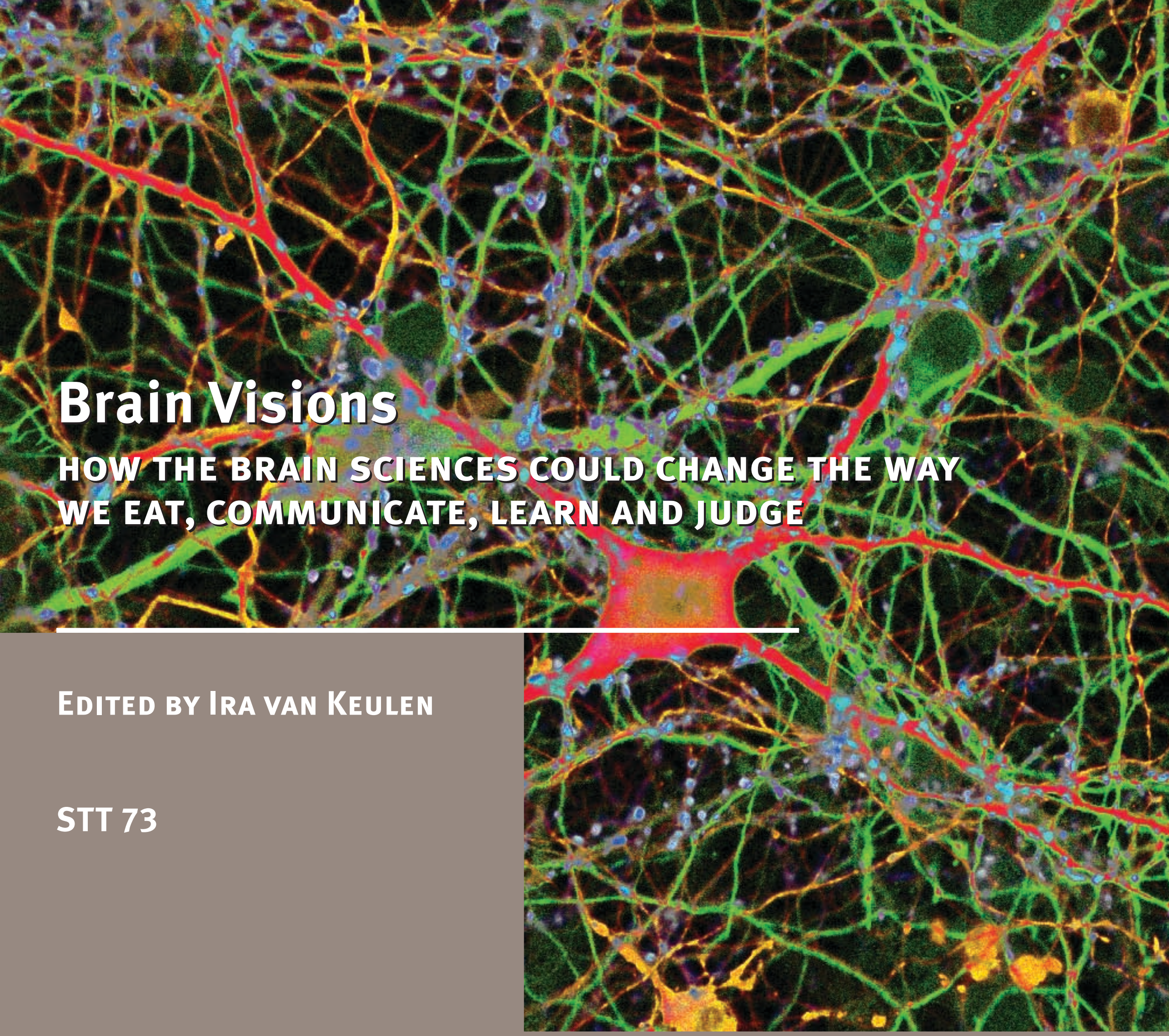

# Brain Visions

## How the brain sciences could change the way we eat, communicate, learn and judge

Edited by Ira van Keulen

STT 73

STT Netherlands
Study Centre for
Technology Trends

# Brain Visions

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The STT Netherlands Study Centre for Technology Trends was established in 1968 by the Royal Institution of Engineers in the Netherlands (KIVI). In 2001, STT merged with Beweton, the Future Shape of Technology Foundation. STT carries out foresights on topics which cross the border between technology and society. Within the foresight process, STT stimulates participants to think innovatively about the future. The most important aim for STT in doing foresight exercises is to encourage the exchange of participants' – each with their own specific academic background and working environment – ideas and experiences. This is referred to as 'knowledge fusion'. This foresight working method arises from the conviction that people themselves are the 'engine' to new developments. In this way, STT develops visions for the future. An STT publication is the tangible result of a foresight exercise. However, the results are also dispersed via the media and lectures. After a foresight on a topic has been completed, the results are transferred and continued into other activities, such as national (applied) research programmes or public-private cooperation. The participants who take part in the foresight process are the most important ambassadors for the forth-setting and dissemination of ideas.

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2008

STT
The Hague, the Netherlands

## Colophon

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# Contents

# Preface

*"The brain struggling to understand the brain is society trying to understand itself."*

This quote, by British neurobiologist Colin Blakemore, contains an important message, namely that studying the brain basically means studying ourselves. The physical brain is the engine that drives the complex and highly developed human mind. Thanks to rapid advances in the neurosciences and cognitive sciences, we are coming to know more and more about how the brain influences the mind — and vice versa. And that is in fact the task that the brain sciences have set themselves for the decades ahead: to understand ourselves, from our molecular basis to our behaviour, via the neural level.

Blakemore's statement also implies that our growing knowledge of the human brain will have all kinds of effects on society, more than any other scientific discipline has ever had. Although we do not yet have a 'grand theory' of the brain similar to the periodic table in chemistry or DNA in genetics, we can already play around with the pieces of the knowledge puzzle that we do possess. After all — as one of the participants in the STT Brain Visions project once commented — during the development of the automobile the horse still surpassed the car as the faster mode of transport for a long time. He wanted to point out that it is certainly not too early to consider how we might use our new neuroscientific knowledge, even if we do not yet fully understand the way the brain works. Our knowledge base in the brain sciences is expanding rapidly. Many discoveries — for example, mirror neurons, the brain as an automatic machine, and the far-reaching plasticity of the brain — are pioneering and will lead to many significant and socially relevant applications.

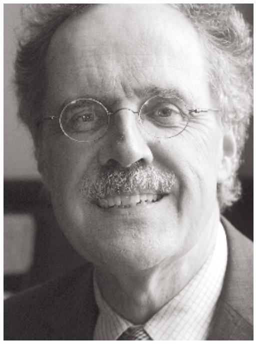
At the same time, it is useful for us to think about how we can use our knowledge of the brain to tackle existing social issues. For example, how can we, in our complex information society, use neuroscientific knowledge to develop interfaces that make optimal use of the potential and limitations of our brain (i.e. neuro-ergonomics)? Can we establish direct connections between our brain and our environment? Can we improve our teaching methods based on neuroscientific knowledge? And will those new methods allow us to tailor our teaching to individual pupils? Can we influence our eating habits through the brain, so that we can control obesity? And how does nutrition influence the way our brain develops? What should we eat if we want to function at our best? Can a person's brain show us whether he is telling the truth? Can we predict criminal behaviour?

Proper, useful applied research obviously requires interdisciplinary and transdisciplinary cooperation, with neuroscientists from different backgrounds (neurobiologists, neurophysiologists, cognitive neuroscientists, neuropsychologists, etc.) collaborating with scientists in other disciplines and with practitioners in the field (government, industry, civil society organisations, etc.) to define and conduct socially relevant research.
Applied research of this kind is already being carried out in the Netherlands in the field of health care, and more specifically in psychopharmacology. The Netherlands needs to concentrate on applied interdisciplinary and transdisciplinary neuroscientific research in a broader range of less obvious fields too, such as those explored in the STT Brain Visions project: nutrition, interface design, education and justice. The Netherlands is one of the international academic leaders when it comes to the brain sciences. Our challenge is to avoid the Netherlands' usual innovation paradox — academic brilliance which is not

exploited in applied research or practices — and to work on developing specific applications in this important field of science at an early stage.

STT's mission — to identify and encourage opportunities for innovation in the Netherlands — has inspired the project Brain Visions to make the first move in considering long-term neuroscientific applications beyond the field of medicine. The result of this project is a network of people in the Netherlands who have challenged one another to think beyond their own (brain) science research and everyday practice. Their thoughts and ideas about how to apply our growing understanding of the brain are the focus of this book. It is the product of the unflagging efforts of a large number of enthusiastic people active in the brain sciences and related areas of application, and of the even greater efforts of project manager Ira van Keulen. We trust that this book will goad others to continue expanding our knowledge of the neurosciences and to study how that knowledge can be applied. We are facing far-reaching changes in our world image — and we must be prepared!

Ir Wiebe Drayer,
Chairman of the Study Centre
for Technology Trends (STT)



Ir Paul 't Hoen,
Chairman of the Brain Visions
Steering Committee

# 1

# Brain Visions: an Overview

*Ira van Keulen (ed.)*[1]

## 1.1 Introduction

Neuroscientific research aims to understand the human brain and mind. Like genetics, it tries to unravel the biological basis of human nature. Never before did scientific research get so personal, however. The brain has slowly come to occupy a key place in the image we have of ourselves and will continue to do so.

Following the explosion of knowledge in the genetic sciences over the past twenty years the same revolution is expected in the neurosciences and cognitive sciences[2] in the decades ahead. According to Eric Kandel, one of many Nobel prize-winning neuroscientists, there is even general consensus in the scientific community that the biology of the mind will be to the 21st century what the biology of the gene was to the 20th.

1 Projectmanager, STT.

2 We define the neurosciences as the study of the central and peripheral nervous system — including the brain and mind — on different levels of aggregation from molecule, cell, tissue, organ to system. The cognitive sciences have a broader perspective, combining the methods and insights of large parts of psychology, neuroscience, evolutionary biology, linguistics, articial intelligence, philosophy, anthropology and other social sciences, and formal methods from computer science, mathematics and physics [Andler, 2005].

Our growing knowledge of the brain has not failed to affect other scientific disciplines such as economics, ethics and even theology. For example, neuro-economics is a new subdiscipline based on functional magnetic resonance imaging (fMRI; see Appendix 1) research on the (until now neglected) effect of emotion on decision-making. Neuro-ethics is another upcoming field, which reflects on the ethical consequences of neuroscientific findings (and considers major issues such as cognitive enhancement and free will); it also explores the neurobiological basis of moral decision-making. Some neuroscientists even refer to the possibility of a brain-based theory of ethics [Gazzaniga, 2005] or the neuroscience of fair play [Pfaff, 2007]. Another example is neurotheology, which explores the neurological and evolutionary basis for subjective experiences categorised as spiritual (as some earlier geneticists did in looking for the 'god gene').

There is great interest in the public domain in the progress of neuroscience and cognitive sciences in general. And, as it turns out the traditional cognitive disciplines such as behavioural psychology have — in the wake of neuro-imaging research — also become the focus of renewed attention. New popular magazines on psychology are popping up and existing ones are gaining subscribers. Newspapers report recent findings in brain and cognition[3] research on a daily basis. Numerous websites, weblogs and television programmes explain scientific discoveries related to the brain and behaviour to the general public. All this public attention can be explained by the fact that neuroscientific findings are closely related to the self and the way we see ourselves.
Our growing knowledge of the brain is also leading us to believe that 'we are our brain', a notion that is gaining credence in society. We increasingly view our brain, rather than our heart or our DNA, as the key and determinative factor of our personality. At the same time, the idea that the human mind[4] can be reduced entirely to brain functions has taken root, not only in academic circles but also among the general public.

One thing is clear: the brain is in the centre of scientific and public attention. That is precisely why the Netherlands Study Centre for Technology Trends (STT) has set up the Brain Visions project: to explore this imminent revolution in science and public thought. STT has placed particular emphasis in this project on how fundamental neurocognitive and cognitive research interacts with social issues. *The main question therefore is: how and where can this growing knowledge of the brain be of use to society?*

Because other research is already exploring neuroscientific advances in medicine in-depth, the STT project has deliberately focused on four other important areas of application outside the medical domain: food, man-machine inter-

3 Cognition refers to mental processes such as memory, action, attention, perception, problem solving, mental imagery, but also emotion.

4 Mind collectively refers to the aspects of intellect and consciousness manifested as combinations of thought, perception, memory, emotion, will and imagination. See www.wikipedia.org.

faces (MMI), education and judicial practice. Inevitably, some of the examples given in this book are related to health, simply because most neuroscientific and cognitive research seeks to understand neurological and psychiatric disorders. Nevertheless, the key goal of the project (and this publication) is to show potential applications or opportunities for applied research in four — for some readers perhaps less obvious — domains outside health care. This chapter presents a selection from the many fascinating ideas — or 'brain visions' as we like to call them — circulating in academia and industry as to how we can apply our growing knowledge of the brain.[3]

In this introductory chapter we summarise and reflect on the outcomes of the STT project. The following questions will be addressed:

- What brain visions can we find in the fields of food, MMI, education and judicial practice (see sections 1.2, 1.3, 1.4 and 1.5)?
- What is the aim of fundamental neuroscientific and cognitive research in the near future? (see section 1.6)
- To what extent are the neurosciences and cognitive sciences ready for applied research? Why are the expectations of research on brain and cognition so high? (see section 1.7)
- What conditions must be in place for the neurosciences and cognitive sciences to continue academic progress and to produce socially and economically relevant applications? (see section 1.7).

### 1.1.1 How to read this chapter

This first chapter, Brain Visions: An Overview, is based on the subsequent chapters: Nutricognition, Neuro-centred Design, Personalised Learning and Evidence-based Judicial Practice. Each section describes a number of the future applications and research topics covered in one of the four chapters. These projections are articulated briefly in propositions (i.e. brain visions) based either on current neuroscientific and cognitive research findings or on present trends in the particular area in which neuroscientific research (or technology) can be of help. This first chapter therefore serves to whet the reader's appetite. You can read more about the background of the various propositions in the chapters themselves; the relevant sections will be indicated at the end of each proposition.[5] The reader should be aware that the propositions are based on contributions by various authors who have differing views about society, science and technology. They therefore do not always form one coherent vision; indeed, some propositions may even contradict one another to a certain extent.

The propositions also differ at domain level (food, MMI, education and judicial practice). For example, those referring to nutricognition are prompted largely

5 Some ideas may even turn out to be unfeasible in the long run.

by the interests of the food industry, but are also relevant for large groups in society. Most of the propositions in the domain of MMI are more futuristic and therefore more debatable; the visions put forward may have a time horizon of more than twenty years. The propositions related to education focus on one specific vision, i.e. personalised learning, and have fewer tangible applications for educational practice in the short run. And finally, the propositions related to judicial practice are very much focused on criminal investigation and the judicial process in the courts (and less on criminal punishment and treatment); more than in the other domains, they also presume ethical and political choices.

## 1.2 Brain visions on food

There are two ways to think about the relationship between food and the brain, or 'nutricognition', as we refer to this field of expertise in this book. On the one hand, there is growing research on the effect of diet and individual nutrients on brain development and cognitive functions (see subsection 1.2.1). One example is the positive effect of folic acid on the ageing brain: it slows down the normal age-related decline in such cognitive functions as memory and information processing. On the other hand, researchers are increasingly examining the neural mechanisms behind eating behaviour, e.g. satiety, food perception and liking, hunger, food addiction or buying patterns (see subsection 1.2.2). Recent neurocognitive research has demonstrated, for instance, that the response of the food reward system in the brain to food cues such as food advertisements varies widely between individuals. People with a strong tendency to overeat have a more sensitive neural reward system.

Although the food industry is increasingly focusing on healthy food — in the past five years, American food companies have introduced more than 10,000 nutritionally improved food products — the relationship between food and the brain has been largely overlooked. Research and development concerning diet and dietary standards used to focus mainly on physical health, such as cholesterol levels, but rarely studied the effect of diet on cognitive performance. This has changed significantly. Nowadays, the brain-food relationship is one of the main pillars of many food companies' research programmes. For example, Nestlé recently agreed to grant the Swiss Federal Institute of Technology 3.1 million euro a year to study the role of nutrition in cognitive functions. Understanding the link between brain function and diet is also one of the main items on the strategic research agenda of the European Technology Platform on Food for Life, which represents the collective European food industry.

This growing mound of nutricognitive research may lead to the introduction of various food products now and in the future: ‘brain food’ (i.e. products affecting brain development and performance), weight-control products (i.e. high-satiety products that reduce the consumer’s appetite) or products based on cross-modal compensation strategies (i.e. replacing different sensory stimuli like taste, odour, texture or colour with one another to achieve the same effect in liking). The rapid introduction of healthy brain food products is a result both of the food industry accepting its corporate social responsibility and of the considerable profit margin of 30 to 40% on functional food products[6] (compared to the very small profit margin on standard products).

But it is not only the food industry that will profit from the increasing research on brain-food interdependency. The public will also receive better nutritional advice, with, for example, the elderly being advised to consume vitamin D to prevent depression or folic acid to prevent dementia. Scientific research into the neural mechanisms behind overeating may lead to better policy measures to fight the obesity epidemic. Nutricognitive research may also make it possible to develop nutritional interventions counteracting the damaging neural effects of naturally occurring arsenic found in the groundwater of 200 million people in Asia.

But we are not there yet. There are still many questions to be answered, for example regarding the impact of various nutrients on the brain for different groups of consumers. Neuro-imaging techniques will be particularly crucial in nutricognitive research. They can provide more sensitive and specific test methodologies to help us understand the underlying mechanisms of preference and liking, sensory perception and integration, and the influence of nutrients on brain development and performance. And whereas more traditional food research relies on long-term nutritional intervention and large groups of respondents, neuro-imaging may speed up research on the effect of nutrients on the brain.

### 1.2.1 Brain food

**Brain food is especially promising for specific consumer groups in developed as well as developing countries**

**– section 2.2**

As mentioned in the introduction to this subsection, there are different ways in which the food industry aims to profit from our growing knowledge of the

6 Food products that claim to improve well-being or health.

brain. The most obvious, of course, is by developing brain food: functional food products that have a positive effect on brain development and/or cognitive functioning. To provide conclusive proof of the feasibility and functionality of brain food, we must answer some key questions, for example: what is the effect of individual nutrients on key molecular processes in the brain, and what is the relationship between these processes and cognitive functioning? So far, most of the evidence for the positive effects of nutrients on cognitive development has come from research on diseased or malnourished individuals. It is therefore likely that the market for brain food products aimed at specific consumer groups — for example, subclinical groups (consumers with a predisposition towards e.g. stress or mood disorders) — will grow. Brain food is likely to have a bigger impact on these groups. The same goes for consumers in the developing world, as the nutritional deficiencies that hamper brain development are more widespread in such regions. In particular, children who are deprived of a well-balanced diet suffer from cognitive underdevelopment because they lack micronutrients such as iodine, vitamin A, iron, zinc and folic acid. On the other hand, the market for brain food for healthy target groups (e.g. children and seniors) is bound to grow as well. There, the food industry will attempt to optimise nutrition in support of brain development (children) and to prevent the erosion of the brain structure and function with food (seniors). Brain food products could either be novelties (for example 'brain bars') or more traditional value-added products optimised during production or processing to naturally contain more of the desired ingredients (e.g. omega-3s in dairy products, eggs or meat). In developing countries, a simple strategy of fortifying staple foods (for example adding minerals to flour) will probably reach more of the target consumers. The average middle-aged consumer with a well-balanced diet will probably not benefit from brain food, however, simply because its effect on top of an optimal diet or even a dietary baseline will be minimal or non-existent.

## Products or strategies based on the direct effects of food may not lead to cognitive enhancement, but the indirect effects of food may – subsection 2.2.4

There are a couple of key nutrition-related factors that have a indirect effect on cognitive development and performance. For example, the gut has to be healthy in order to absorb the essential nutrients from the brain food ingested. Another key factor is a healthy cardiovascular system, which has a positive effect on cognitive performance, especially later in life.[7] Since lifestyle (including nutrition) is one of the ways to control the key risk factors for car-

7 Elderly people nowadays are encouraged to take more physical exercise to stave off neurodegeneration.

diovascular diseases (such as blood pressure and LDL cholesterol), nutrition can play an indirect role in improving brain function by ensuring a healthy cardiovascular system. Another example of an indirect route is recovery (i.e. sleep), which influences our ability to concentrate and thus 'exercise' our brain. These indirect effects may compel the food industry to consider strategies that combine food products with activities promoting a healthy lifestyle. Nike's 'Start to Run' initiative is a good example; it is a training programme for people who need a little extra motivation to start running (in a new pair of running shoes, of course). The food industry may also find this an interesting strategy for its brain food sector, for example in combination exercise-food programmes,[8] especially as it has been suggested that the direct effects of nutrients can only lead to normal or optimal brain and cognitive development. In other words, under normal circumstances it will likely be impossible to enhance cognitive functioning by means of nutrition. However, the indirect effects might represent the differentiating factors that boost development and performance 'above baseline'. This is still a topic of great debate among scientists, however.

### 1.2.2 Overeating

Brain vision

**Neuroscience can help to improve strategies of replacement of potentially harmful nutrients and satiety (i.e. achieving a feeling of being full) in product development** – subsections 2.3.2 and 2.4.2

Besides brain food, there are other ways in which brain research can be of service to the food industry and to consumers. These have to do with the shifting focus of industry towards health-related goals such as vitality and wellness. Companies nowadays make considerable efforts to develop food products that support a healthy life style, e.g. products aimed at weight management. Two product strategies are interesting in this respect and could benefit from the neurosciences.

In the first place, there are the cross-modal compensation strategies: how can potentially harmful nutrients such as fat, salt or sugar be replaced with harmless ones without the consumer perceiving a difference? For example, because taste affects smell and vice versa, adding strawberry aroma to sucrose solutions increases their perceived sweetness (taste). A major challenge for the neurosciences here is to understand how we sense 'fat content' or creaminess

8 The American start-up BrainSavers (www.brainsavers.com) is using just such an indirect strategy. They have developed "a total lifestyle program that helps people adopt healthier habits through physical and mental exercise, support, education, nutritional guidance, and supplemental nature-based nutritional products."

in food products. Some neuroscientific research suggests that we have a separate oral sensory mechanism to sense fat. This means that we might be able to replace fat by another single compound. However, it is more likely that a good understanding of how our brain 'sees' fat will allow product developers to find suitable alternative mixes that exploit colour, flavour and taste to recreate that rich, creamy feeling of fat in the mouth, without the calories.

Another weight management strategy involves satiety. Some foods are more satiating than others because they have a lower energy density (i.e. small number of calories per volume), more weight or volume or a high fibre content. In future, more and more products will be designed to produce higher satiation per calorie. In other words, these new food products will give the consumer a feeling of fullness in an early stage of consumption. The main strategies so far have been to add fibre or protein, but a better understanding of the neural mechanisms behind satiety could help to develop new satiety product strategies. Furthermore, neuro-imaging methodologies can also monitor the subconscious brain responses of subjects directly when it comes to satiety, instead of measuring responses indirectly by means of questionnaires.

Brain vision

## The first year of life is the largest window of opportunity for conditioning food preferences – subsection 2.3.4

Food preferences are remarkably stable and those acquired early in life may have particularly long-lasting influences. Hedonic (i.e. like versus dislike) *taste* aspects are largely inherited, but may be shaped by experience during development. The hedonic value of *smell*, on the other hand, is learned and varies widely between subjects and cultures. Although heredity plays some role, most sensory preferences seem to be learned through repeated exposure to particular sensory events and their associated consequences. A fondness for certain foods established in the early years of childhood may even predict preferences in early adulthood, especially for vegetables, cheese and meat. For example, neonatal exposure to vanilla odour resulted in a preference for vanilla-flavoured tomato ketchup during adulthood. Flavouring formula milk with vegetable flavours could be one way of stimulating children to eat healthy food, although we do not yet know whether such flavoured milk will indeed make vegetables more acceptable to them later. In summary, the first year of life seems to be a large window of opportunity for developing stable food preferences.[9] Whether and how this window can be used to condition a preference is not clear yet. Determining the neural mechanisms underlying human preference behaviour could help us design strategies to influence that

9 Although it is also possible in adults to establish, for example, an association between novel — non-existent — smells and a particular feeling (e.g. happy or sad).

behaviour. Future neuroscientific research should therefore focus in particular on the processes involved in the neural linkage between the hedonic and perceptual aspects of food.

## Individual neural differences appear to determine a proneness to overeating – example I

If the taste, smell and appearance of food is highly appetising, the rewards can override satiety signals in the body, and thus promote overeating. Neuroimaging research shows individual brain differences in these reward responses to food cues. At the same time, behavioural research has shown that people with a high reward sensitivity have a higher body weight, more food cravings and a stronger tendency to overeat than people who are less sensitive to appetising food cues. In short, it seems that some people are more prone to overeating than others. This means that there is more to obesity than a lack of individual willpower resulting in overeating, a notion that has led to prevention strategies aimed at the individual. The latest neuroscientific findings, however, show that collective strategies — such as banning food advertisements for sweetened food products and beverages from children's television — may work too.

## Obesity affects brain and cognitive development; for example, it leads to a higher risk of dementia – subsection 2.5.3

The discussion of the medical consequences of obesity has so far neglected the effects of overeating on the brain and cognition. The emphasis in that discussion is usually on cardiovascular risks, insulin resistance syndrome and other lung, liver, kidney and muscoskeletal complications. But scientific evidence for the negative neural and cognitive consequences of obesity is mounting. For example, early postnatal catch-up of a low birth weight up to one year of age is negatively correlated with IQ. Other research shows that this particular effect of postnatal compensatory growth may also negatively influence IQ scores at the age of eleven, when adjusted for socio-economic factors.

Obesity in middle age also increases the risk of dementia later. Research has shown that people who were obese in mid-life were 74% more likely to suffer dementia. Overweight people were also 35% more likely than people of normal weight to suffer dementia [Whitmer, 2005].[10] Programming of obesity during

10 A Body Mass Index (BMI, statistical measure of an individual's weight scaled according to their height) of more than 30 indicates obesity; between 25 and 30 indicates overweight.

pregnancy also appears to contribute to the potential risk of Alzheimer's disease. In general, it seems that the more organ fat, the higher the risk of dementia, the result of neurodegenerative, vascular and metabolic processes affecting the brain structures underlying cognitive decline and dementia. More research is needed to describe these disconcerting neural and cognitive consequences of obesity in detail.

### 1.2.3 Product development

Brain vision

**A better understanding of the sensory properties of food could help reduce product development cycles**

**– subsections 2.3.1 and 2.3.5**

Greater insight into the sensory and physiological functionalities of ingredients and food structures could help the food industry predict consumer liking and, in particular, long-term acceptance of new products. Of special interest here is the possibility of using neuro-imaging to directly measure hedonic brain responses to different sensory properties, such as the taste, smell and texture of specific ingredients. For example, there is a positive hedonic value when hedonic brain systems such as the dopaminergic and opioid pathways are activated. Different brain regions, for example the orbitofrontal cortex, are important in liking and craving behaviour. These areas are more active — and thus light up on imaging scans — when chocolate lovers see or eat chocolate, for example. According to the renowned neuroscientist Edmund Rolls, this means that *"We can tell what people will like from their brain response"* [Farrow, 2007]. Research in Rolls' lab showed that there are indeed individual differences in brain processing for very pleasant food, depending not only on the amount of food eaten — the more you eat, the less you crave that particular food (i.e. sensory-specific satiety) — but also on people's particular liking and craving for food. Understanding these individual brain differences in relation to food choice and food craving could help industry design product development rules. At the same time, neuroscientific methods may allow us to measure consumer perception more objectively than by means of consumer panels or interviews. Such insights could reduce the amount of time spent on trial and error in laboratory testing and solve one of the food industry's trickiest problems: the fact that more than 70% of new products disappear from the shop shelves within three months.

## 1.3 Brain visions on man-machine interfaces (MMI)

The most obvious application of neuroscientific knowledge in the field of MMI[11] is, of course, brain-machine interfaces (BMIs; see subsection 1.3.1). One of the most mind-boggling examples of a BMI is the brain implant that Mathew Nagle — paralysed from the neck down — received in 2006.[12] This neuroprosthetic device enabled him to communicate his intentions directly to the outside world by thinking. For example, he was able to move a cursor by thinking about moving it. This seemingly insignificant action helped him compose a letter, play a computer game, open his e-mail and browse the Internet — an enormous improvement in the quality of his life (see also example V).

There are two principal BMI approaches: invasive (inserting electrodes directly into the brain) and non-invasive (attaching sensors to a cap or headband worn on the scalp), both of which can read brain activity — for example by measuring electrical signals, blood supply or oxygen level — and translate it into a digital form that computers can convert into action of some kind. The brain activity measured by BMIs is sometimes related to a particular cognitive activity. Microsoft, for example, sent in a patent application in August 2007[13] for *"using electroencephalograph signals for task classification and activity recognition"*. They — and many others — hope to use an electroencephalogram (EEG; see Appendix 1)) to recognise the brain activity patterns of cognitive workload, task engagement, surprise, satisfaction and frustration. Such information, derived directly from the brain, could lead to adjustments to the computer system, for example in case of cognitive overload the amount of information offered to the user. Progress in understanding the neural activity patterns behind different mental processes could eventually lead to the ultimate adaptive system. Sometimes brain activity does not contain any information at cognitive level, but is used merely as an output measure that can be detected by the computer system in order to recognise the user's need. For example, when a user watching a random sequence of letters sees one letter that he wants to communicate, a P300 brainwave[14] — measured by EEG — spikes.

Neuroscientific research can also be of use outside the field of BMI, however. Two other areas that might benefit from our growing knowledge of the brain in MMI are neuro-ergonomics and neuro-mimicry. Neuro-ergonomics (see subsection 1.3.2) is an emerging field combining neuroscience with man-machine interaction studies in order to evaluate and optimise the match between a particular technology or interface and the capabilities and limitations of the human brain. One example is the recent brain-imaging research on mobile phone use while driving, which indicates that even hands-free or voice-activated use of a mobile phone is as dangerous as driving under the influence

11 MMI studies the means by which people interact with a system, e.g. a particular machine, a device, a computer program or another complex tool.

12 An 96-electrode array was placed on the surface of Nagel's motor cortex in the region that controlled his left arm and hand. The electrode was connected to a computer trained to recognise Nagel's thought patterns while Nagel attempted to make certain movements. Nagel had the BMI for a year. In July 2007 Matthew Nagel died.

13 United States patent application 20070185697.

14 A P300 brainwave is a positive deflection in voltage indicating that the user is experiencing a significant sensory stimulus.

of alcohol.[15] Neuro-mimicry (see subsection 1.3.3) is about using our growing knowledge of how the brain works to imitate neural mechanisms in novel interfaces, machines or robots. An example of this is the whiskerbot: a small mobile robot with whiskers that can assess surroundings which are difficult to enter such as pipe-lines or collapsed buildings.[16] The design is based on computational models of whisker-related brain areas in the rat brain. Another example is the American company Numenta — owned by Jeff Hawkins, the founder of Palm Computing — which is working on developing an intelligent computer that does not need to be programmed but, like the human brain, learns by identifying patterns in complex data. Hawkins calls it a hierarchical temporal memory system (HTM) patterned after the human neocortex.

Last but not least, a totally different perspective on the symbiosis of the neurosciences and MMI claims that the neurosciences can also benefit from MMI research and development (see subsection 1.3.4). MMI can offer the cognitive neurosciences interesting research tools such as Virtual Reality (VR). Research participants being tested in an fMRI scanner must lie still. The research stimuli can only be given on a computer screen, requiring no movement from the participants. Combining fMRI and a well-designed VR environment that gives participants a strong sense of reality could lead to a better understanding of the relationship between what people are thinking and experiencing and the associated patterns of brain activity. MMI can also support the neurosciences in designing applied research projects proposing to investigate the neural and cognitive processes underlying the interaction of humans with technology. That way, MMI would support fundamental neuroscientific research anchored in the real world and extend the ecological validity (i.e. approximating the real-life situation under investigation as closely as possible) of neuroscientific findings.

The various ways in which MMI can exploit neuroscientific knowledge and vice versa could lead to a new field, and perhaps even a new era: the neuro-centred design of interfaces.

15 Neurocognitive research shows that the listening-and-drive mode produced a 37% decrease in activity in the parietal lobe, which is associated with spatial processing, critical for navigation. Activity also decreased in the occipital lobe, which processes visual information [Just et al., 2008].

16 See www.whiskerbot.org.

## 1.3.1 Brain-machine interfaces (BMIs)

### A better understanding of the communication between brain areas or neuronal networks will lead to the broad application of BMIs in future – subsections 3.2.2 and 3.2.3

Only the most fundamental brain functions (motor and sensory functions) are regulated by one specific part of the brain, i.e. are localised in the brain. Cognitive functions such as attention and perception are more complex[17] and controlled by networks of different brain areas. The degree to which these networks are activated depends on the task at hand. Although it is a much more complicated matter to measure network activity, doing so will most likely improve any future BMIs that aim to convey information on the cognitive state of the user to a system. As we become capable of measuring more specific and selective activation patterns, it will be easier for us to interpret them in terms of mental activity.

Many questions remain, however. For example, how do neurons communicate with one another in a network? Much of the neuron activity measured during motor tasks is related to the task at hand but not really essential to performing that task. It seems likely that populations of neurons — sensing similar aspects of the environment — compete with one another in order to perform a certain action as quickly as possible. We need to understand the encoding of information in neural population activity in order to grasp the fundamental computations underlying brain function and to interpret signals that may be useful for BMIs intended to control external devices. Until now most of these BMIs have measured the brain activity related to motor activity, or more accurately, most of them measure the activity related to the user *imagining* a certain motor action, for example grasping a glass. Current BMIs used to direct devices therefore do not measure the user's intention before the actual action, but merely use a small area of the cortex that — through training — has become an artificial output channel for control. This means that a user with a BMI may have to imagine moving his foot in order to move his prosthetic arm. Direct measurement of intentions would be an important step towards BMIs controlling external devices on a widespread basis. Although BMI research has so far focused mainly on less able/disabled users, we can also imagine it being useful for healthy users in specific environments (gamers, surgeons or soldiers). To facilitate the general, day-to-day use of BMIs, various engineering issues must also be addressed: interfaces should be portable, non-invasive, wireless and automated — or at least easy to use (see subsection 3.2.4). BMIs

17 When it comes to cognitive functions, it is more difficult to assess the neural translation process from stimulus to action or mental activity.

will probably not replace conventional interfaces in conventional settings; they will not surpass the limbs as the most efficient output channel for the brain.

## In future smart environments, BMIs will make it possible to understand and anticipate user intentions – subsection 3.2.1

Smart environments are environments that are sensitive, adaptive, and responsive to the needs, habits, gestures and emotions of their users. The trend towards smart environments indicates a growing need to understand the user in the man-machine interaction. An example of a smart environment is a home control system that recognises the mood you're in when you come home after a long day at work. Based on this information, the system immediately starts to create your preferred relaxed atmosphere by setting the various lights at a certain colour and level and turning on your favourite music. These settings are automatic because they are derived from your profile, created on the basis of previous experiences in similar situations. In future, BMIs could help track and measure the conscious and unconscious intentions of users in smart environments directly — an improvement, as the complexity of human intentions cannot always be captured just by looking at overt actions. Some restrictions will apply, and the environment would have to be very specific, for instance a car. One odd example is the automobile company Honda, which is already thinking of using BMIs to decode drivers' intentions and communicate them to the car or other drivers and pedestrians. In the far future, BMIs may even be able to track user's intentions before the user himself is conscious of them. That means that smart environments will understand what the user wants before he is even aware of his own intentions. Neuroscientists were recently able to predict which of two buttons a subject in an fMRI brain scanner would press [Haynes et al., 2007]. They could predict the action ten seconds before the research participant consciously took his decision by measuring the activity in a network of brain areas in the prefrontal cortex that prepare upcoming decisions. EEG can also measure a 'readiness potential' (RP) in the case of simple motor tasks. An RP is detected only 350 to 400 milliseconds before the participant becomes consciously aware of his intention. However, it is not clear whether the same is true of higher intentions or more complex choices, i.e. beyond motor or movement intentions. Also, although the brain is already preparing an action before someone consciously takes a decision, that person may still be free to consciously decide to *interrupt* the preparations. Anyway, using fMRI to read someone's hidden intentions is not the same as reading those intentions with the help of a non-invasive BMI on an everyday basis. There are many technological and scientific challenges ahead of us.

## Some BMIs are intended to exploit or bypass unique characteristics of the brain – example VIII

One current line of research involves sorting and classifying images by combining the processing power of the human brain with computer vision. The Cortically Coupled Computer Vision system, or C3 Vision, helps people search through large numbers of images or video footage much faster than humans or computers can. As it happens, the human brain is much better and faster than current artificial intelligence systems at pattern recognition, even without the user consciously knowing what he is doing. The C3 Vision system makes use of this by registering the images in an image stream that elicits the P300 peak. This peak in brain activity occurs when a person sees an image that is novel, unusual or rare, even before it enters that person's consciousness. The C3 Vision system has been tested to identify helicopter platforms on overhead satellite images. The system turned out to be not only faster but also more efficient, i.e. identifying more targets than if done by visual inspection. Another interesting way to exploit the unique characteristics of the individual brain was developed at Carleton University in Canada. The researchers' goal was to use brain-machine interfaces as a biometric device. As their identification method, they used the unique response of the individual brain to stimuli such as sounds or images. The Defense Advanced Research Projects Agency (DARPA) — the R&D organisation for the American Department of Defense — is following the same path by developing the Cognitive Technology Threat Wiring System (CT2WS). This is a military device that is supposed to be ten times more powerful than today's binoculars, enabled by an alerting system based on EEG technology. The binoculars should be able to spot neural signals for target detection before the soldier becomes consciously aware of the potential threat. DARPA is taking the idea of the C3 Vision system a step further with this project. What the CT2WS does is an attempt to bypass a special feature of the human brain, i.e. the prefrontal cortex's selection task, which inhibits false alarms.

### 1.3.2 Neuro-ergonomics: improving conventional interfaces

## Neuro-imaging methods can be used to evaluate and optimise man-machine interfaces – subsection 3.2.2

Alongside the futuristic potential of brain-machine interfaces, the neurosciences and, in particular, the relevant imaging methods can be used to evaluate more conventional interfaces. We need to design man-machine interfaces that stimulate the particular brain regions involved in a task, and we can use imaging methods to evaluate the effectiveness of the stimulation. This is relatively ‘easy’ to do, since the human brain is a highly modular and parallel system. The visual system, for example, contains functionally specialised modules (i.e. brain areas) for colour vision, motion vision, stereovision, form vision, texture vision, object representation, face recognition, and so on. Separate neural pathways (i.e. circuits of anatomically and functionally connected brain areas) encode visual information specifically for localising objects in the environment, for recognising and performing actions, for recognising objects, and for recognising the surface properties of objects. More than one of these pathways is involved in many real-world tasks. An interesting example here is that tools, unlike ‘normal’ objects, also activate brain areas that encode their use, presumably so as to prepare for their being used. In short, the best interfaces will be self-explanatory, in the sense that they will activate the relevant brain areas (i.e. those that would also be involved in using the device or in performing an action). Neuro-imaging techniques could be used to determine the degree of activation of such areas, making it possible to select interfaces that fit the relevant criteria best. Other desirable criteria on which interfaces could be evaluated by means of neuro-imaging methods are: cognitive workload, task engagement, surprise, satisfaction or frustration. Recent evaluation methodology in the MMI field has also focused on the emotional criteria of interfaces or interaction, such as enjoyment, fun, engagement, beauty and hedonic quality. Neuro-imaging research has already explored the neurological underpinnings for such basic emotions as anger, fear, happiness, empathy, indignation, love and even personal taste and the influence of marketing (see example III). Such research could generate the neural substrates of emotional criteria needed to evaluate the efficiency of interfaces in the experience economy.[18]

**18** An economy in which businesses focus on orchestrating memorable events for their customers; the product is the experience. See www.wikipedia.org.

Brain vision

**The discovery of mirror neurons implies that man-machine interaction will improve if the interface acts more human, not looks more human** – subsection 3.2.2

The human brain appears to use the brain areas involved in performing actions to observe and understand the actions of others as well. These areas contain ‘mirror neurons’: neurons that are active both when one *observes* someone performing an action and when one *performs* the action him or herself.[19] This action recognition system is broadly tuned, e.g. the human brain tends to treat robots that perform simple actions similarly to humans who

**19** This means that the action systems in our brain can be stimulated even while we are doing nothing physical ourselves (except observing).

perform these actions. Even people without arms and hands who have learned to perform actions with their feet nevertheless have the same regions of the brain activated as people with hands when observing others perform actions. This implies that at least part of the coding of information in the brain is in the form of action *goals*, rather than specific actions. Some have even suggested that the mirror neuron system is aimed at response preparation (and thus anticipation). In other words, humans use the neural systems that initiate their own actions to understand the actions of other organisms. These findings suggest that man-machine interfaces do not need to *look* very human-like in order to be effective. However, *acting* human-like may facilitate the recognition processes. In order to be properly 'understood' by their users, the interfaces should thus activate the brain areas that encode the behaviour in question. The neuroscientific discovery of mirror neurons may result in machines that act more like humans and in interactions that are more humanoid. It could also result in less visible and intrusive interfaces, so that the user can engage in the task at hand rather than have to concentrate on controlling or interacting with the product.

Brain vision

## Manipulating the neural mechanisms behind physical ownership may trick the brain into perceiving fiction as reality – subsection 3.6.4

Neuroscientific research based on the rubber hand illusion has added to the mounting evidence that our bodily self-identification — the ability to distinguish what is contained within versus what is outside our own body — is highly flexible. The experiment is as follows: when a person watches a fake rubber hand being stroked in precise synchrony with his own unseen hand, the person will, within a few minutes of stimulation, start experiencing the rubber hand as an actual part of his own body. In order words, our brain can perceive an artificial limb as our own. The feeling of body ownership is mediated by the brain's ability to detect correlated multisensory signals. In the rubber hand illusion, the temporally-correlated and matching visual, touch and proprioceptive (i.e. position sense) signals are enough to induce a feeling of ownership of the rubber hand. When the signals no longer match, for example when participants try to move the fake hand or when there is a small delay between seen and felt stimulation, the illusion will diminish or disappear completely. Recent cognitive research has revealed that mediated environments, such as computer-generated images, can also influence our sense of body ownership and, consequently, our sense of self, albeit to a lesser extent. This opens up opportunities for improving virtual reality. A fully immersive virtual environment that contains a real-time responsive and realistic representation of our body, mapped onto our bodily movements in minute detail, would probably bring about a significant level of identification with the virtual body, and consequently a sense of presence in the virtual space. Moreover, depending on the fidelity of the haptic feedback,[20] a sense of body ownership is likely to develop. Virtual reality could then turn into real virtuality. The presence of a believable virtual body will likely improve our interaction performance in mediated environments. Before this can be achieved, however, we must address a number of research questions, e.g. on the fidelity required of the virtual body or the required level of body tracking and proprioceptive matching.

### 1.3.3 Neuro-mimicry

**The brain can be used as a model for the development of interfaces and robotic systems – subsections 3.2.2, 3.6.1 and example VI**

Man-machine interaction is still hampered by fundamental limitations. Computers and robotic systems cannot react properly to unexpected commands, since they have only a rigid set of responses. To overcome these limitations, we must develop smart systems capable of learning complex skills and performing them autonomously (i.e. without remote control) in novel and unanticipated situations. Such autonomous robotic systems could be useful in conditions that are hostile or dangerous for humans (e.g. deep-sea and space exploration and construction; mine detection and dismantling; construction and repair in radioactive, toxic or disease-infected areas). One way to improve the autonomy of current artificial systems and interfaces and make them more capable of learning from experience is through neuro-mimicry, i.e. by imitating the workings of the brain.[21] We can derive particular inspiration for such autonomous learning systems from the neural wiring connecting the different (e.g. memory or control) brain modules (i.e. areas). Our knowledge of modularity helps us understand how neural modules classify and store patterns of input, how they associate input patterns with motor responses, and how they control input and output processes in the service of particular tasks or goals. It is possible that we can implement this knowledge in computational systems to develop smart robots.[22] Unlike present-day robots that perform well-defined tasks in pre-specified conditions, smart robots would learn autonomously to carry out tasks in unspecified conditions, flexibly adapting to unanticipated events and circumstances. One additional issue when developing smart robots is the role of emotion in decision-making, which is very

20 Haptic feedback is feedback in the form of sensations transmitted by special input or output devices (joysticks, data gloves, etc.) to the hand or any other part of the body.

21 The introduction to this section already gave two examples of neuro-mimicry: the whiskerbot (i.e. a robot with a multi-whisker sensory system based on that of a rat) and the intelligent artificial system of Numenta (i.e. a machine learning model based on the structural and algorithm properties of the human neocortex).

22 See for example the research project at www.paco-plus.org.

important in the human brain. It affects learning and memory and continuously influences our goals and decisions. But how do we implement that in a robot?

Another interesting example of brain-inspired technology is developed by the research group headed by Bart ter Haar Romeny in Eindhoven, the Netherlands. They use the visual system — the best-studied part of the human brain — to develop biologically inspired computer vision systems for computer-aided diagnosis (e.g. to find tumours or polyps). Their algorithms are based on the concept of the visual system as a multiscale image machine. This particular part of the brain consists of different layers of neurons, each one using different derivatives of the actual image. In other words, each layer is doing different — and more complex — information processing jobs. Another source of inspiration is the retina, conceived of as a multi-resolution camera that sends a stack of images of different resolutions to the visual system of the brain. More knowledge of the complex structure and workings of the brain would allow us to optimise the advantages of neuro-mimicry in man-machine interaction.

### 1.3.4 Other

**Many conventional interfaces work well because of the flexibility of the brain** – example XI

The main thrust of our arguments favouring the symbiosis of neurosciences and man-machine interfaces is that current and future technology must be adapted more effectively to the peculiarities of the brain. This is an important and relevant issue in a rapidly evolving, complex information society, one for which the brain is not especially equipped by evolution. On the other hand, we should not forget that the brain has adapted itself to all different kinds of tools and environments down through the ages. Thanks to its enormous plasticity, it has always been able to recruit and exploit non-biological resources. Take, for example, today's children and youngsters: on average they are much better at using digital technology than their parents. Some research shows video-game players outperform non-players on different aspects of visual processing, for example the fast temporal processing of visual information (see example XI). Our human cognitive adaptability means that many current interface designs already work quite well as an integral part of our own problem-solving system, i.e. the brain. What we need is a more detailed understanding of how the human brain tailors its problem-solving activities to a variety of non-biological devices. An interesting question in this respect is: could neuro-imaging detect whether an average user's brain is adapting effortlessly to a novel interface? Such research is essential for the development of novel interfaces, but also for our understanding of the potential positive and negative effects of existing technology — such as video games — on the brain. In summary, in most cases — i.e. for healthy users — it would be better to improve conventional interfaces by exploiting neuroscientific knowledge or imaging technology than to implement electrodes inside the brain, as in case of an invasive BMI. Non-invasive BMIs carry fewer health risks (e.g. infection) than invasive ones, but even so, their efficiency compared to a conventional interface should always be considered.

## The field of MMI, especially virtual reality (VR), can also be of use to neuroscientific research – subsection 3.6.4

Neuro-imaging technology such as fMRI requires the research participant to lie very still within the scanner, and in particular to keep his head immobile. The research design therefore usually involves viewing movies, hearing sounds, and performing cognitive tasks such as memorisation, all of which require little movement. Well-designed VR on a computer screen (i.e. desktop VR) — preferably with a wide field of view and even VR goggles or spectacles — would give cognitive neuroscientists the opportunity to study complex mental processes without the participants needing to move, e.g. using a driving simulator to study spatial cognition. Brain activity patterns elicited by immersive VR stimuli may be more ecologically valid than brain activity elicited by conventional stimuli. VR also makes it possible to study brain activity associated with the illusion of presence (i.e. a feeling of 'being there') in a virtual environment. Based on one of the preceding propositions (on manipulating the neural mechanisms behind physical ownership), researchers might consider influencing the research participants' perception of their bodies within a virtual environment in order to learn something about the neural mechanisms behind bodily self-perception. New virtual environments that support the physical identification of the user with his virtual alter ego (i.e. avatar) open up a range of research possibilities. For example, respondents could have an experimentally induced, transformed perception of self, based on a well-controlled virtual body. Such experiments could include simple body shape alterations (body weight or height) or more complicated changes (race, gender, age, etc.). The workings of the brain behind self-perception and self-representation related to such socially meaningful bodily transformations could then be studied in an fMRI experiment. More importantly, a virtual environment within an fMRI experiment could lead to studies that would otherwise be difficult (in the case of a small clinical population) or unethical (since we do not want to purposely inflict body agnosia, neglect syndrome or body dysmorphia[23] on a research participant). More research is naturally needed on the required fidelity of the virtual body, i.e. the extent to which a full and accurate representation of the participant's body is required for him or her to experience ownership.

## 1.4 Brain Visions on education

Neural plasticity is the main principle behind learning and currently the subject of exhaustive neuroscientific research. It will therefore come as no surprise that there are many international and national initiatives uniting the neurosciences, the cognitive sciences and educational sciences in the search for *evidence-based learning*. In other words, the disciplines are joining forces to develop educational curricula and instruction methods based on neuroscientific and other insights. The prevailing opinion is that the brain sciences can make a valuable contribution to education by investigating what type of training at which intensity and for what length of time is most effective and for whom, based on differences in the way the brain is organised.

One future line of research in — as some call it — the educational neurosciences is *personalised learning*. Both educational practice and science appear to be particularly interested in how the neurosciences and cognitive sciences can contribute to personalised or customised learning. The biggest challenge in educational practice is how to gear instruction towards individual needs, largely because we lack insight into the various strategies and procedures of learning that people apply during a learning task. Our lack of knowledge means that instructional materials and traditional teaching methods do not take these differences into account. Many of the instruction methods used in schools do not invite children to participate, stimulate them enough, or fit in with the way they learn. The neurosciences are expected to give the educational sciences a more solid basis for developing theories about these individual differences in learning abilities and strategies (see subsection 1.4.1) and motivational aspects (see subsection 1.4.2). Such research may also provide clues on how to adapt instruction to individual differences.

Many questions remain, however. There are only a few examples of neuroscientific findings that can be used unconditionally to justify specific recommendations for educational policy and practice. For instance, we only have a limited understanding of *human* brain development, since most basic neuro-

23 Body agnosia is the inability to recognise (part of) one's own body; neglect syndrome is the inability to perceive the left or right half of the physical environment; body dysmorphia is the obsession with an imagined or minor defect in one's body.

scientific research so far has been conducted on animals. More quantitative and histological research on human brain development is required, including investigations of possible sensitive periods (or 'windows of opportunity') during which specific brain areas or functions related to formal education (reading, arithmetic, writing, etc.) develop optimally. The use of neuro-imaging in educational settings is also still a long way off (see subsection 1.4.3), mainly because the current techniques are either too expensive and too complex to use. Whether imaging techniques will have added value for existing behavioural or learning outcome measures remains questionable. It is also difficult to read individual fMRI scans owing to the individual differences in brain structure. Still, there are some instances of neuroscientific research that may, in the short term, have an impact on educational practice, for example the research on gender differences in brain structure and functioning, mirror neurons and the development of memory-enhancing drugs (see subsection 1.4.3).

### 1.4.1 Individual differences

Brain vision

**The many differences in individuals' learning ability, are a result of the interaction between genes and environment during brain and cognitive development** – section 4.4

Brain development and the development of cognitive abilities (e.g. memory, attention, decision-making, etc.) mutually influence each other. As the brain develops, it permits cognitive abilities to develop; using those cognitive abilities allows the brain to continue developing. Both genetic and environmental influences are decisive in brain and cognitive development and result in considerable individual differences in children's ability to learn, and in how, and how efficiently, they acquire information and experience. *Genes* define the mechanisms for brain development, which in turn specify the neural circuitry for information processing and learning. Genes and their expression can be permanently changed by mutation (e.g. resulting in intellectual disability) or even milder mutations known as polymorphisms (e.g. involved in determining IQ variations in the general population). Environmental factors such as education can also control the expression of genes indirectly through neuronal electric activity generated by our sensory organs (vision, hearing, taste, smell, touch). The environment, however, has a much more dramatic and direct influence on brain development.[24] Particularly during the first years of life — including during pregnancy — dramatic environmental influences such as isolation, stress and alcohol and drug can play a decisive role in language, social and intellectual functions. Other more generally important environmental

**24** Monozygotic twins, for example, already have different brain structures at birth, although they are genetically identical.

factors known from research on rodents are early (i.e. in childhood) sensory stimulation (resulting in structural and functional fine-tuning of the underlying brain circuitry and enhancement of information processing), enriched environments (resulting in a sharp increase in many of the properties of cerebral cortex connectivity[25]) and maternal care[26] (resulting in a better adaptive stress response and better performance on learning tests in adulthood). Genome and experience interact to develop cognitive and learning abilities, resulting in individual differences. However, we need much more quantitative information on circuitry formation during human brain development. As stated before, most of what the basic neurosciences know comes from research on rodents. And although the underlying genetic and cellular mechanisms are highly similar, differences in timing, magnitude and complexity will affect human brain development non-linearly in a way that cannot be easily extrapolated from rodent models.

## The neurosciences can give the educational sciences a solid biological basis for developing theories about learning and individual differences – subsections 4.2.1, 4.5.1 and example XII

As already stated in the introduction to this section, educational practice still works with instructional materials and teaching methods that are not based on individual differences in learning strategies and procedures. The basic and cognitive neurosciences could change that by giving the cognitive — or more specifically the educational — sciences a biological basis for developing theories about learning and individual differences. This might involve discovering which teaching methods promote formation of the most efficient neural connections or studying the role of the mirror neuron system as it relates to learning and social cognition in normal development (e.g. children use mirror neurons more as they become more socially adept [Pfeifer, 2008]). As a result, cognitive theories can test — on a fundamental level — notions as to which parts of the brain are involved in various types of information processing. That means that we will be able to validate theories about information processing in relation to various types of learning tasks as well as theories about individual differences in information processing. Likewise, neuroscience can provide behavioural or learning outcome measures for individual students. This in turn will allow educational researchers to develop and test various strategies for adapting instruction to these differences. For example, fMRI research has shown that individual memorisation strategies are based in different areas in the brain. Each strategy may influence memory performance separately; the

25 It even seems that enrichment — introducing toys and other opportunities for exploration – can partly counteract deficiencies in neuronal connectivity and learning ability caused by genetic mutations.

26 In research on rats, a 'good' mother stands for a high incidence of licking and grooming.

verbal elaboration strategy and the visual inspection strategy are the most effective strategies for memorising a series of objects, research shows (see example XII). Findings such as these can help us adapt instruction methods so that pupils study more effectively.

## There are significant differences in the brain development of girls and boys that may have consequences for future educational practice – subsection 4.6.1

Although the variation between individual brains is more significant, more and more research is pointing to major differences between male and female brains. For example, Dutch neuroscientific researchers recently showed that men suffering from depression have other stress hormones in their brain than depressed women, leading to the development of different antidepressants for males and females. It is not always clear, however, what the neural differences between the sexes actually mean. For example, research has shown that male brains are more voluminous in certain areas, e.g. the temporal lobes, whereas other areas appear to be larger in women, e.g. the anterior cingulate cortex and the orbitofrontal cortex. Both these areas are involved in emotional processing. When it comes to the brain development of boys and girls, there are strong indications that boys' brains generally develop more slowly and reach full maturity some years later than girls' brains. Areas of the brain cortex underlying the 'executive functions' tend to reach full maturity a few years earlier in girls than in boys. The executive functions help individuals act according to a plan and to prioritise on the basis of social and emotional consequences in the short, medium and long term. These areas — which are responsible for impulse control — are not fully mature yet in adolescent males. Boys therefore suffer from the 'boy problem': they are more playful and aggressive in primary and secondary school. Whether this has any consequences for the educational system is unclear yet. The same cannot be said of the neuroscientific finding that the brain functions related to language develop earlier in the female than in the male brain. For example, fMRI research suggests more intense activity in brain language areas in girls between the ages of nine and fifteen than in boys of that age; girls even activate more brain areas during language processing tasks than boys. Boys also appear to use 'lower-level' linguistic processing strategies (i.e. based on the visual properties of words), whereas girls rely on more efficient processing strategies at a 'higher level' (i.e. using abstract, conceptual knowledge of words) [Burman et al., 2008]. This may explain why girls tend to choose language subjects over science subjects — in which they have not yet developed an interest — when asked to decide on their educational future. In countries where children are allowed to choose later on in their school career, boys and girls do not differ as radically in their choice of language or science subjects. Research on sex differences in the brain is booming; some findings, like the one on linguistic strategies, may very well have consequences for future educational practice.

## Adaptive cognitive systems are useful for presenting instructional material in such a way that it matches the pupil's individual cognitive profile – section 4.3

While it is true that the present state of knowledge does not permit us to generalise about the most effective learning methods for particular subjects and individual pupils, by offering a pupil material on a computer and registering his response digitally, we can in fact construct an accurate model. Once we have set the parameters, the model will — in time — tell us how a pupil will respond to specific instructional material. How does such a cognitive learning system (or educational software) work? Most important is that the system knows what the pupil knows. That means that the system must be used as much as possible in the learning process itself. By building up a database on a pupil's progress, the system can construct a cognitive profile of the pupil. The underlying parameters can be estimated; they may, for example, indicate how quickly a pupil learns different types of material, what he is having trouble learning and how soon he forgets what he has learned. Such cognitive learning systems make it possible to track, predict and manage a pupil's progress and, most importantly, optimise the learning process. The latter can be achieved by enriching cognitive learning systems based on insights into meta-cognitive methods (i.e. tips on how to learn) gained in cognitive psychology, for example on spacing (i.e. offering instructional material in time stages) or elaboration methods (i.e. ways of making the material easier to remember). The usefulness of such systems is greatest when they are applied in school subjects or skills that pupils work on individually; in group settings, they have many other social skills to learn. By working with cognitive learning systems, pupils are likely to feel more motivated because they have much more choice, understand the learning process better, receive more relevant feedback and perform better. An additional advantage is that cognitive systems can contribute to evidence-based education by facilitating the evaluation of new methods for their effectiveness and applicability. Nevertheless, two important challenges remain: how can we get computer systems to analyse the pupil's own compositions for comprehension (i.e. semantic analysis)? And: is it useful to incorporate neurocognitive measures (e.g. based on EEG) into the system in order to understand pupil responses better?

## So far there is little evidence supporting the existence of specific windows of opportunity in brain development relevant for educational practice – subsections 4.4.3, 4.5.1, 4.5.2 and 4.8.1

Of special interest to educational practice are the 'sensitive periods' in brain development: specific, limited periods of neural plasticity in which certain brain areas or functions develop. In the past thirty years, research has shown that the brain needs certain kinds of stimulation at specific times — mostly during early childhood — for the sensory and motor systems to develop normally. Appropriate stimulation of the sensory and motor systems is generally available in any environment, at a very basic level, and early deprivation of certain stimuli does not usually lead to irreversible damage, except in the case of binocular vision.[27] The brain areas and corresponding sensory functions are usually able to recover to some extent at a later stage. However, until now most of the relevant research has involved animals and concerned the development of sensory skills, rather than non-sensory ones. There is therefore much debate in the neurosciences and cognitive sciences as to whether these sensitive periods exist and how important they are,[28] with no strong evidence having been found of sensitive periods for any skills *related to formal education*. (There is some proof that sensitive periods for language development exist, but not for vocabulary learning, which is possible throughout life.) Nevertheless, most scientists seem to agree that the developing individual cannot learn everything in every developmental phase. A child cannot learn certain skills to best advantage if it has not yet mastered the basic underlying skill. Scientists also agree that these sensitive periods of brain and cognitive development differ enormously in timing — not in sequence — between children. More research is needed on the sensitive periods for specific cognitive abilities underlying school subjects such as reading, writing or arithmetic. The concept of sensitive periods of plasticity could be relevant for evidence-based innovation in education, as represented by personalised learning. If it turns out that sensitive periods do exist for various brain or cognitive functions, we could facilitate brain development by adapting instruction to them.

**27** Bionocular cells are necessary for the two eyes to work together and are the basis of in-depth perception. If these cells are not exposed to visual experience early in life, they become smaller in size, vision is reduced and depth perception is lost.

**28** For example, the OECD was very reluctant in its report 'Understanding the Brain: The Birth of a Learning Science' to support the theory of specific windows of opportunity in brain development.

## 1.4.2 Motivation

**Emotional stimuli and motivational factors are essential for optimal learning and memory consolidation** – subsection 4.6.1

Personal motivation and emotional engagement are vital for proper information processing and learning. Memory consolidation, for example, depends on a minimum level of emotional or motivational stimulation. Motivations and emotions are meant to help the brain fend off particular stimuli and resist acting impulsively. The neurosciences see motivations as essential biological drivers for bodily survival and survival of the species (hunger, thirst, sex, sleep, etc.).[29] Emotions, on the other hand, help to alert the individual to potentially important stimuli. The brain structure involved is the limbic system.[30] Its role is to apply an emotional value to sensory stimuli, ensuring that the individual recognises the importance of a particular stimulus later on. Consequently, educational practice should bear in mind the role played by basic motivations and emotions. Negative emotions, such as stress, anxiety and fear, make it more difficult to learn because they reduce the pupil's ability to pay attention to the task at hand. Positive emotions that result from adapting instruction to the motivations of the individual pupil naturally also have an effect on learning and knowledge acquisition. Interesting in this context is the DANA Foundation's project concerning the relationship between arts training and better academic performance. The researchers found that *"an interest in a performing art leads to a high state of motivation that produces the sustained attention necessary to improve performance."* As a consequence, *"the training of attention leads to improvement in other domains of cognition"*.[31] Nevertheless, more neurocognitive research is needed to demonstrate that higher levels of motivation change specific neural pathways. Above all, a pupil needs to be emotionally competent in order to learn optimally, i.e. be able to restrain himself and his impulse reactions. Research has shown that learning to control one's impulses at a young age may lead to future academic success.[32] In future, the neurosciences and cognitive sciences may help us understand how to teach children to become emotionally competent.

29 These are regulated by major brain structures, e.g. the thalamus and the hypothalamus.

30 The limbic system is an ancient system in the basic forebrain and includes the hippocampus and the amygdala.

31 See www.dana.org/news/publications for the Dana Foundation Annual Report 2007, including an essay on the results of a three-year Arts and Cognition project led by neuroscientist Michael S. Gazzaniga.

32 See the research of psychologist Walter Mischel at Columbia University in New York.

## Research shows that the brain matures until well after the 20th year of life, suggesting that it needs an external motivator until adulthood – subsection 4.6.1

Recent cognitive neuroscientific research shows that the medial prefrontal cortex matures from early to mid-adolescence until well into adulthood. These anterior parts of the brain become fully developed around the age of 25 in males and a few years earlier in females. It is certainly not an autonomous biological process. It is only the very earliest stage of development that is guided by biological factors in which genes play a role. Environmental factors determine the proper functioning of these brain structures, which are responsible for the executive functions. As stated above, the executive functions enable individuals to act according to a plan and to prioritise on the basis of social and emotional consequences. The immature state of the prefrontal cortex therefore partly explains why adolescents are more inclined to act on impulse and show risk-taking behaviour.[33] Self-evaluation and social monitoring are also executive functions, making the prefrontal cortex of utmost importance to learning. Based on these findings, we can conclude that pupils need guidance when it comes to planning and prioritising. A teacher (or parent) should act as an external motivator, helping the pupil acquire relevant knowledge and make choices in day-to-day classroom situations or even in their future educational career planning. Such guidance should not stop at the age of eighteen, when someone is legally an adult in Western societies, but should continue for quite a few years thereafter. This neuroscientific finding is at conflict with Dutch educational concepts implying that the teacher should retreat and that education should facilitate the autonomous learning process in students. Neuroscientific research, however, suggests that a teacher should not only be a passive facilitator who offers instruction when asked; he or she should also take a more pro-active approach and motivate the pupil to engage in fields or domains that he would never have entered on his own. More research is required on the subject, however, for example comparing self-initiated learning and learning based upon external motivators.

33 One of the reasons why the U.S. Supreme Court decided in 2004 that capital punishment for juveniles under eighteen is in conflict with the Constitution. See subsection 1.5.2.

### Playing action video games improves visual skills and attention – example XI

Teachers and developers of instructional materials devote much of their time and effort to motivating learners, and with good reason, since motivation affects all teaching and learning processes. They often look on jealously while children are immersed in computer games. They would obviously like to understand the motivational aspects behind gaming and whether the same incentives can be used in the educational system. Another question interesting to educational practitioners is the influence of gaming on children's brain development. Some research has been done on this subject, with positive results. For instance, students who play action video games habitually tracked objects better, reacted faster and located visual targets better than non-players. The same skills were shown to improve in non-players who began to play these games regularly. Other research shows that playing an action video game for only ten hours results in a substantial improvement in spatial attention[34] and mental rotation, with women benefiting more than men. Whereas training usually induces improvements specifically in the relevant task, playing action video games alters a range of visual skills. It trains players to distribute their attention and perform various tasks simultaneously, which apparently results in brain changes that improve an array of visual skills. These findings suggest that educational gaming software can be developed to help pupils (and others) train their visual and spatial skills in an entertaining way.

## 1.4.3 Other

### Basic neuroscience is set to influence the development of pharmacological agents that promote learning and memory consolidation – section 4.4

Pharmaceutical and biotech companies are searching for potential nootropic drugs (i.e. cognitive enhancers or 'smart drugs') based on new insights into the neurobiological basis of learning, memory and cognition. These drugs are primarily intended to battle cognitive problems in neurodegenerative disorders such as Alzheimer's disease or specific forms of mental retardation (e.g. fragile X syndrome). Various mechanisms are targeted for their possible memory-enhancing effect, such as neurotransmission mediated by acetylcholine, which has been shown to be involved in various memory processes. Agents in this group generally enhance the effects of acetylcholine at its nicotinergic

34 Better spatial attention is the ability to tolerate smaller distances between a target and a distracting object.

receptor. Another example is research into the mechanisms underlying long-term potentiation (LTP), identified in 1973 as the cellular correlate of learning and memory. This has led to the development of Ampakines.[35] Other targeted mechanisms are epigenetic regulation[36] in memory processes and the dynamics of synaptic connectivity. Last but not least, over one hundred genes have been identified as causally involved in certain forms of intellectual disability. At least some of these genes will be targeted for nootropic drug development. Given the scale of robotised high-throughput screening for drugs that can interact with targets of interest, it will not be long before potential nootropic pharmaceuticals can be identified. In view of the economic potential of nootropic drugs (estimated at 5 billion US-dollars annually), their application may just be a matter of time. These memory-enhancing drugs may well come into more general use in future as a 'learning or exam pill', as is the case with Ritalin and Adderol. Both stimulants are already used by healthy children in the United States to improve concentration before exams.

## The general use of neuro-imaging in educational practice is conceivable but still a long way off – section 4.3 and example VII

Neuro-imaging techniques are in general use in research and clinical settings, but some people think that they will be used in educational settings in future. Whether they are depends on their ease of use, cost and practical advantages for learning. fMRI is still too bulky and too expensive; EEG is easier to use and cheap, but the brain signals are difficult to read, i.e. there is too much 'noise'. Various technical breakthroughs are required before neuro-imaging techniques become advantageous for educational practice, but they can already be used for educational purposes in some interesting ways. For example, we can already see whether a pupil's working memory is activated. If the working memory does not show up on the fMRI as having been activated and the pupil keeps making mistakes while doing mental arithmetic, then he is evidently having trouble remembering the interim results, a problem that requires separate attention. Another example of an interesting neuro-imaging application concerns the degree of consciousness at which processing takes place. Highly automated processes have a weaker effect on the frontal lobes than thought processes requiring conscious attention. Learning generally follows a pattern from highly conscious monitoring and attention to nearly unconscious performance. fMRI scans can be used to track these processes so as to see whether a pupil has mastered (i.e. automated) a certain skill. EEG can be deployed in a comparable manner, for example to show individual efficiency at excluding irrelevant information from storage in the short-term visual memory [Vogel et

35 These drugs enhance the function of the AMPA receptor, which shows enhanced synaptic expression upon induction of LTP.

36 Epigenetic regulation entails the long-term modification of DNA and/or accessory proteins that could lead to life-long alteration of the expression of specific genes.

al., 2005]. Whether these individual differences in memory storage need to be or even *can* be undone by specific training is unknown yet. Another way in which EEG may be useful in future educational practice is through neurofeedback, a technique whereby individuals learn how to influence the electrical activity in their brain cortex, visualised via EEG. In a neurofeedback session, a participant gets feedback from a computer on which brain waves are present in the brain region of interest. If the desired frequencies are present, the brain receives a reward, e.g. points in a computer game. So far there is little proof that neurofeedback will result in better cognitive performance, but evidence is mounting that it offers an effective treatment for epilepsy and ADHD.

## Like physical training, mental simulation of movements and observation of movements result in improved performance – example IX

Research shows that just by practising a five-finger piano exercise *mentally* for five days, participants were able to improve their performance markedly. The areas of the brain involved in finger movement enlarged over the period of practice, as they did in participants who practiced physically. Mental simulation of movements apparently promotes changes in the neural circuits involved in motor skills learning and at the same improves performance. Other research shows that *observing* the movements of others also enhances progress. For example, the DANA project on arts training and academic performance demonstrated that effective observation can be a highly successful method for learning dance steps. Learning by observation and learning by physical practice seemingly accomplish the same effects in the neural substrates that support dancing, i.e. the management of complex actions. Both types of learning involve common processes in the brain, with a major overlap between the brain areas used for observation and for movement. This has been articulated in the neuroscientific theory of mirror neurons. Mirror neurons are activated not only by performing a given action but also by observing someone who performs the action. One important research question for future educational practice is whether effective observational learning can be transferred to other cognitive skills. For example, to what extent does observing a teacher doing math on a blackboard have the same effect on a pupil's learning performance as working on math problems himself?

## 1.5 Brain Visions on judicial practice

The neurosciences and cognitive sciences help us understand the functioning of the brain in relation to human thought processes and behaviour, including those of delinquents, witnesses, police investigators, judges, lawyers and public prosecutors. In fact, much of the current knowledge derived from the cognitive sciences could already be applied in judicial practice, but it has unfortunately not always penetrated the administration of justice yet. A simple example: judges tend to put more faith in suspect statements made at a later date than the initial statement, even though we already know that memories do not become more accurate in time. Our growing understanding of the workings of memory (the influence of stress, the origins of false memories, facial recognition, etc.) could be particularly important to many aspects of judicial practice, for example interrogation techniques and the status of witnesses' and victims' statements (see subsection 1.5.1).

Other, more basic neuroscientific findings — which depict the brain as an automatic device that controls our perception, attention, emotions, judgements and decisions — may have a more profound impact on judicial practice (see subsection 1.5.2). These recent findings will reawaken the philosophical discussion as to whether human beings actually possess free will. If not, the concept of what constitutes personal responsibility for one's actions may have to be reconsidered. Consequently, the legal system may have to change its assumptions about criminal responsibility. Whether it should in fact do so is a matter for careful examination. It is likely that a better understanding of the interactions between the neurobiological and environmental factors underlying behaviour will reinforce the belief that delinquent behaviour is the product of forces beyond the control of the offender. This belief might result in a legal system that emphasises treatment more than punishment.

The contribution of the neurosciences and cognitive sciences to the judicial system will obviously not be limited to investigative practice and the courtroom (i.e. lie detection, profiling, neuro-imaging evidence, determination of accountability, decision supportive systems). The brain sciences are also expected to influence the punishment or treatment of delinquents, for example by improving the diagnostics of psychopathologies, facilitating better (i.e. customised) and different treatments and treatment combinations for psychopathologies, anti-social behaviour and addiction, and providing better insights into the effect of punishment on delinquents and how it varies from one person to the next.

In summary, our current and future knowledge of the brain will make judicial practice more evidence-based in future, but in order to integrate the neurosciences into judicial process, brain researchers must understand the law, and lawyers must understand the neurosciences. It is important for the first steps to be taken in that direction, in the form of transdisciplinary research involving neuroscience, cognitive science and legal practice. This section represents one of those first steps, as it is based on the outcomes of the well-attended transdisciplinary conference Justice and Cognition, held in November 2008 in Zeist, the Netherlands.

### 1.5.1 Memory

Brain vision

## fMRI technology is not yet suitable for lie detection

**– section 5.4**

fMRI is not yet suitable as a lie detection system, even though two American companies are already marketing it as such.[37] There are several reasons why fMRI is not appropriate for detecting deception. In the first place, there is no such a thing as a 'lie centre' in the brain. fMRI can only visualise cognitive processes that are indirectly associated with lying. For example, one theory is that if someone is lying, the standard setting of the brain — i.e. telling the truth — has to be switched off. This involves the prefrontal cortex; if that area becomes activated in response to questions concerning charges ('Did you kill him?'), the defendant is innocent. The question then is: how does fMRI lie detection work if a guilty person has gradually grown convinced of his own innocence? In the second place, fMRI findings usually describe a group average, as there is individual variation in the way the human brain is organised. The regions shown as active on individual scans may differ from those indicated on the average scan. The connections between regions within a brain may also differ from one person to the next.[38] That makes it difficult to interpret one person's brain activity on a fMRI scan; for example, does it mean he is trying to hide something, or does it mean something else? Individual brain scans therefore do not offer the certainty required in a judicial process. In short, fMRI technology is not yet ready to be used for lie detection purposes, but the associated research has been an important impetus towards developing a theory of lie detection, something that has been lacking for a long time.

**37** See www.noliemri.com and www.cephoscorp.com.

**38** The differences in individual brain structures are not so large that it would be pointless to average the brain scans of different respondents; on the contrary.

## EEG recordings of the P300 combined with the guilty knowledge test can detect the presence of criminal knowledge quite accurately, although not yet sufficiently

– section 5.4

Another neuro-imaging method that is being developed — especially in the United States — for lie detection purposes is EEG. EEG recordings can show a brain wave that occurs 300 milliseconds after something unusual has happened. This is known as the P300, and it reveals a moment of 'conflict' in the brain's electrical activity. The P300 can be useful when combined with the guilty knowledge test. The test (which may involve showing a suspect a picture of the get-away car in a line-up of random cars) can demonstrate criminal knowledge (i.e. usually knowledge of the crime scene), since the picture of the get-away car will evoke a P300 peak in the perpetrator. In this case, we should refer to memory detection instead of lie detection. So far some 25 studies have been carried out with this technique; the findings are uniform and reliability averages 80% in the case of guilty persons and 90% in the case of innocent ones. In one Dutch study, the P300 peak correctly showed in 92% of the cases that the subject had seen a familiar face. That is useful when someone is a member of a criminal organisation but is trying to hide it. EEG recordings are, in fact, no more reliable than measuring the skin conductivity of the fingers, i.e. the suspect's perspiration, combined with the guilty knowledge test. The percentages are about the same, but the skin conductivity method has been tested more extensively (including with high-stake lies), and it is also cheaper and easier to perform. The question remains whether the reliability percentages of both of these memory detection techniques are good enough to satisfy the criteria of judicial practice (although the risk of false positives is quite small, with the chance of someone innocent ending up in jail being minimal).

## An eye-witness's first statement is of crucial importance, since every recollection thereafter re-installs and changes the memory in question – section 5.6

Our memory is an active and dynamic system, *not* a passive filing cabinet. When we recall something, the neural network involved becomes temporarily instable and the memory is re-installed in a stable form. This means that every time we remember something, that memory is changed, coloured by the circumstances during recollection. The initial recollection of an event is therefore probably the most accurate and closest to what actually happened. An eye-witness's first statement is thus of eminent importance. Witnesses should preferably write down everything they remember as soon as possible. Police investigators should always try to record or retrieve a witness's first statement, even if it was made to a family member or someone else. And finally, if a witness suddenly claims that he recalls more than he did before, or only reports a crime to the police weeks after the event, investigators should check who the witness has spoken to in the meantime.

## When the brain retrieves information, it has to reassemble various elements of memory and therefore easily gets things wrong – section 5.11

False memories are easily created, even in intelligent research participants. Recent findings from cognitive neuroscience offer an explanation for flawed memories. Experience always leaves traces behind in our brain. These traces are chopped up into bits and saved in various parts of the cerebral cortex, for example the visual elements in the occipital lobe, the auditory elements in the temporal lobe, and so forth. When our brain retrieves information, it has to reassemble all these various elements of memory, and quite easily gets things wrong. This means, for example, that when a witness has only a vague recollection of an offender, his merely glancing at a photograph of a suspect is enough to replace that vague recollection with the subject's face.

## It is not yet possible to use fMRI to distinguish between false and correct memories outside the laboratory – section 5.11

Several neurocognitive studies support the notion that correct memories differ at a neural level from false memories because the former uniquely activate areas of the brain involved in processing perceptual details. Unfortunately, those areas differ considerably per study. That is partly owing to the nature of the stimulus material, but even in studies that use the same material, correct memories have activated different areas of the brain. The studies in question also induced false memories in one specific way, namely through the DRM paradigm[39], whereas in the real world, false memories are induced in various different ways. Research methods in which the participants recall

39 The Deese-Roediger-McDermott (DRM) paradigm involves using lists of words that all converge or relate to a critical word that is not listed. If a list contains words such as 'thread', 'pin', 'eye', 'sew', and 'sharp', a participant often falsely recalls and recognises the word 'needle' (i.e. the critical lure) as having been on the list.

non-existent amateur videos of public events or fictitious incidents from their childhood bear a closer resemblance to actual false memories. It is therefore important to know whether the false memories induced by these methods activate other areas of the brain than do real memories. What we need is research in which subjects recall true and fictitious life events while lying in a scanner. If research of this kind systematically shows that correct memories activate other areas of the brain than false memories do, and that those areas activated by correct memories are always the same ones, then there may well be a place in the future for brain scans in determining the veracity of an eyewitness's or suspect's memories.

### 1.5.2 Free will and responsibility

**So far, neuroscientific findings on the absence of free will are not at odds with the judicial practice of personal responsibility** – sections 5.2 and 5.3

There is growing evidence in neuroscientific research of a mechanistic basis to human decision-making: by the time we want to decide something, our brain has already done it. Recently, neuroscientists demonstrated that as much as ten seconds before someone consciously takes a decision, a network of high-level-control brain areas are already busy preparing the upcoming decision, for example whether to push a button with one's left or right hand.[40] The decision concerned, however, may not be representative of more complicated choices that go beyond coordinating motor activity. It is also not clear from research whether the participant in question is free to deviate from the decision-making process at the very last moment. Nevertheless, neuroscience has already shed some light on why people believe that they have free will, based on research on split-brain patients. Studies show that the left hemisphere of the brain has a module, called the 'brain interpreter', that is constantly looking for patterns and relationships between perceptions in order to concoct a plausible story and come up with reasons for behaviour *afterwards*.

So do these neuroscientific findings have implications for prevailing assumptions about personal responsibility in judicial practice? A difficult question. Interestingly, legal specialists postulate the idea of free will without really considering the extent to which a defendant does indeed possess it. They tend to base judgements of intent — the exercise of one's free will — on the circumstances in which a person acted. For example, a person in a pub fight pulled a pistol and fired a shot, hitting someone he did not know in the leg.

40 This research [Haynes, 2008] is an update of a famous study by Benjamin Libet in the seventies and eighties, which showed that it takes approximately half a second for a decision taken by a brain region involved in coordinating motor activity to reach our consciousness.

The judge considered that the person acted with intent and convicted the man for attempted murder, because someone who deliberately shoots off a pistol in a crowded pub must have the intention of hitting someone. The bottom line is that the neuroscientific findings on the absence of free will have so far concerned only simple motor tasks. Based on the current findings, no far-reaching conclusions should be drawn and no one should be exempted from legal responsibility for their actions.

## Brain research findings will shift the emphasis in judicial process from punishment and retribution to treatment and forgiveness – section 5.2 and 5.12

As stated before, the fact that the neurosciences reveal the brain to be an automatic mechanism does not mean that we shouldn't hold perpetrators accountable under criminal law. At the same time, a better understanding of the brain and how it generates emotion, behaviour, morality and thought — including, for instance, the effects of drug and alcohol abuse on brain development — might make our criminal justice system more compassionate. Brain research may show that the behaviour of excessively aggressive persons or ADHD sufferers who received the wrong treatment is the product of forces beyond their control. In future, neuroscientists will collaborate with other specialists such as psychiatrists, legal experts and social workers to produce more accurate diagnoses of psychiatric and neurological disorders and better treatment programmes.

One current example of a shift towards a more merciful criminal justice system is the case of Roper versus Simmons, in which the U.S. Supreme Court decided in 2004 that capital punishment for juveniles under eighteen is in conflict with the Constitution. This decision was based partly on neuroscientific evidence claiming that the prefrontal cortex of young adolescents is not yet fully developed. The immaturity of the prefrontal cortex affects adolescents' mental capacities, for example their ability to consider the pros and cons and the emotional impact of their decisions. They are therefore more likely to exhibit high-risk behaviour and have trouble controlling their impulses. In the Netherlands, this neuroscientific finding calls into question court decisions to try young delinquents accused of serious crimes under adult criminal law.

## 1.5.3 Neuroscientific evidence

### Much of the neuro-imaging data in brain research cannot be used as evidence yet, but it nevertheless influences judges, lawyers and public prosecutors – section 5.2 and 5.3

There are currently 912 cases before the American courts in which the brain sciences play a role. For the most part, these cases involve lawyers presenting brain scans of a suspect showing that he is suffering brain damage, for example a tumour. It is true that brain damage can alter people's behaviour. Damage to the prefrontal cortex may make someone more aggressive, but not everyone who suffers damage in that part of the brain becomes uncontrollably aggressive. Brain scans showing certain brain damage can therefore hardly exempt someone from his legal responsibility and should not be used as evidence. This might change in the future, when scans are used to diagnose certain neurological disorders and psychiatric diseases such as schizophrenia, drug addiction or autism spectrum disorders. Another problem associated with using brain scans as evidence is the individual variation in the way the brain is organised, the same problem involved in using fMRI as a lie detection device. FMRI findings usually describe a group average, making it very difficult to interpret the brain activity of a single person on a scan. Nevertheless, brain scans — even when dismissed as evidence — can set off a train of thought in a judge or jury that might remove the last lingering doubt about the defendant's criminal intent. Judges, lawyers and public prosecutors are all tempted to believe in the hard data of a brain scan. Recent research [Weisberg et al., 2008] showed that the mere presence in a text of trivial sentences starting with 'Brain scans show that…' make a scientific claim more credible for lay persons and even brain science students. Brain researchers should therefore be aware that their interpretation of neuroscientific data can have a major impact on the taking of evidence, and legal experts should not overestimate the value of such data. If in future neuro-imaging is to be admitted as courtroom evidence, however, there must first be a rigorous legal and ethical debate on the concept of 'cognitive privacy'. At the moment, individuals can be compelled by law to provide fingerprints, blood, tissue for DNA tests, and photographs. Should the same apply for brain scans? And should brain-imaging data have the same privacy status as genetic information? Unless the law in the Netherlands is amended, the brain will remain a legal private domain.

**Our growing knowledge of the brain will contribute to the list of risk indicators for criminal behaviour, reinforcing the trend towards pre-emptive criminal law** – section 5.3

Criminal intelligence units were first introduced in the Dutch police force in 1985. Since then, the Dutch police have made increasing use of profiles and risk indicators, i.e. data showing that someone is highly likely to commit a crime. There is growing pressure — influenced by the fight against terrorism — to apply this strategy to catch criminals red-handed. Our growing knowledge of neurological disorders, psychiatric diseases, stress, aggression, empathy, etcetera will undoubtedly contribute to the list of risk indicators. At the same time, biological and neurobiological risks will probably not act as a deciding factor for taking pre-emptive measures. The gravity of the anticipated criminal offences and the likelihood that they will actually occur are too uncertain when based on biological/neurobiological risk factors alone. However, the greater the potential role of biological/neurobiological data, the greater the role of investigative risk analyses and pre-emptive criminal law. At the same time, a better knowledge of biological/neurobiological and other risk factors will help us develop strategies to prevent children and adults being drawn — or drawn back — into a life of crime. Some argue that this is commendable but should not lead to what the World Health Organisation (WHO) in 2002 called a ‘public health approach to crime’. The claim is that a medicalised approach to criminal behaviour has one important drawback: objective health does not exist. Health is subject to social norms and illness is a state that deviates from the relevant person’s ideal or from a statistical average. A public health approach to crime might therefore result in a scenario in which social risk and costs determine who is healthy and who is not, with the latter group being subject to preventive treatment, prosecution or incarceration. Our growing knowledge of biological/neurobiological risk factors should not lead us to use mental health care as a furtive means of applying pre-emptive criminal law.

## 1.6 Progress in the neurosciences and cognitive sciences

*Wytse Wadman*[41]

Despite more than 150 years of intense activity, the neurosciences and cognitive sciences are still in their infancy. That is not surprising if we realize that the subject of study — the human brain — is the most complex system known to mankind. The research efforts have increased exponentially and since 2004 the annual meeting of the (American) Society for Neuroscience attracts

41 Professor of Neurobiology, Swammerdam Institute of Life Science (SILS), University of Amsterdam.

over 30,000 participants that are active in all branches of brain research. An experimental science in this stage is expected to be technologically driven and that clearly shows up if we look at history. Every new (research) technology pushes forward the field with a large step. That can be illustrated by a multitude of examples of which we will only mention a few here. It held for the patch-clamp technology in neurophysiology (allowing researchers to record the activity from identified individual neurons in the central nervous system), for the multitude of tools provided by genetics (linking function to molecules at all possible levels of brain functioning) and for the inventions that allowed non-invasive imaging of activity in the functioning brain (finally opening up the possibility to couple higher functions in the brain with activity in the underlying neural substrate[42]). Such breakthroughs are very difficult to predict, even for insiders. The only thing we can do here is mention where major questions are still waiting and where new technologies are currently being developed or expected.

A very important aspect of the brain sciences is its interdisciplinarity. In the early days scientists obtained the Nobel prize for excellent anatomical work and later for work in physiology, biophysics, molecular biology, etcetera. These days, high ranking journals are mostly filled with articles that approach important questions about the brain with a multitude of techniques, most of the time written by teams of scientists with various background and expertise. With a little overstatement, we can conclude that we know a lot about the elements of the brain. Nothing is complete yet, but we have great knowledge about the detailed anatomy of the brain, about the way individual neurons process information and how they communicate with each other, how the major sensory input systems collect and represent information and how output systems (such as muscles, glands, etc.) are addressed. Despite this enormous and continuously growing collection of brain facts we still face major obstacles in understanding the brain and mind. We mention here a few in random order, each of them will need major breakthroughs in our experimental skills and/or conceptual ideas.

– Lack of concepts on how to analyse such a huge complex system. New branches in science like systems biology[43] have started to tackle this problem, but no solution is yet in view. We sometimes feel like chemists in the age before the periodic system was understood.
– How to handle the strong dynamic aspects of the brain? The types of analysis employed over the past century (histology[44], genetics, but even physiology and imaging) have biased our model of the brain to a quite static model. It has become clear that membranes, cells and connections between cells are very dynamic at scales of seconds, hours, days and

42 By ‘neural substrate’ is meant the set of brain structures that underlies specific behaviour or psychological state.

43 System biology is a field that focuses on the systematic study of complex interactions in biological systems while using a new perspective (i.e. integration instead of reduction). See www.wikipedia.org.

44 Histology is the study of fixed (i.e. non-functioning) tissue, in this case of the brain, sectioned as thin slices under a light microscope.

years. It is much easier to implement important properties like plasticity, development or adaptation in a dynamic system, where the final result is an equilibrium between all the constantly active transitions than to imagine how they occur in a rigid static configuration. Dynamic systems thus facilitate the implementation of these important biological properties, but they also impose huge problems for our basic understanding of how the organisation of the brain is maintained.

– Matching the bridge between molecular aspects and higher functions. This development, that has started in particular with the possibilities of genetics and of in-vivo neuro-imaging, in principle allows relating higher functions to molecules in the brain. However, except a few clear cases of disease, it is not clear at all what types of conceptual theories are needed to describe such relations. It becomes more and more clear that each and every higher function involves many neurotransmitter systems and multiple genes.
– Research on brain function has concentrated mostly on neuronal function, but it has become clear that the other cell type present in the brain (summarized as glial cells), outnumbers neurons by a factor ten and they are at least equally important for brain function. Their role needs to be further revealed.
– It is clear from many studies and from conceptual models that in the brain information is processed and stored in a distributed way. That concept does not match well with the intuitive desire of scientists to find a location for each and every function we define (see the many examples in this book). New theories are needed to integrate both ways of thinking into a new one that pays tribute to both possibilities.
– The organisation of the brain is so complex and extensive that it can be easily shown that its building plan can not be included in the DNA. Most likely, higher levels of self-organisation regulate the development of brain structures. Many scientific disciplines are currently involved in analyzing complex (dynamic) systems. Unravelling and investigating these principles in brain science will most likely find applications at many other places in society.
– In the last decade the possibilities for computational approaches have reached a level that can be extremely helpful in our understanding of brain function. The new Blue Gene project[45] and actions of the international neuro-informatics[46] society are examples of this development. These projects are expected to push brain research forward in a similar manner as the cloning of the human genome did for genetics. However, we should realize that the demand on computer resources is several orders of magnitude bigger.
– From an experimental point of view, recording simultaneously from many

45 Blue Gene is a computer architective project designed to produce several supercomputers. See www.research.ibm.com/bluegene.

46 Neuroinformatics is a research field that focuses on the integration of data on different levels of the brain by developing neuroscience data- and knowledge bases, analytical and modelling tools and computational models. See www.incf.org.

neurons and structures with high spatial and temporal resolution and link their activity to higher functions is still a key necessity of brain research. However, improvements of this aspect alone, will only generate more data. The key to progress will be a parallel development of new concepts on how to integrate this knowledge, involving all disciplines that contribute to the brain sciences.

All questions and topics mentioned above (in no way claiming to be exhaustive) will at some point lead to new developments in every one of the four application fields explained in detail in this book. Undoubtedly our knowledge on brain function will greatly increase in the coming decades, but like scientists fifty years ago could not imagine that we would know the structure of DNA, the detailed functioning of membrane ion channels or that we could follow brain activity in living individuals, we better be modest in predicting what will be known in another fifty years.

## 1.7 Opportunities in the applied neurosciences and cognitive sciences

*Ira van Keulen*

The well-known cognitive neuroscientist Antonio R. Damasio, who discovered that emotions play a central role in human decision-making, once said in an interview: "*Knowing about the workings of mind and brain can help us deal more effectively with the social problems we face today.*" Several of the propositions — or brain visions — presented at the beginning of this chapter support Damasio's claim and demonstrate that his prediction could come true both in the near and more distant future, at least if we interpret social problems broadly, including healthy nutrition, obesity, human-technology interaction, educational instruction, gaming, juvenile delinquency, and so on. Of course, we still have much to learn about the workings of the brain and mind, and some applications — for example lie detection — have not turned out to be as straightforward as we once imagined. Moreover, more knowledge about the neural mechanisms behind our behaviour will not always lead to spectacular new applications or sensational solutions to old problems. But it is indisputable that our growing knowledge of the brain will make a very valuable contribution to existing academic and non-academic knowledge and expertise in many different areas.

This is why in the final section of this book, we focus on four conditions that will ensure that the neurosciences and cognitive sciences will continue to make a significant and positive contribution to both science and society. These four conditions rose to the surface during meetings of the STT Brain Visions expert and steering groups. In short, the brain sciences should:

- Try to maintain a proper balance between making promises and preventing hypes by avoiding or challenging oversimplification and overvaluation of their scientific findings (subsection 1.7.2).
- Continue the trend towards interdisciplinary research[47] in order to support the successful academic development of the field and work towards a comprehensive theory of the brain (subsection 1.7.3).
- Increase transdisciplinary research[48] in order to stimulate socially relevant applications and disseminate neuroscientific and cognitive knowledge in different relevant practices (see subsection 1.7.4, which includes some themes suitable for transdisciplinary research).
- Set-up a research agenda and public debate on the ethical, legal and social implications (ELSI) of the neurosciences and cognitive sciences (see subsection 1.7.5).

It speaks for itself that the brain sciences can only achieve those conditions in cooperation with others (government, industry, the relevant professions and other related scientific disciplines). But before treating the favourable conditions for their blooming, let us first examine the reasons behind the expected, broad impact of the neurosciences and cognitive sciences on society.

### 1.7.1 Broad impact on society

*Ira van Keulen, Michel Decré* [49]

One important message of this book is that the knowledge of the neurosciences and cognitive sciences will inevitably result in innovation in research and development in at least four different domains of society: food, education, man-machine interfaces and law. But there are other domains — not described in this book since they have been studied in depth in by others — in which our rapidly advancing insights into the brain and cognition will also turn out novel applications. Two are worth mentioning here: health care and the military or national security. Most obvious is of course health care, which will feel the impact of our growing knowledge of the brain in the form of new drugs, therapeutic devices and diagnostics. After all, most brain research has medical clinical applications as a goal. That is no surprise, with two billion people worldwide suffering from brain-related illnesses and, according to the Neurotechnology Industry 2008 Report,[50] revenues in the global neurotech industry (i.e. drugs, devices and diagnostics) rising 8.3% to 130.5 billion US dollars in 2008. It is supposed to be the largest unmet medical market.

47 Interdisciplinarity involves confronting a problem from the perspective of different scientific disciplines while integrating concepts, methods and data.

48 Transdisciplinarity signifies the integration of scientific and non-scientific knowledge (i.e. the lay expertise of patients, teachers, consumers, etc.).

49 Principal Scientist at the Health Care Devices & Instrumentation Department, Philips Research Europe.

50 See www.neuroinsights.com.

Another domain which can profit extensively from neuroscientific research is the military or national security. Many neuroscientific findings have caught the attention of national defence agencies, for example DARPA's Cognitive Technology Threat Warning System (CT2WS) described in example VIII. Other areas of interest to the military are: improving the endurance and psychological performance of soldiers (e.g. drugs to keep sleep-deprived soldiers alert); cognitive profiling of terrorists; and information systems to aid soldiers' cognition.[51]

An important reason for the broad societal impact of the neurosciences and cognitive sciences is that sciences and technologies so far have dealt with the world outside ourselves (e.g. reconsidering our place in the universe, gaining control over our environment, increasing our material quality of life, increasing our health, etc.) as opposed to genetics and even more the brain sciences. These sciences deal with our very selves: our biological inheritance, our hidden (genetic) blueprints, and our conscious and unconscious behaviour, which make our identities and personalities. We stand on the brim of unveiling biological bases and organic explanations for some of the most intimate aspects of our lives. If we ever come to fully understand the workings of the brain and the mind, we will understand how we ourselves think and behave, with potential relevance in every domain of life. Furthermore, our understanding of ourselves will only be accelerated by the fact that various forms of social behaviour (bargaining, imitation, moral judgement and fairness) are increasingly subject to neuroscientific research. This emerging field of social cognitive neuroscience aims to understand social behaviour in neurobiological terms.[52]

The impact of neuroscientific findings on society will probably even be more profound than was and ever will be the case for genetic research, because most people think our brain tells us more about ourselves than our genetic profile. We simply identify ourselves more with our behaviour[53] than with our biological inheritance. But more importantly, 'neural essentialism' seems much more grounded than genetic essentialism.[54] This is nicely explained by Alex Mauron [2003]: "*Genomes are inherently replicable… Brains are precisely the opposite. Because their structure does not come about by merely 'unwrapping' some pre-existing genetic program, but by the constant interplay of internal developmental processes and external stimuli, they are inherently unique and irreproducible… This is why the brain provides a much better material home for the numerical and biographical identity of persons than the genome does. Every brain necessarily has a history of its own and thus much more resembles the human self 'itself' than the static database represented by the genome.*"[55] In short, the genetic and environmental aspects of your personal history are 'written' in your brain. The prominent British neuropharma-

51 For an overview, see the book 'Mind Wars: Brain Research and National Defense' [Moreno, 2005].

52 Examples of social neuroscientific research are studies on mirror neurons in relation to empathy and on the neurotransmitter oxytocin in relation to social recognition, bonding and trust.

53 Some people think the brain tells us more about ourselves because memory (in stead of behaviour) resided in our brain, fundamentally makes us who we are.

54 Neural or genetic reductionism are forms of biological reductionism. A neural or genetic essentialist view proposes that behaviour (sexuality, delinquency) can be fully explained in biological terms: neural mechanisms or genes. It is the belief that a person is his genes or his neurons operating in a certain way.

55 Even though epigenetic studies have proven that gene *expression*, at least, is not that static and can be changed in multiple generations under the influence of environmental factors.

cologist Susan Greenfield argues that our mind is nothing less than a personalised brain: a brain customised from conception onward under the influences of our genes and our biological and social environment. Brain-based explanations can therefore (theoretically[56]) be complete, while genomic explanations always remain partial.

*Shift in public thinking*

Besides the broad impact in terms of novel applications in different domains, there is also the impact of the neurosciences on our thinking, i.e. people increasingly tend to explain themselves, others and their behaviour in terms of the brain. This shift in thinking is being influenced by the media's growing interest in the results of brain and cognitive research. As a result, people increasingly draw upon languages, concepts, and explanatory logics that set up the brain as the essential locus of their identity. Some social scientists speak of 'folk neurology' in this respect. For instance, many people refer to the pleasure they experience after physical exercise as an 'endorphin rush', or they explain their addiction to alcohol in neuroscientific terms: "*I am not an alcoholic, I am endorphin challenged*" [Vrecko, 2006]. The Dutch neuroscientist Peter Hagoort too predicts the growing use of expert neuroscience to explain behaviour: "*I picture a patient visiting his GP in 2025 saying: 'I think it's my amygdala' instead of 'I think I'm agoraphobic'*" [Neurofederatie, 2005].

There is also a certain attractiveness in perceiving the brain as the central locus of our identity, especially as we have recently learned that the brain is much more plastic than we ever thought. This is best illustrated by the famous neurocognitive plasticity study on juggling. Certain areas of the brain involved in juggling — motion perception and predictive skills as to where the ball will land — grew steadily in volume during the three months of training. But as soon as the subjects stopped juggling, those areas immediately shrank again (see also example IX). Such studies have contributed to the idea that *if* the brain is the origin of our behaviour and even of our identity, *and* the brain is highly flexible, we can change ourselves by training our brain. Or, as the subtitle of Dutch neuropsychologist Margriet Sitskoorn's highly popular book 'Het Maakbare Brein' ['The Mutable Brain'] expresses it: "Use Your Brain and Become Who You Want To Be". The prevalence of this idea is reflected in, for example, the popularity of Nintendo's DS Light Brain Games, but also in the trend towards lifelong learning (i.e. the idea that it is never too soon or too late to learn).[57] Such public ideas are typical of the optimism that generally rules the early stages of a rapidly developing scientific field.

56 Theoretically, because there are still many breakthroughs needed before we are able to completely understand the brain and mind, as referred to in section 1.6.

57 See www.wikipedia.org.

### 1.7.2 High hopes for the brain sciences

*Ira van Keulen, Michel Decré* [58]

The first condition that we deem necessary to favour positive contributions of the brain sciences to academia and society concerns hopes, hypes and expectation management. Both the broad coverage of brain research results in the popular media and academic journals and the growing financial support for neuroscientific and cognitive research suggest overall optimism about this pioneering scientific field. All this is raising expectations in the public domain, and in particular in such professional areas as education, the food industry, criminal investigation and the law. During the STT project, which involved more than fifty experts from various professional backgrounds (see the Project Organisation section), representatives of the food industry[59] and the educational sector were particularly optimistic about the value of neuroscientific knowledge for their professions. Or at least, as we will illustrate below, they had high hopes for the potential usefulness of our growing knowledge of the brain. This contrasts with the observation during the STT project that the neuroscientists themselves were frequently reluctant to make recommendations for policy or practice, based on neuroscientific findings.

Take, for example, the concept of sensitive (or even critical) periods in which specific brain areas or functions would develop. This concept is embraced by both the food industry and educational practice (see also subsection 1.4.1), although the academic debate is still vivid as to whether such periods actually exist. For the food industry, such sensitive periods might entail opportunities to develop products that have the biggest effect during a certain period and for a certain target group. Hence, the expert group on brain-food interdependency broadly supported the idea of the 'right nutrition at the right time for optimal brain development'. Similarly, educational practice sees opportunities for adjusting educational curricula to sensitive periods in brain development in which specific learning abilities develop best. To what extent the expectations of the food industry and educational practice will be borne out is still doubtful, however. This example illustrates that there are high hopes for the brain sciences in non-academic circles.[60] This does not necessarily mean that the 'lay experts' are overly optimistic because they lack information; it could very well be that the neuroscientists are too cautious. Time will tell.

However, some participants in the STT project claimed that a lot of useful neuroscientific findings are as yet insufficiently adopted by industry, government, etcetera. They explained this by the fact that many neuroscientists are too much focused on fundamental research — there is after all still a vast area

58 Principal Scientist at the Health Care Devices & Instrumentation Department, Philips Research Europe.

59 The optimism in the food industry is nicely illustrated by an earlier quote from the CEO of Nestlé: *"We now know that diet can have very beneficial effects on the mature and ageing brain"*.

60 In the STT project, experts from other scientific disciplines such as food or education were also more optimistic than the neuroscientists.

of research to cover — and not on applying their recent findings in practice (see also subsection 1.7.4). They think research has already given rise to many broadly accepted ideas about the workings of the brain (e.g. the 'interpreter' theory or mirror neurons) and to scientifically sound results that can already be applied in daily practice. For example, elderly people should take as much mental but certainly also physical exercise as possible to prevent neurodegeneration [Hamer and Chida, 2008].[61] An intense focus on fundamental research may, however, result in an innovation paradox, i.e. the failure to exploit academic brilliance in applied research or practice. Other participants in the STT project argued the opposite. According to them many intellectually rich findings of brain research are not directly suitable as policy or practical recommendations. In some cases, the neurosciences explain behavioural mechanisms that we already know. For instance, 'practice makes perfect' has been confirmed by basic neuroscientific studies showing that in skills acquisition, repeated exercise helps the nervous system learn the right response.[62] The truth (about the applicability of current neuroscientific findings) will probably lie somewhere in the middle.

Back to the high hopes, which are leading many different parties to take an interest in the neuroscientific field. The rhetoric of expectations and promises in every scientific discipline, increases the visibility of the research and its possible applications. Such publicity is needed to set research and innovation agendas and mobilise more students, PhD candidates and financing. Hype is inevitable, and some people probably think it is already a factor in the neurosciences. Nevertheless, in the early stages, hype is difficult to distinguish from justified hope [Van Doorn, 2006]. Whether hype or hope, it is clearly to the advantage of the field that academia, industry, government, and other stakeholders extrapolate about the possible contribution of the brain sciences to their particular area of expertise. The phenomenon also has its downsides though, like oversimplification leading to jumping to conclusions, or hasted policy making driven by public hopes.

*Oversimplification*

As section 1.6 has shown, the field of neurosciences and cognitive sciences is very complex: methodologies, experimental protocols, (statistical) interpretation of results are often correspondingly delicate and elaborate. It is therefore very tempting to indulge in (over)simplification when bringing these results to a broader, or lay, public. Both media and (to a lesser extent) neuroscientists are found oversimplifying. This should, however, be banned from the field, because perhaps more than in any other field, nothing can be stated in black or white terms when dealing with matters of the brain.

**61** Neurodegeneration is the loss of neuron structure or functions. See www.wikipedia.org.

**62** This also explains why it is so difficult to unlearn an old habit. If you have learned to play a note on the violin in a particular way, it is very difficult to change it; it has become automated, i.e. 'engraved' in the relevant neural pathways.

One reason for rising public expectations about the benefits of neuroscientific research are reports on fMRI studies containing colourful and attractive images of brain activity. These powerful representations are bound to elicit a response from the public and fellow scientists; the images seem "*to imply visual proof of the fundamental nature of reality and subjectivity*" [Racine et al., 2006]. For instance, some people seem to believe that these images make behavioural observation more real (i.e. 'neurorealism'). fMRI images have an objective aura, although — unlike photographs — they are not in fact a direct image of reality [De Rijcke and Beaulieu, 2004]. They are a representation of the scanned brain being subjected to different statistical methods. Misinterpretations of the technical details behind neuro-imaging encourage oversimplification of the scientific results, especially in media coverage but also in new disciplines that have enthusiastically adopted neuro-imaging techniques as research tools, for example neuro-marketing or neuro-economics.

Oversimplification of results is a hot topic among neuroscientists themselves. In November 2008, an — according to some neuroscientists — oversimplified fMRI story about the cognitive state of twenty undecided voters in the upcoming American presidential election appeared in The New York Times. The critique was that the research was based on 'reverse inference', i.e. inferring a particular cognitive process — in this case anxiety and mixed feelings of voters — from the activation of a particular brain region. This is actually a common way to look at fMRI data; however, some neuroscientists argue that although anxiety engages the amygdala, for example, so do many other things such as pornography or intense smells. The Times article resulted in a letter to the editor by sixteen American cognitive neuroscientists, who stated that "...*we are distressed by the publication of research in the press that has not undergone peer review, and that uses flawed reasoning to draw unfounded conclusions about topics as important as the presidential election.*" [63] According to these neuroscientists [Miller, 2008], oversimplification of fMRI results should be suppressed and the field itself should concentrate on introducing more rigour into fMRI research.[64]

Summarising, it is hard for scientists to find the right balance between making promises and avoiding hypes. In the end, especially the media, but also cognitive and neuroscientists and non-academics alike, must exercise some caution when it comes to interpreting neuroscientific results (risk of oversimplification) and making claims or recommendations based on brain research (risk of overvaluation or of stating the obvious). The challenge may lie therein that in fields like education, law, or MMI (and to a lesser extent in food), systems to verify the validity of statements are much less developed than they are for health care. These fields have no equivalent to the American Food en Drug

**63** See www.nytimes.com/2007/11/14/opinion/lweb-14brain.html?_r=1&oref=slogin.

**64** More information on the pros and cons of fMRI can be found in Appendix I.

Administration (FDA), or the European directives, regulations and guidelines for drug approval. Mechanisms are thus missing to prevent the application of unvalidated findings in less regulated societal fields. This puts consumers at greater risks, and should therefore be tackled collectively (see subsection 1.7.5).

### 1.7.3 Interdisciplinary research

Traditionally, psychology studies higher cognitive functions and behaviour without looking at the brain. Psychology is accustomed to approaching the mind as a black box, only to focus on the transformations between input (environmental stimuli) and output (behaviour). Studying the brain is traditionally the domain of biology, which investigates the workings of neurons without involving the final goal of these workings: behaviour. Fortunately, the two fields, each with its own research strategies, have in the past two decades been working together more and more often. The up-and-coming discipline of cognitive neuroscience, with its neuro-imaging techniques for investigating brain function 'live', has encouraged interdisciplinarity between psychology and basic neuroscience. According to a recent Rathenau study with bibliometric analysis (of citation relations in relevant journals) [Merkx and Van Koten, in press], the cognitive neurosciences are in fact a growing interdisciplinary field, situated in between the fields of basic neuroscience and cognitive science (including psychology). This indicates that the latter fields have not necessarily been integrating, but that a new monodiscipline — cognitive neuroscience — has been created, with its own theoretical framework and body of knowledge.[65] Still, there are also other signs showing a developing overall interdisciplinarity in the field of brain and cognition. For example, about forty percent of the members of the Society for Neuroscience (SfN) have a background in psychology. And in the past five years, neuroscientists in their turn have increasingly participated in the US Cognitive Science Society, traditionally populated by psychologists [Ishii, 2005].

Cooperation between the different disciplines within biology that study the brain at different levels of brain organisation (molecular, cellular, etc.) has also increased. As with neuro-imaging, the development of new research tools makes it easier for the different disciplines to work together. For example, the function of groups of neurons can nowadays be linked with certain genes by recording neural activity in living active animals. Transgenic and gene knock-out technology[66] in animal models makes it possible to study the interaction between many different genes and proteins and the patterned (behavioural or mental) responses they elicit. In short, interdisciplinarity in the neurosciences and cognitive sciences seems to be much more common and accepted than ten years ago.

**65** In fact their analysis of the relevant journals in the neuroscientific and cognitive field revealed a trend suggesting increasing specialisation and fragmentation instead of overall integration in the neurosciences and cognitive sciences.

**66** A gene knock-out is a genetic technique in which an organism is engineered to carry genes that have been made inoperative in order to learn about the function of those genes. See www.wikipedia.org.

A fully developed interdisciplinary approach within the neurosciences and cognitive sciences has not been attained as yet and will take time. At the same time, the cooperation between the brain sciences and more 'foreign' scientific disciplines such as educational sciences or food sciences, MMI and law is in its infancy.[67] The Rathenau report mentioned earlier also studied the citation relations between neuroscientific, cognitive scientific and education journals. It states that even in the interdisciplinary field of 'educational neurosciences' — which has captured the attention of educational policy-makers and practitioners — interdisciplinarity (and also transdisciplinarity) has not really taken off. Bibliometric analyses show that educational psychology uses only cognitive psychology as a knowledge base, and not any of other fields such as basic neurosciences, cognitive neurosciences or cognitive sciences. The latter, in turn, do not quote any articles from educational psychology journals [Merkx and Van Koten, in press]. Even in the recently established journal 'Mind, Brain and Education' — whose mission is "*to create a new field...with educators and researchers expertly collaborating in integrating the variety of fields connecting mind, brain, and education in research, theory, and/or practice*" — the quotation charts are dominated by journals in the cognitive neurosciences, whereas educational journals make only a modest contribution.

*Stimulating interdisciplinary research*

As section 1.6 already stated, interdisciplinarity is an important aspect of the brain sciences; big steps towards a fully integrated scientific field have already been taken. Still, based on the discussions in the steering and expert groups of STT project, there seems to be a need for more academics who feel comfortable integrating the molecular and cellular level (neurobiology) with the behavioural level (psychology), using theory and methods drawn from mathematics, physics and chemistry. This means that we need more students to enrol in interdisciplinary academic programmes. Generally, the problem as such is not to find students who are interested in interdisciplinary studies, but to make institutional changes facilitating the assessment of interdisciplinary programmes. The Royal Netherlands Academy of Arts and Sciences has even advised bestowing 'science status' ('beta status') on Master's programmes in the cognitive sciences (in its report on the organisational structure of the neurosciences and cognitive sciences in the Netherlands).

Besides changes in academic programmes, another way to attain a fully interdisciplinary neuroscientific and cognitive field is to encourage research facilities. Particularly important in this respect is what the Royal Academy calls "*an interdisciplinary effort to develop a complex and extensive system of computer networks for simulation, analysis and cooperation tailored to the cognitive sciences and making it possible to usefully store and analyse the huge*

67 There has been some interdisciplinary cooperation between the brain sciences and less obvious scientific disciplines, however. This has resulted in totally new fields, for example neuroethics and neurotheology, which look for neurobiological explanations of (in this case) morality or spirituality.

*amount of data produced*". The rapid expansion of the field has produced an enormous wealth of data at every level, from the molecular level to the brain as a whole. And these data are gaining higher levels of granularity.[68] In order to handle the complexity and model the organisation of the brain, an extensive system of computer networks and accompanying software is needed to manage and exchange data (in section 1.6 explained as one of the major challenges of the brain sciences). As early as 2005, five directors of the National Institutes of Health (NIH) pointed out the growing need for an undertaking similar to the Human Genome Project, with network systems and databases enabling "*a more rapid and comprehensive pursuit of the brain's physiology*" [Insel et al., 2004].

When it comes to stimulating interdisciplinarity between the brain sciences and more 'foreign' scientific disciplines, the STT project Brain Visions has made some first steps in acquainting the different scientific disciplines with each other. Interestingly, the STT expert group on MMI suggested that collaboration between disciplines (in this case between the neurosciences and MMI research and development) focusing on a specific application would be useful, as is happening with brain-machine interfaces (BMIs). Such an application then becomes the driver that speeds up interdisciplinarity and innovativeness in the relevant scientific disciplines in general and the specific field of application in particular. At the same time, driver applications are a vital means of focusing the research agenda. The propositions at the beginning of this chapter suggest some promising driver applications — or at least directions for applied research — emerging from the interaction between scientific/technological push and societal pull (as both sides were represented in the STT transdisciplinary expert groups). Examples are: weight management food products that stimulate early satiety; conditioning of food preferences in the first year; obesity and higher risk of dementia; evaluation of conventional interfaces through neuro-imaging; and attaining a sense of body ownership in virtual reality.

**68** Granularity is a measure of the size of the components that make up the system, in this case the brain.

### 1.7.4 Transdisciplinary research

One step beyond interdisciplinarity is transdisciplinarity. One particular advantage of transdisciplinary research is that intensive interaction between scientific disciplines and cooperation with societal actors makes it possible to gear knowledge generation more towards applications. Both science and practice are encouraged to think about socially relevant applied research and applications. That's why STT's Brain Visions study, which aims to explore the possibilities of neuroscientific applications, was set up as a transdisciplinary project.[69] At the same time, as a dialogue between different stakeholders, transdisciplinarity is also — although on small scale — a good way of counter-

**69** The expert groups on Education and Food and the conference "Justice and Cognition" were transdisciplinary in nature, whereas the MMI expert group was more interdisciplinary. See the Project Organisation section at the end of the book.

acting some of the hype, unrealistic expectations, and neuromyths or faulty knowledge of the workings of the brain and the mind. In short, it fosters the embedding of neuroscientific and cognitive knowledge into society and avoids the earlier referred to 'innovation paradox' so common in the Netherlands.

### *Difficulties in transdisciplinary research*

It was clear from the very start of the STT project that transdisciplinary research is not yet common in the neurosciences and cognitive sciences. This comes as no surprise, since — as we have repeatedly argued — there is still plenty of fundamental research to be done in the field. Most of the relevant scientists focus primarily on fundamental (and not applied) research. This makes many neuroscientists — at least within the STT project — circumspect about our current knowledge of the brain and reserved in their statements about the extent to which brain science results will lead to applications in various domains. This circumspection might be due to the sometimes overly optimistic media coverage of neuroscientific applications, something that has made many neuroscientists more reserved. The European intellectual legacy of "*a certain pessimism about science-based cures to social and political ills*" [Andler, 2005] might also play a role here.

Besides the fact that neuroscientists and cognitive scientists tend to focus on fundamental research, the path to more transdisciplinary research on the brain and cognition is also strewn with such obstacles as differences in jargon, paradigms (e.g. reductionism in the life sciences versus subjectivism in the social sciences and practice) and assumptions that are difficult to reconcile. These cultural differences will become evident in the following chapters of this book. While a representative from industry may concentrate on opportunities to develop new products (see subsection 2.2.6 on sensitive periods in brain development), the scientist focuses on weaknesses in research on the effect of fatty acids on brain and cognition (see subsection 2.2.5 by Renate de Groot). Or someone in educational practice (see subsection 4.6.2 by Harry Gankema) may use the concept of *motivation* as related to (and even as the first sign of) intelligence while seeing *drives* (hunger, thirst, sleep, sex) as the biological necessities of life, whereas a neuropsychologist (see subsection 4.6.1 by Jelle Jolles) conceives of these 'drives' as motivational factors. These cultural differences usually result in issues that are epistemological in nature. When so many different disciplines and practices come together, a discussion of what is 'good' knowledge can naturally be expected. For example, ideas on properly conducted scientific research may differ per discipline and opinions of the value of lay expertise may also vary.[70]

70 True transdisciplinary research assumes that knowledge is intersubjective. That makes opinions, ideas and facts difficult to distinguish from one another and places equal value on everyone's contribution.

*Cautious trends towards transdisciplinary research*

Nevertheless, a cautious trend towards transdisciplinary research can be detected, especially in the field of education (and even more cautious in the fields of food, justice and MMI, according to the STT project). For example, there is the new journal referred to earlier, 'Mind, Brain and Education', and the OECD study 'Understanding the Brain: the Birth of a Learning Science', actively promoting a transdisciplinary learning science. At national level, the Brain and Learning Centre at Maastricht University is starting up transdisciplinary research initiatives. This cautious rapprochement between the neurosciences, cognitive sciences and educational practice can be attributed in part to the current notion that transdisciplinary research may help jazz up the impact of academic research on educational practice [Onderwijsraad, 2003], which in the Netherlands traditionally has been very low. However, the study conducted by the Rathenau Institute [Merkx and Van Koten, in press] claims that in international terms, a transdisciplinary learning science does not yet constitute a substantial field of research.

There are a few signs of emerging transdisciplinary research in the other fields studied in the STT Brain Visions project. One nice example in the area of law is the Law and Neuroscience Project in the United States, which is receiving 10 million US dollars from the McArthur Foundation. Its mission is "*to address the diverse and complex issues that neuroscience raises for our legal system*".[71] To accomplish this mission, the project consists of three transdisciplinary research networks (on diminished brains, addiction and decision-making) headed by a neuroscientist *and* a legal expert, and an educational programme informing people working in judicial practice of relevant neuroscientific findings. The Netherlands has a few smaller scale transdisciplinary initiatives, mostly focused on exploring new pharmaceutical treatment methods for delinquents in detention suffering from schizophrenia, autism, addiction, or other conditions.[72]

There is quite a lot of interdisciplinary and transdisciplinary research and development taking place in the field of BMI, involving researchers from the fields of nanotechnology, biotechnology, information technology, neuroscience, cognitive science, biomedical engineering and applied mathematics. The Netherlands has a major research project on BMIs called BrainGain (see Box 1 in Chapter 3, Neuro-centred design). This project also has a transdisciplinary line of approach since it has three patient organisations as partners (Parkinson, epilepsy and ALS). Their lay expertise is being used to improve specific BMIs.

**71** See www.lawandneuroscienceproject.org.

**72** For example: the Research and Documentation Centre at the Dutch Ministry of Justice (WODC) has recently done a review on neurobiological research in relation to sanctioning and crime prevention, and the Pompestichting detention clinic in Nijmegen has set up a study group on the possible contribution of neuroscientific research to treatment during detention.

*Encouraging transdisciplinary research*

If we want neuroscientists and cognitive scientists to "*seek more links with societal issues*"[73] in order to earn a spot in the national knowledge and innovation debate alongside genomics, nanotechnology and information technology, then more transdisciplinary research in the brain sciences is one way to go. There are several ways to encourage transdisciplinary research. Various Dutch reports have made recommendations for increasing transdisciplinary research or processes, for example adjustments to assessment systems, disciplinary structures, career counselling for scientists, and new funding structures [AWT, 2003; Klein 2001]. It is beyond the remit of this book to discuss these different recommendations in detail. However, we would like to review some of the ideas posed by participants in STT's transdisciplinary Brain Visions project.

*Academic practices in existing teaching hospitals and academic schools.* These institutions are actively involved in education and in research involving user groups (patients, pupils/teachers, etc.). They cooperate extensively with universities, offer opportunities for innovation, and set an example for other practices [RGO, 2000]. Such practices could also be relevant as small-scale initiatives in which scientists and non-scientists work together on applied neuroscientific and cognitive scientific research. Examples include academic primary and secondary schools focused on brain, mind and learning, or academic courts of law, law offices, and police forces that collaborate with relevant academic faculties. It is important that academic practices are initiated from the bottom up by the academic and non-academic stakeholders themselves to turn them into long-lasting, firmly grounded practices.

*Direct funding programmes for small-scale transdisciplinary research by national or local government.* For instance, the Dutch Ministry of Education, Culture and Science recently launched a funding programme on Evidence-based Education, which is making 25 million euro available over the course of four years. Schools and research institutes can apply for funding together.[74] The programme's mission is to come to understand what does and does not work in educational practice by means of hands-on (cognitive, neuroscientific or other scientific) experiments.

*Create scope for transdisciplinary research within large-scale national research projects*. Examples include the current National Brain and Cognition Initiative or BrainGain on BMIs. Between 3 and 5% of the annual budgets spent on the Human Genome Project were devoted to the ethical, legal and social issues (ELSI) surrounding the availability of genetic information (see subsection 1.7.5).

73 A quote from the proposal of the National Brain and Cognition Initiative. See www.nwo.nl/nwohome.nsf/pages/NWOA_6MXKBK.

74 www.minocw.nl/onderwijsbewijs.

**Box 1: Themes suitable for transdisciplinary research**

During the STT project, a number of overarching themes emerged from the different areas of application (food, MMI, education and law). These themes can be seen as society's demands or as market opportunities that can channel transdisciplinary research or neuroscientific and cognitive research in general. In other words, they are examples of questions that the food industry, interface design, educational and judicial practice have in common and therefore represent promising themes for further transdisciplinary research.

*Sensitive periods in brain development as windows of opportunity*. As mentioned earlier (see subsection 1.7.2), the expert groups on both food and education were very interested in opportunities to adjust functional food products and curricula alike to the periods in which particular brain (e.g. vision, language) and cognitive (e.g. decision-making, planning) functions develop. The common assumption is that functional food products and instruction can have an optimal effect on the brain in this way. There is still no convincing scientific evidence that these periods exist, especially not for cognitive functions (more so for brain areas, such as the visual cortex, the auditory cortex and prefrontal cortex). In both education and the food industry, the common goal behind using such sensitive periods is to influence the brain and cognitive functions at an early stage of development (i.e. in infants and toddlers).

*Motivation and how it is neurally wired*. This is another important theme running through the discussions of all STT expert groups. Neuroscientific research shows that emotional stimuli influence cognitive performance. Some might even say that "*Will and wanting is not an extra to the brain; it is at the core of its functioning*" [Nørretranders, 2007]. But what do these recent findings mean for the different application domains? Stakeholders from the food industry and national government are interested in several of the motivational aspects of eating behaviour; some of these are related to food addiction resulting in overweight or even obesity. But they are also interested in the conditioning of food preferences in young children: how can we teach them to appreciate healthy food such as fruit and vegetables? People from educational practice are interested in the motivational processes behind learning in relation to age and intervention methods; they want to understand the relationship between motivation and involvement, boredom or self-esteem/uncertainty; they want to know what to expect from self-guided learning and dependence on the teacher, and in particular why children in general are so motivated to play computer games. Finally, the MMI scientists and developers were interested in evaluating interfaces and systems against the motivational mechanism in the brain and in developing 'persuasive technology' (i.e. technology that helps change the user's behaviour, as is the case with weight management) and systems that keep users engaged without feeling they are losing control.

*Multimodal sensory integration.* We use more than just words to convey our message and we look for cues to understand people or things: hand gestures, the look in someone's eyes, the smell and texture of food, and so on. We use different sensory modalities to interpret other people and the world around us. A better understanding of multi-sensory information processing or how various input signals result in one coherent, complex interpretation in the brain (the 'binding problem' referred to earlier) could be useful in many different application domains. The various expert groups raised the following questions: how do different sensory modalities such as vision, hearing, taste, smell and texture integrate in the brain to form an overall perception? How do all these bits of sensory information influence one another and how do they influence final perception? How does the brain weigh various sensorial inputs? In what situations (for example under stress) can which sensory modalities be used to communicate best? Is it always better to address multiple sensory modalities to convey a message? Which modalities bind better than others? In the domain of interface design, insights into human multimodal communication may help in developing multimodal interfaces that go beyond the use of keyboard and mouse [Andler, 2005] or that increase the face validity and immersive experience of a virtual environment. In the area of education, the question is how different educational material can be presented in such a way that pupils are able to learn best: which sensory modalities should be addressed for the best results? Are there differences in the 'sensory preferences' (i.e. visual, auditory or tactile strategies) of individual pupils, and what is the best way to deal with this? In the food domain, the interest in sensory integration stems from the food industry's aim of influencing food perception and liking, for example replacing one sensory stimulus (salt or fat) by another, less potentially harmful one, or developing more experience-intensifying and taste-intensifying products. Interestingly, one of the goals behind understanding sensory integration is the same for the three domains, namely *intensifying* the experience of virtual reality (MMI), *intensifying* the learning process (education) and *intensifying* the experience of eating (food).

*Effect of ICT use on brain development and cognitive functions.* Another theme common to the expert groups on MMI and on education was how technical environments such as video game culture influence brain and cognitive development. We know now that the brain is much more plastic than we previously assumed, but this also implies that it is much more flexible and vulnerable than we had thought.[75] Several experts mentioned the use of information and communication technology and its possible effect on the brain as an important topic of future research. Not only should such research focus on the potentially damaging impact of gaming or surfing the web on the brain, but it should also explore the extent to which the present ICT generation, including infants and toddlers who grow up in an environ-

75 The latter is illustrated by current public concern about the very harmful effects of alcohol on adolescents' brains, which was relatively unknown before.

**ment saturated with media — called 'new millennium learners' by the OECD — has developed a 'different brain' and new cognitive skills. The following cognitive traits are frequently mentioned as different: a short attention span, the need for an instant response, and the ability to multitask. Educational practitioners wonder whether this generation really does have other competencies and skills compared to older generations, and whether educational curricula should be adapted accordingly. In interface design, the question is how the brain tailors its problem-solving activities to a variety of technological information and communication devices. Based on that knowledge, is it possible to detect whether a user's brain — of the digital or non-digital generation — is adapting effortlessly to conventional or new interfaces?**

### 1.7.5 Ethical, social and legal agenda

*Ira van Keulen, Maurits Kreijveld* [76]

The first two subsections, covering changes in how we understand our brain, ourselves and others (see subsection 1.7.1) and the risk of hype (see subsection 1.7.2), already pointed out two reasons to call for an ethical, social and legal issues (ELSI) agenda parallel to the research agenda in the neurosciences and cognitive sciences. An ELSI agenda, including public consultation and debate, can help maintain and enhance current public support for the brain sciences. Public aversion or even resistance can lead to restraints against the flourishing of the brain sciences in the coming decades (as happened with tissue-engineering after the experiment with the mouse with a human ear on its back became news). It is without a doubt that the neurosciences and cognitive sciences will confront us with new moral dilemma's which might even ask for policy measures and adjustments in the legislation. As the sciences on brain and cognition will penetrate our daily life more and more, either through supplying novel applications or influencing public thinking, the ethical questions become more relevant. A public debate on ethical, social and legal issues should be initiated in time. Therefore it is important to analyse these issues and set an ELSI agenda. Just like the Human Genome Project (HUGO) had an ELSI agenda, raising issues such as the intellectual property dilemmas associated with accessing and using genetic information, the use of genetic information and technologies in non-health care settings (such as employment, insurance, criminal justice, etc.), and the impact of genomics on concepts of race, ethnicity, kinship, and individual and group identity.[77]

So far, detailed analyses of the ethical, social, legal but also economic implications of the neurosciences and cognitive sciences are nascent. There has

76 Senior Policy Advisor of ICT and Innovation, Ministry of Economic Affairs

77 See www.genome.gov/10001618. There has been a lot of debate on the significance of the ELSI agenda for the development of the HUGO project.

been little formal consideration (a European ELSI agenda for example) of the implications of these rapidly advancing scientific fields. At the same time, the field of neuroethics is developing equally quickly, with a substantial amount of scientific literature having already been produced in this area, including specialised academic journals ('AJOB[78]/Neuroscience and Neuroethics'). In addition, the Neuroethics Society[79] was recently founded in the United States and the European Neuroscience and Society Network (ENSN)[80] was set up in Europe.

### *Neuroethics*

Neuroethics addresses two main research themes: the ethics of neuroscience and the neuroscience of ethics. The first refers to the ethical evaluation of applications or technologies produced by the neurosciences and cognitive sciences; it concerns issues analogous to those in the traditional field of bioethics, for example medicalisation, treatment versus enhancement, social justice and privacy issues. The second theme concerns neuroscientific findings on traditional ethical and philosophical issues, such as the existence of free will, human rationality and the nature of morality or spirituality. Brain research increasingly produces illuminating data about the neurobiological underpinnings of what makes us human; these findings are unique and have no precedent in any other science [Levy, 2008; Farah, 2005]. Some of the latter issues have been briefly addressed in this introductory chapter and will be considered in more detail in the following chapters.

Despite the growing academic interest in the ethics of neuroscience, the field has so far been largely speculative, *"fruitlessly piling speculation on top of conjecture"* according to Hank Greely [2007], legal and ethical expert on brain sciences at Stanford. One of the most prominent European neuro-ethicists, Nikolas Rose, argued in his lecture at the first conference of ENSN that very little social scientific research on the implications of our growing knowledge of the brain has been *"grounded in sound empirical knowledge of what is actually happening in those fields and what are the actual implications when they move from the laboratory to the field. Neuroethics and social neuroscience have been largely speculative…as to the possible implications of the neuroscientific advances on human behaviour and 'human nature'. Hence the need to try to transform those hypothetical implications into a more substantive and informed debate"* [Rached, 2007]. The same conference also concluded that up to now there have been very few ethical analyses involving industry representatives in order to assess how the neurotech industry is addressing neuro-ethical questions.

**78** AJOB stands for American Journal of Bioethics.

**79** See www.neuroethicssociety.org. Their mission is "to promote the development and responsible application of neuroscience through better understanding of its capabilities and its consequences".

**80** See www.neurosocieties.eu. The ENSN serves as "a multidisciplinary forum for timely engagement with the social, political and economic implications of developments in the neurosciences".

*Relevant ethical issues*

Another shortcoming of current social and ethical research is that most of it has focused on the implications of the brain sciences for health care, including medical BMIs, and to some extent for the law (concerning such issues as lie detection and the alleged absence of free will). Other fields of application have been largely overlooked by social scientists; obviously, since most of the applied neuroscientific research has focused on the medical field. But an ELSI agenda would definitely be relevant too for the other fields addressed in this book: food, education and interface design. Because of our deliberate choice not to embark into extensive discussions of ethical issues in the book, chapters 2, 3 and 4 have separate yet brief subsections on the ethical and social issues involved in applications in the three areas (see sections 2.6, 3.4 and subsection 4.7.5). Still, based on the results of the STT project, in this chapter we would like to pay attention to three relevant ethical issues. Doing that, we should bear in mind that many of the applications of brain research mentioned in this book are still being studied and are partly speculative. More research and discussions between scientists, industry and end-users are definitely needed.

**Cognitive enhancement**. A broad definition of cognitive enhancement is an improvement in mood, cognition or behaviour that is 'better than normal' (as a physical analogy, think of the widespread non-medical use of Viagra). In education, the issue comes up when healthy pupils and students start to use nootropic drugs (or 'smart drugs') to enhance attention and memory, for example. These drugs are primarily intended to battle cognitive problems such as ADHD and neurodegenerative disorders such as Alzheimer's disease. As it turns out, many healthy children in the United States have already discovered the enhancing effects of Ritalin and Adderol [Farah, 2002]. Cognitive enhancement can also be achieved through BMIs, which may someday enable healthy individuals to extend their information management capacities. DARPA is conducting significant research on 'augmented cognition'; the aim is to improve the cognitive abilities of soldiers in the field. Or as Honeywell Aerospace Industries, working under the authority of DARPA, states on its website: *"AugCog technology [which uses EEG technology - Ed] identifies soldiers facing information overload and prompts real-time tactical changes by allowing commanders to redirect that information and any required action to other soldiers."* It is doubtful whether brain food products will have a 'boosting effect above baseline', but food products — or medication for that matter — that suppress our appetite are more within reach.[81] Ethical issues surrounding cognitive enhancement are numerous: possible side effects in the long run, unfair distribution of enhancing products, the moral objection against 'gain without pain' and the idea that the extensive use of enhancing technologies will raise

**81** An interesting ethical issue is that of autonomy: any intervention that frees the patient from the inability to eat enhances, not undermines, his or her autonomy (see section 2.6).

our standards of normality, placing people who choose not to enhance at a disadvantage [Farah, 2002]. At the core of the above issues is a certain uneasiness most people have with manipulating brain functions: it feels wrong and even dangerous.

**Medicalisation**. A term defined in Chapter 4 (Personalised Learning) as the increasing medical interference with 'natural' life events such as childbirth, ageing and dying; the broader definition is the solving of societal issues by medical means. Medicalisation is an issue that pops up in education as well as in the food domain. Within the 'brain vision' of personalised learning, it refers to the possibility that neuro-imaging techniques will be used increasingly in educational practice in order to monitor pupils' cognitive and/or neurocognitive profile. Monitoring, however, might easily lead to a divide between 'normal' and 'deviating' profiles, perhaps leading to the medical diagnosis and even treatment of some pupils. In the food domain, medicalisation is at issue when it comes to functional brain food that stimulates brain development or prevents neurodegeneration. Product development in this case walks a thin line between medical drugs and food products, resulting in the medicalisation of food (as testified by the term 'medical food' with 172,000 Google hits).

**Privacy concerns**. Another important bioethical issue is that of privacy or confidentiality. As with any technology that reveals sensitive information about a person (e.g. prenatal testing or genetic testing for breast cancer), it is not always in a person's best interest to have brain-imaging information available to others, for example insurance companies or future employers. Brain scans are not as revealing about our behaviour (e.g. lying, sexual identity) as some people think.[82] They can detect a possible brain tumour but they are not yet suitable as a major psychiatric diagnostic tool. Many research groups are working on this, however, and there have been some encouraging results with schizophrenia and ADHD, for instance. It is therefore not too early, to consider who is entitled to have access to whose brain-imaging information, and for what purpose. This matter will become even more urgent in the future, when neuro-imaging techniques enter non-medical domains such as the law, education and career planning. In the United States, some people — including the non-governmental organisation Center for Cognitive Liberty and Ethics (CCLE) — have already called for a legal system based on the new concept of 'cognitive liberty', in response to research into brain-scanning technology as a mind-reading device. In the Netherlands, the brain is still a legal private domain, unlike fingerprints, blood and tissue, which persons can be compelled by law to provide (for DNA tests). Other compelling ethical questions related to privacy are: where is the information store? Who has access to the information? Can it be combined with other personal characteristics, like age,

82 There has, however, been fMRI research on neural correlates of racial attitudes and group identity (see example XVI).

gender, profession, etcetera? Important questions, since personal ‘neuro-information’ has potential commercial value.

It is clear that the search for the biological basis of behaviour has always raised ethical questions and led to shifts in public thinking. This will not be any different for the future developments of the neurosciences and cognitive sciences. In the case of the ethics of neuroscience, the traditional bioethical questions might even be more pressing, since — as we have already said — the neural aspects of human nature are more grounded and have more direct relevance than, for example, the genetic underpinnings of human nature. But what must feature prominently on any ELSI agenda are questions arising from the neuroscience of ethics, which addresses the mysteries of the mind in disturbing ways and questions the very core of what makes us human (rationality, free will, morality, etc.).

### *The initiation of an ELSI agenda*

An ELSI agenda is a joint effort of scientists, companies and public institutions on both national and international level. A prominent role lies with the neurosciences and cognitive sciences themselves. This is not self-evident since most scientists usually distant themselves from the ethical consequences from their findings or downplay the risks involved in their (applied) research. But in the end, public debate and scientific research on the social impact of the brain sciences could be to their advantage, resulting in better public understanding of their work and greater likelihood that novel applications will be accepted. One way for the sciences themselves to encourage ELSI research is by allocating it a certain percentage of large-scale research budgets (the 3-5% reserved for the Human Genome Project is a good example). One could also think of a Centre for Society and Brain Research, similar to the Netherlands Centre for Society and Genomics (CSG). The latter is embedded in the Netherlands Genomics Initiative (NGI) scientific network. The mission of CSG is: *“Understanding and improving the interaction between society and genomics…through interdisciplinary research as well as innovative communication and education activities.”*[83] Industry, although in general oriented towards commercial interests in the short term, should also take up their corporate responsibility by initiating or participating in ethical research into its particular neurotechnological or neuroscientific applications. It would even be preferable for industry to work on the ethical, legal and social issues in relation to the development of specific applications in order to avoid speculation and encourage practicable policy measures, for example privacy by design[84]. At the same time, companies can do consumer research in order to find out about the desires and fears of consumers and use those results to determine which R&D should be stimulated or not. Government and public expertise

83 See www.society-genomics.nl.

84 Privacy by design involves thinking on the appropriate use of personal information within an organisation in an early stage of technology development.

centres such as the Dutch organisations the Brain Foundation, the Nutrition Centre or the Rathenau Institute[85], are also relevant stakeholders who can be the drivers behind the initiation of an ELSI agenda. National states and the European authorities can give financial support. The public expertise centres play an important role in educating the public, in increasing neuroscience literacy among the general public, and in encouraging public debate on the various neuro-ethical questions.

85 The Rathenau Institute has as its mission "to focus on the influence of science and technology on our daily lives and map its dynamics, through independent research and debate".

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# 2

# Nutricognition

## 2.1 Introduction

*Ira van Keulen[1], Erik van de Linde[2]*

Until recently, the relationship between nutrition and cognition — called nutricognition[3] in this chapter — was largely overlooked. Many of the authoritative publications on diet and dietary standards focused on physical health issues but scarcely mentioned cognitive performance. For a number of years now, however, science and industry have become increasingly interested in the connection between nutrition, brain and cognition. The food industry in particular is investing heavily in functional foods for the brain, or 'brain food' as some companies call it. For example, Nestlé recently agreed to give the Swiss Federal Institute of Technology 3.1 million euro a year to study the role of nutrition in cognitive functions. Understanding the link between brain function and diet is also one of the main items on the strategic research agenda of the European Technology Platform on Food for Life, which represents the collective European food industry [ETP, 2007]. It is clear that great things are expected of research and development in the field of nutricognition.

1 Projectmanager, STT.

2 Director, Erik van de Linde Innovation Management Consultancy.

3 Nutricognition is a new term coined by STT to describe research and development exploring the effect of food on brain and cognition and on the brain mechanisms behind eating behaviour.

There are enough indications that diet can affect cognitive development and performance (see for example the work of Alex Richardson), particularly at the extremes of the spectrum. It may well be that people in most Western countries already have optimally balanced diets in this respect.[4] What remains is to optimise diets in developing countries and for certain minority groups in the developed world. Diet may also make it possible to postpone or eradicate certain brain dysfunctions that accompany old age, but that involves looking more closely at the period in which brain tissue develops during pregnancy and infancy. Such research may also give us a better understanding of craving, satiety and liking mechanisms, including cross-modality effects[5], so that we can work towards nutritional strategies for battling obesity and encouraging a healthy lifestyle.

### 2.1.1 Understanding brain function in relation to diet

Our understanding of the relationship between nutrition and cognition is increasing for several different reasons. One is our growing knowledge of the brain itself. For example, we now know that the brain has much more plasticity than previously thought. It continues to change throughout a person's life, with synapses being generated, eliminated and moulded. Although the brains of children and adolescents are much more plastic than the brains of the elderly. The CEO of Nestlé regards the degree of neural plasticity in adults as an epoch-making finding: *"We now know that diet can have very beneficial effects on the mature and ageing brain"*.

Neuro-imaging techniques are another breakthrough of enormous interest to the food industry, which until recently depended on behavioural performance tests to demonstrate the developmental or performance benefits of nutrients. Functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electro-encephalography (EEG) and diffusion tensor imaging (DTI) can provide additional, more sensitive and specific test methodologies to demonstrate and understand these benefits. Traditional behavioural tests require long-term nutritional intervention and need large groups of respondents to obtain significant results. New imaging methods might speed up research on the effect of micronutrients and macronutrients on the brain.

In the pharmaceutical industry, brain imaging is already being used to develop drugs more quickly and with greater confidence of their effect. Imaging provides more sensitive measures of patient characteristics, more precise selection of the right dose of drugs, and better prediction of their effect. It also allows drug researchers to spend less time on animal models and more time studying the 'live' effect of experimental medicines on human brains [Matthews, 2007].
It is clear that the advantages of neuro-imaging are also relevant for the food

4 Not everyone agrees on what is optimal. For some nutrients that might be quite different from what is currently recommended.

5 Cross-modality means replacing different sensory stimuli like taste, odour, texture or colour with one another to achieve the same effect in liking.

industry. Box 1 looks at what neuro-imaging could mean to research on food and cognition.

**Box 1: Neuro-imaging and food research**

As is the case in several other scientific disciplines, incremental changes and new insights in food research have been boosted by technical advances that give scientists the chance to ask radically different questions. Neuro-imaging allows scientists to push the boundaries of our knowledge of how the brain develops and functions. Food scientists are actively exploring and exploiting neuro-imaging tools to advance their research. A few examples:

***Preference and liking***. This application involves investigating the processes that influence liking and preference for certain food products and types. Although it is still early days, using neuro-imaging tools (especially fMRI and PET) in combination with traditional tools, for example preference mapping, or more advanced tests such as implicit association tests (IAT) have given us a deeper insight into the pathways that control our behaviour. The food industry expects that a better understanding of the processes that drive our behaviour will allow us to develop more healthy food products that will be as attractive to us as products that exploit our programmed preferences for sweet, salty and fatty foods.

***Sensory perception and integration***. Linked to the above application but fundamentally different is the use of neuro-imaging tools to elucidate the neural encoding of our sensory perception system. For example, we do not have receptors for 'wet', but by combining the signals emitted by the temperature and touch or pressure receptors in our skin, our brain knows what 'wet' is. A major challenge for food scientists here is to understand how we sense 'fat content' or creaminess in food products. There are some suggestions that we might have specific receptors for this class of ingredients, and that we might be able to replace fat by another single compound. However, it is more likely that a good understanding of how our brain 'sees' fat will allow product developers to find suitable alternative mixes that exploit colour, flavour and taste to recreate that rich, creamy feeling of fat in the mouth, without the calories. Again, fMRI is playing a major role in helping scientists to understand the underlying processes.

***Brain development and performance***. With equipment becoming increasingly sensitive and access to it less restricted by the increasing number of research-only (not for clinical purpose) scanning equipment, it will be possible to gather vast amounts of data from large population groups, thereby improving our understanding of what 'normal' brain development and functioning looks like and giving us deeper insights into the links between deviations in structural brain development, exhibited behaviour and the role that environmental factors such as food can play across large populations. It is in this area in particular that a wide variety of tools and techniques are being deployed: structural MRI, functional MRI, and PET to visualise chemical

**processes; arterial spin labelling to visualise and quantify blood flow in the brain; EEG to measure the immediate electrical reactions occurring in the brain, etcetera.**

**Although we can envisage many additional applications, it is the integration of these new tools and existing expertise and insights that has already brought us many breakthroughs and will continue to do so in the future.**

*Paul van der Logt*[6]

Another reason for the growing interest in brain functions in relation to diet is that governments and non-governmental organisations are now asking the worldwide food industry to produce more healthy products. Of the 65 million people who die every year, 25 million die as a consequence of unhealthy diets, including undereating and overeating. Shareholders are also putting more pressure on the food industry, as they can earn more money from health products such as functional foods than they can from traditional products such as soft drinks or dairy. Campina, for example, earns only one cent per litre on standard milk or yoghurt, but has a profit margin of 30% to 40% on such products as Optimel Control [Balthesen, 2007].

In attempting to understand the relationship between brain function and diet, we face some major research challenges. The strategic research agenda of the collaborating European food industries summarises them as follows [ETP, 2007]:

- to chart the scope of diet and individual nutrients to influence brain health and performance. To interpret these results and maximize the impact, mapping will be required of the underlying mechanisms through which dietary components are capable of modulating brain development and cognitive performance (see section 2.2).
- to increase understanding of the neural pathways controlling functions such as food intake, hunger and satiety (see section 2.4 and 2.5).
- but also (not mentioned in the ETP report): to enhance our knowledge of multi-sensory information processing (i.e. how different sensory stimuli integrate in the brain to produce perception and liking), so that we can replace a particular sensory input (such as salt or fat) or intensify product appreciation (see section 2.3).

6 Principle Scientist, Unilever Foods and Health Research Institute.

**Example I**

# The brain's reward circuit tells who will overeat

**How somebody responds to a picture of a chocolate cake depends on how his or her brain is wired. The response of the food reward system in the brain to food cues differs widely between individuals. This may be the reason why some people are more prone to overeating than others.**

The taste, smell and appearance of a food product has a powerful influence on a person's decision to eat it, and on the quantity he or she will eat. If the food is highly appetising, these rewarding properties can override satiety signals in the body and promote overeating. However, sensitivity to such rewarding stimuli varies between individuals.

An extensive network of interconnected brain areas is involved in experiencing the reward effect of foods. Brain scans reveal that components of this network are activated in people who see images of appetising foods. And when the circuit is stimulated by pharmacological compounds in rats, the animals eat more than usual, and preferably fatty and sugary foods.

Not just the sensitivity to food traits is visible in this brain network, but also the variability in this sensitivity, British neuroscientists have shown. In people who are highly sensitive to the rewarding aspects of foods, the network is more active when they look at pictures of delicious foods than in people who are not as sensitive.

The scientists compared the effect of pictures of palatable foods, such as ice cream or chocolate cake, with that of bland foods, like rice or potatoes, and of non-food, such as a videocassette. They also included aversive food pictures, for example of rotten meat or mouldy bread. While lying in a functional magnetic resonance imaging (fMRI) brain scanner, participants had to indicate to which extent they found the pictures disgusting, pleasant, arousing, nauseating or appetising.

Before the scan session, participants had filled out a questionnaire that measured their reward sensitivity. In all five brain regions implicated in reward, appetising foods elicited more activity than bland foods in persons who scored high on reward sensitivity. A high score on another measure, fun seeking, did not correlate with activity in these regions.

Original publication: Beaver et al. (2006). *Journal of Neurosciences*, 26, 5160

Behavioural research has shown that people with high reward sensitivity have a larger body weight, more food cravings and a stronger tendency to overeating than people who are less sensitive to appetising food cues. This puts them at a higher risk of developing obesity, bulimia nervosa and binge-eating disorder.

The British study is one of the first to show that these behavioural findings can be related to properties of the brain. Knowing the neurobiological correlates of behaviour that can instigate the development of overeating disorders may help in finding ways to normalise these behaviours.

## 2.1.2 Social and economic relevance of research on the brain-food relationship

*Cor Wever*[7]*, Ira van Keulen*

There is enormous social relevance in answering the above research questions. Take, for example, children in the developing world who suffer from cognitive underdevelopment because they lack micronutrients such as iodine, vitamin A, iron, zinc and folate [UNICEF, 2007]. Or the growing population of elderly people, particularly in the Western world, who are suffering cognitive decline owing to diseases associated with old age. In 2004, for example, the prevalence of dementia in the Netherlands was 207,701, with the direct and indirect costs running to 3.1 billion euro [Andlin-Sobocki et al., 2005]. Nutrition might be able to slow down or even prevent the process of neurodegeneration. There is also the fact that nutrients have a positive — i.e. preventive — effect on other neurological and psychiatric disorders such as depression[8] or ADHD[9]. This means that changing food patterns can help lower health care budgets and improve the quality of life in the Western world. Another important factor is the obesity epidemic. It may be possible to combat obesity by considering new insights into the brain mechanisms behind satiety and addiction. This is important because the number of overweight people in the Western world is growing fast, even in the Netherlands with its bicycles and bike lanes. In 2005/2006, about half the Dutch adult population (18-70 years) was overweight, i.e. had a Body Mass Index (BMI)[10] above 25 [RIVM, 2008].

The economic relevance of the brain food market should also not be underestimated. Research shows that in 2007, 77% of the Dutch population was prepared to pay for functional food such as brain food, an increase of 41% compared with 2005 [Balthesen, 2007]. It is also economically important for the Dutch food industry and food science sector to retain their international position as front-runners. The agro-food sector in the Netherlands contributes 10% of the country's gross national product and accounts for 600,000 jobs.

Societal, scientific and economic progress can go hand in hand. Indeed, several advances in our knowledge of the brain could lead to beneficial new products for the food industry and help solve society's problems at the same time. Box 2 gives some examples, including corresponding research questions (some of which will be addressed in this chapter).

7 Policy Coordinator Food Quality, Ministry of Agriculture, Nature and Food Quality.

8 Prevalence of 715,038 and total costs of 4,255 million in the Netherlands in 2004. See www.fondspsychischegezondheid.nl.

9 At least three out of every hundred children in the Netherlands suffer from ADHD, one of them severely. This is 40,000 children between five and fourteen years of age. See www.fondspsychischegezondheid.nl.

10 BMI is a statistical measure of an individual's weight scaled according to their height. A low BMI (< 18,5) indicates underweight and a high BMI (> 25)overweight or obesity (> 30).

**Box 2: Socially and economically desirable neuroscience applications in the food sector**

***New healthy, sustainable and enjoyable food***

Many consumers want to buy healthy food and snacks, but they do not enjoy the taste [Data Monitor, 2007]. Food must be fun, but improving its health value by lowering the fat, salt or sugar content or adding bitter ingredients makes it less enjoyable. Consumers miss the fun of eating it. Another recent development is the demand for sustainable food, i.e. products that require less energy when grown or processed. Consumers and the food industry want to use meat-replacement products such as tofu and Valess or Quorn, but such novelties entail an extra need to predict whether consumers will like and buy them.

The food industry must respond swiftly to changes in consumer demand – and that demand will change more frequently and more rapidly in the future as consumers are increasingly exposed to tastes from other countries. Consumer trends also come and go at an ever-increasing pace. Nowadays, the food industry uses consumer panels to develop attractive food products because it lacks an objective method.

Research must answer the following questions:

– Can neuroscience use new imaging methods to contribute to our understanding of food perception?
– How can a better understanding of the sensory and physiological functionalities of ingredients and food structures allow the food industry to dramatically reduce product development cycles?
– Is it possible for the food industry to judge consumer appreciation of food better and quickly, e.g. by using brain imaging methods?

***Children's food choice***

Children use a lot of energy and need specific nutrients to support their rapid growth. It is important for young children to develop healthy food and eating habits, and such habits also prevent overweight. It seems that many children do not always have breakfast before they go to school; most children do not eat enough fruit and have other bad eating and drinking habits [Ocke et al., 2008; ZonMW, 2007]. The Netherlands is trying to tackle the problem with popular school programmes (School Breakfast, School Fruit, Taste Lessons, etc.). Our knowledge of the effect of eating behaviour on cognitive performance has increased, but we still do not understand how to motivate children to improve their eating patterns and how this can help children control their weight and improve their educational performance.

Research must answer the following questions:

– Which food products and eating patterns support children's weight control and cognitive performance? And how can we alter the often negative perception of healthy food?

- How can we motivate children to eat more healthy foods such as fruit, vegetables and fish?
- Are there food products and eating patterns that physicians or clinics should recommend to children with abnormal cognitive development?
- Do specific foods promote the development of certain brain functions in specific critical periods? For example, are the nutrients necessary for language development (early in life) different than those for executive functioning (later in life and through adulthood).

***The obese consumer***

We live in an obese society. Food intake is driven not by our need for energy, but by abundance and the desire for food [Dagevos and Munnichs, 2007]. Hedonic and cognitive motives drive the quantity that we eat. These factors are leading to problems such as obesity and eating disorders. Unhealthy diets cause a considerable decline in health. In general, we eat too much and our diets are not balanced [Van Kreijl and Knaap, 2004].

We do not fully understand why consumers choose the foods they do and how they perceive them. The brain has one brain circuit for liking and another for wanting the same sweet reward [Finlayson, 2007]. Liking and wanting therefore do not always go hand-in-hand. For example, it is easier to activate desire than pleasure. A better understanding of these neural functions can help us develop interventions and food to control weight and eating disorders.

Research must answer the following questions:

- How will knowledge of the neural pathways involved in liking and wanting food stimuli help us understand how to control food intake?
- How can this knowledge prevent overweight and other eating disorders? And how can it contribute to the development of healthy food and eating habits?

*Cor Wever*[11]

### 2.1.3 The effect of food on the brain and cognition

Nutrition can affect the brain and cognition in many different ways. First of all, it can stimulate the cognitive development of foetuses, neonates, infants and young children. There are already products being sold in the Western world (Blue Band Idee! and Amaze Brainfood, both by Unilever) that contain nutrients said to support children's brain development and brain function. In the developing world, 32% of lives are at risk from iodine deficiency, resulting in *"insufficient thyroid hormone production, which can prevent normal growth in the brain and nervous system and lead to poor school performance, reduced*

11 Policy Coordinator Food Quality, Ministry of Agriculture, Nature and Food Quality.

*intellectual ability and impaired work capacity."* [UNICEF, 2006]. Secondly, nutrition may prevent or slow down cognitive decline in the elderly. For example, folic acid (supplementation) seems to dampen the normal decline of cognitive functions that comes with age (see example IV on folid acid). A product that makes similar claims is a beverage that Numico will release in 2008 which inhibits mild forms of Alzheimer's.[12] The product will only be available through medical channels such as pharmacies and hospitals, touching on the question of whether it should be classified as a food or a drug. Thirdly, nutrition can improve mood and mental performance, including stress, attention, or sleep. There are already many — mostly dubious — products on the market in this area, for example milk that makes you sleepy, beverages that improve your alertness or attention, etcetera. Fourthly, nutrients have a positive impact on mental illness or aggressive behaviour, and may perhaps even be used to prevent such disorders in the future. Research has been carried out on the effect of diet on depression, schizophrenia and ADHD. There is also some evidence that poor diet causes antisocial or aggressive behaviour, based on research with prisoners receiving modified diets with nutritional supplements [Gesch et al., 2002]. Another similar experiment was conducted in the Netherlands recently, in cooperation with the Dutch Ministry of Justice.[13] The results were moderately positive — prisoners showed less aggressive behaviour — but too inconclusive for actual interventions as yet. In summary, nutrition can have varying effects on different groups at different times (see also box 3 on arsenic poisoning and neural defects). Overeating also appears to affect cognition; obesity can lead to cognitive decline and some research indicates a relationship between obesity and Alzheimer's.

**Box 3: Arsenic poisoning and neural defects**

An estimated 200 million people in Asia are currently threatened by what the World Health Organization (WHO) calls *"the greatest mass-poisoning in history"*. Arsenic, a metal that occurs naturally in sediment around the world, dissolves into the groundwater in large quantities. Unfiltered groundwater has been used as drinking water from the 1970s on, especially in rural areas in Bangladesh and India. Arsenic is not harmful in small amounts, but in large quantities – such as in the groundwater supply in these countries – it is highly poisonous. Ingestion of contaminated drinking water is the most common source of arsenic poisoning, although contaminated food grown on arsenic-rich soil or irrigated with contaminated water is another pressing problem [Duxburry and Panaullah, 2007].
Although long overlooked, the effect of arsenic poisoning on the developing brain is very serious. Poisoning can result in mental retardation, neural tube defects, exencephaly and even foetal death [Dakeishi et al., 2006; Ehrenstein et al., 2007; Grandjean and Murata, 2007]. Arsenic can cross the placenta barrier and affect the

**12** See newspaper article in Dagblad van het Noorden: 'Numico: drankje tegen dementie; Product in 2008 op de markt', 4 August 2006.

**13** See press release on www.minjus.nl/actueel/persberichten, 2 November 2007.

foetus during pregnancy. It is not present in breast milk, however. In adults, arsenic poisoning can lead to memory loss, learning and concentration disabilities and peripheral nerve damage.

While the solution lies in filtering groundwater and thereby preventing arsenic poisoning in the first place, this would be difficult to do in many rural communities for social, cultural and economic reasons. One way to mitigate the problem of arsenic poisoning is through nutrition. A sufficient intake of vitamins A, C, and E and protein-rich food can decrease the adverse effects [Smith and Lingas et al., 2000]. Heavy metals such as arsenic are bound in cells and have to bind to other metal-binding molecules to be excreted from the body. The right diet would have to include a combination of supplements: chelating agents, anti-oxidants and possibly other micronutrients.

What researchers must do is find out which combination of nutrients can mitigate the adverse affects of arsenic poisoning best, and in what quantity, depending on the level of poisoning. Adequate nutrition might even prevent neural damage during foetal development.

More research is needed into the adverse effects of arsenic poisoning on neural development and how these clinical symptoms occur. An animal model could help explain the relationship between the level of arsenic poisoning and the risk of mental retardation and other neural and/or cognitive defects. On another level, researchers could use cell cultures or brain slices to study the effects of arsenic poisoning on neurons (see, for example Chattopadhyay and Bhaumik et al., [2002]). It has been shown that sub-clinical arsenic poisoning can lead to cell apoptosis and necrosis and deficiencies in neuronal growth. Longitudinal studies involving both laboratory animals and human populations may help us understand the best time for nutritional interventions and the most appropriate means (perhaps in combination with other strategies). Windows of opportunity may occur during pregnancy, after breastfeeding and in early childhood.

*Joske Bunders*[14], *Reinout van Koten*[15]

Although we know that there is, at times, a positive or negative relationship between the intake of food and our behaviour, we do not always know exactly what happens on the various physiological — molecular, neural network — levels between the moment we eat something and the moment it affects our behaviour. In many cases, we do not even know the relative contribution of psychological and neurophysiological factors to behaviour. There are also many individual components or ingredients whose precise effect on cognitive development and performance is unknown. Advances in the neurosciences can help us understand this process. *"In twenty years, we hope to be able to deploy nutrition with demonstrated efficiency. The development of such techniques as fMRI, EEG, MEG and PET will help us to understand the link between*

14 Director of the Athena Institute for Research on Communication and Innovation in Health and Life Sciences, VU University.

15 Researcher Science Communication, VU University.

*food and behaviour. In the future, tests will demonstrate the precise effect of food on behaviour."* (quote Van der Logt, Unilever).

Just how great an impact can nutrition have on brain development and performance? We can find an example in the way changing eating habits have led to a decline in mortality through heart failure in recent decades. Perhaps nutrition can have a similar positive influence on the brain and cognition, but compared with pharmaceutical interventions, the effect of nutrition is generally limited, especially in the Western world. It may depend in particular on the dietary baseline, i.e. the quality of the existing diet. Two examples are illustrative. First, a meta-analysis of eighteen studies [Bleichrodt and Born, 1994] indicated a general loss of 13.5 IQ points in chronically iodine-deficient populations compared with non-iodine-deficient groups. Secondly, several studies have shown a positive relationship between excessive eating behaviour and the early onset of dementia.

The question is: is it possible for nutrition to make a cognitive difference on top of the dietary baseline, or even on top of an optimal diet? Food can be expected to have the biggest impact on the brain or behaviour when the subject is sensitive to certain micronutrient deficiencies. Even in the Western world, diets may be deficient in iron or iodine, although not on the same scale as in developing countries. The excessive intake of food common in the Western world can also cause certain deficiencies.

Experts do not agree on how the body and brain work in this respect. The most popular explanation is indeed that physical and cognitive development is influenced at its most fundamental level by diet. The body and the brain are sensitive to certain deficiencies and an altered diet may influence their development. Another explanation, however, is that the body takes only what it needs, and that an overabundance of nutrients will not make a difference on top of a dietary baseline.

So what exactly is a deficiency or when is a diet considered deficient? The problem here is that the definition of deficiency varies enormously, depending on the nutrient concerned. For example, a recent study shows that if all the different areas of the brain need to be saturated with DHA — a fatty acid — then baby food should be much more enriched than is currently considered acceptable [Kuipers et al., 2007; Levant et al., 2006]. There are also many contradictory studies on food deficiencies in relation to cognitive abilities.

In summary, there is still a lot we do not know. So far, three things are clear: there are indications that diet can have a positive and negative effect on our mental health and cognitive performance; the best path to optimal cognitive development and performance is a balanced diet; and actual cognitive enhancement through nutrition is likely to be impossible, if only because it is hard to make a clear distinction between fulfilling one's cognitive potential and actual enhancement.

### 2.1.4 Brain mechanisms behind eating behaviour

The link between food and the brain is not only about the effect of nutrition on behaviour, brain development and performance. It is also about the mechanisms of the brain behind eating behaviour, for example satiety, hunger, addiction or buying patterns. Eating behaviour is a complicated system involving many different parts of the brain, for example the craving and reward systems, and it is difficult to influence. *"The system involved in satiety is staggeringly complicated and encrypted. Evolution has safeguarded us well against feeling hungry. The signal to start and stop eating or eating frequency involve several different brain substances and neural networks. Mechanisms like grazing, binge eating, etcetera also differ per person."* (quote Kroeze, Wageningen University and Research Center).

Our eating behaviour is also deeply rooted in our early food experiences, i.e. brain conditioning. Our early exposure to dietary components is crucial to our taste perception and food preferences later in life. There is still a lot we do not know about how we acquire food preferences. For example: the perception of a bad smell is located at a different area in the brain than a good one [Rolls et al., 2003]. Are bad odours located in those specific areas because they smell bad, or because that particular odour is located there? To what extent is the food conditioning system stabile? Is it easy to influence? What precisely happens in the brain when food habits are changed? These are all questions exploring unknown territory, the neural plasticity behind food intake and regulation.

Research on perception plays an important role in the study of the brain mechanisms behind eating behaviour since it focuses on multi-sensory information processing: how do different sensory stimuli such as taste, smell, texture, etcetera come together in the brain to produce perception, liking and (eventually) consumer behaviour? How do all these sensory signals influence one another and how do they influence perception? Can different sensory stimuli replace one another to achieve the same effect in liking (i.e. cross-modality)? These are socially relevant questions if the aim is to encourage healthy and ethically acceptable food choices. A better understanding of perception and liking could also result in new guidelines for product development to replace the current method of trial and error.

Nevertheless, we will have to overcome some major challenges before we can answer these questions, including being able to measure behaviour and perception objectively and link sensory input and perception to behaviour. *"We hope to be able to measure a consumer's perception objectively in future by means of neuroscientific methods. This is important because by asking consumers something, you are already influencing them. We not only want to influence their choices, we want to figure out what they want without influencing them."* (quote Van der Logt, Unilever Vlaardingen; see also example III on neuromarketing).

### 2.1.5 How to read this chapter

*Ira van Keulen, Erik van de Linde*[16]

This chapter explores four views of how the field of food and cognition will develop in future. These are views that propose over the next fifteen years a growing cooperation between the neurosciences and cognitive sciences on the one hand and food science, policy and practice on the other.
View 1: The right nutrition at the right time for optimal brain development (see section 2.2).
View 2: Influencing food perception and liking (see section 2.3).
View 3: Conditioning food preferences (see subsection 2.3.4).
View 4: Influencing the mechanisms of food intake (see sections 2.4 and 2.5).
By choosing to elaborate these four views of the future, we were unable to address other interesting areas, for example psychological disorders such as bulimia or anorexia nervosa or personalised food.[17]

Figure 1 shows the chapter in a nutshell. On the one hand, we have the positive and negative effect of our nutritional pattern on neural and cognitive processes; on the other hand, we have the effect of the interaction between the brain, sensoring and metabolic processes on food intake.

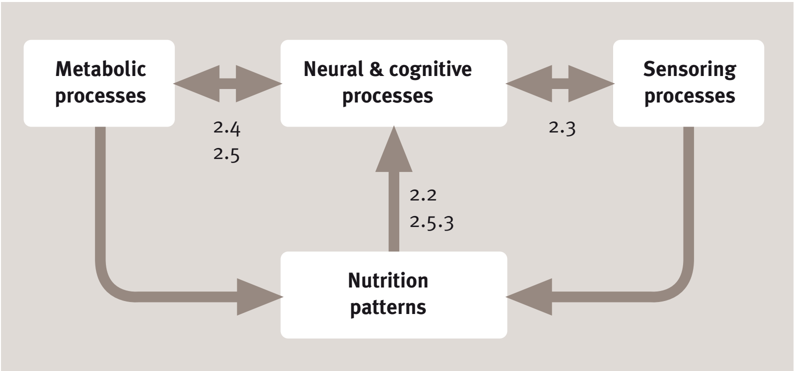



**Figure 1**
*Chapter 2 in a nutshell.*

**16** Director, Erik van de Linde Innovation Management Consultancy.

**17** Personalised food is an interesting idea in the field of nutricognition, however, especially since pharmacological research shows that individual brains differ dramatically (e.g. in the permeability of the blood-brain barrier). The range of optimal doses of pharmaceuticals is broad, and that probably also applies to nutrients.

## 2.2 The right nutrition at the right time for optimal brain development

It is important to begin this section by reminding ourselves that many different environmental factors play a key role in how our brain and cognitive abilities develop, function and are maintained. In addition to genetic predisposition, external stimulation and a healthy lifestyle, nutrition is one of these factors.

### 2.2.1 Introduction

*Paul van der Logt*[18]

Our knowledge of how diet and specific nutrients influence our brain's development and functioning is still limited but has increased significantly in the past few years, with evidence being produced for the role of some ingredients and plausible associations for others. Although the evidence for diet-brain interactions obtained in direct intervention studies and mechanistic work is growing, much of the data still comes from epidemiological and cross-sectional studies. It is therefore a field replete with unanswered questions and potential research queries. A few points should be considered at the outset.

As with many other developmental processes and diseases, we first became aware of the specific role of nutritional factors when epidemiological studies suggested correlations between certain dietary deficiencies and impairments in the mental development or functioning of the brain. Since correlations do not automatically imply causality, and because we do not understand the underlying mechanisms, we need to be careful when drawing conclusions about the function of specific dietary ingredients. We also have to be careful not to assume that, because the absence of some essential building blocks or components have a negative effect, providing extra doses via diet will have a potentially positive effect ('boost above baseline'). On the contrary, overdosing with individual nutrients may have either no effect whatsoever or even a negative effect (as suggested for some minerals and even DHA).

In addition, the positive effects of adding specific micronutrients or macronutrients to a sick person's diet cannot automatically be extrapolated to the healthy population. For example, the positive effects of fish oils on cognitive development are seen almost exclusively in diseased populations (children with ADHD and elderly people with mild cognitive decline), with only limited data supporting an effect on cognitive abilities in healthy target groups.[19] Another aspect to consider — one that we will look at in detail later in this chapter — is whether there are critical periods in the development of the brain

18 Principle Scientist, Unilever Foods and Health Research Institute.

19 However, there is still some discussion of what constitutes a 'healthy population'. Our diet changed for the worse in the Industrial Revolution, with more sugar, more fat and a unhealthier fatty acid pattern. Some say that this implies that the current population is not as healthy as it could be.

when the impact of deficiencies or supplementation will be greater than at other times.

Recent evidence has also emerged concerning the role genetics may play in our ability to use certain nutrients in the diet more effectively. Particularly notable are studies [Caspi, 2007] linking the presence of various alleles of the FADS2 gene — which encodes for delta-6 desaturase — and the IQ scores of breastfed children, especially as this gene is thought to be associated with the desaturation of omega-3 and omega-6 fatty acids and may therefore contribute to brain development and function. It may also explain the need for preformed long-chain polyunsaturated fatty acids in our diets, and in the diets of infants in particular.

Finally, we also have to consider the 'magic bullets', ingredients (mainly phytochemicals[20]) said to have a boosting effect ('above baseline') but whose underlying mechanism is not known. Some examples are gingko biloba, curcumin and many other herbal substances. Although there is some observational data to support the claim that these ingredients have a boosting effect, much more work is needed to elucidate the underlying molecular mechanisms.

So where does this leave us? With all these ifs, ands and buts, can we still claim that diet and nutrition affect brain development and cognitive abilities? So far, the balance of evidence looks to be favourable, but the scientific community will need to answer a number of questions before it can provide conclusive proof and recommendations for optimal nutrition to support brain development. The most important questions will be considered — but *not* answered — in this section 2.2:

– What role do individual dietary ingredients play in the key molecular processes involved in the development and functioning of the brain (see subsections 2.2.2 and 2.2.5)?
– What is the relationship between molecular processes and cognitive abilities (see subsection 2.2.3)?
– What role do the indirect effects of diet or nutrition play on brain development and cognitive performance (see subsection 2.2.4)?
  – gut health
  – cardio vascular health
  – cognitive activity ('brain training')
  – recovery and sleep.
– How do we ensure that the functional components are delivered to the target site (see subsection 2.2.7)?
– Brain development is non-linear: what are the 'windows of opportunity' (see subsection 2.2.6)?

**20** Non-nutritive plant chemicals that have protective or disease preventive properties.

### 2.2.2 Nutrients that may play a role in brain development and cognitive functioning

Many micronutrients and macronutrients have been implicated as playing a key role in the process of brain development and cognitive functioning (see Table 1).

**Micronutrients:** It has been suggested that an inadequate intake of vitamin A may lead to iron deficiency aneamia. Improving vitamin A intake will thus have a positive effect on the level of iron, thereby supporting the beneficial effects of iron on mental health [Roodenburg et al., 1994]. Animal studies have suggested a link between vitamin B2 deficiency and neurodegeneration, for example because it functions as the precursor of the FAD enzyme that plays a role in the energy production. In addition, there are signs that it is involved in the take-up and metabolic use of other micronutrients such as iron, folic acid and vitamins B6 and B12 [Powers, 2003]. Supplementing the diets of elderly people and Alzheimer's patients with vitamin B6 has also been reported to have beneficial effects. The underlying mechanism is thought to involve various reactions, including neurotransmitter synthesis and homocysteine metabolism [Calvaresi and Bryan et al., 2001]. The exact mode of action for folic acid is also not known, but there is convincing evidence that it is involved in the development of the neural tube. Other studies involving elderly have confirmed an association between folic acid supplementation and cognitive performance [Durga et al., 2007]. A lack of vitamin B12 has been shown to cause demyelination of neural axons, with implications for the cognitive development of children [Roodenburg et al., 1994]. Vitamin C has been reported to act as a cofactor in the biosynthesis of neurotransmitters, but the main effect of vitamin C on cognitive development is probably its ability to enhance iron absorption by converting ferric iron into ferrous iron and chelating it in the gut [Lynch and Stoltzfus, 2003]. Iodine has the clearest relationship with mental development and performance. It is required for the production of several thyroid hormones that are also essential for brain growth and development. This makes iodine deficiency the commonest cause of preventable mental retardation in the world [Briel et al., 2000]. It has been demonstrated that iron deficiency has a negative effect on the structure and function of the central nervous system, perhaps owing to the role iron plays in myelin formation (as a co-factor for lipid biosynthesis), reduced oxygen availability and changes in neurotransmitter levels [Haas and Brownlie, 2001]. Zinc has also been implicated as a key micronutrient with respect to attention, activity and neuropsychological behaviour. The literature is divided as to the role of zinc, with there being some disagreement about what constitutes reliable indicators for assessing zinc status, as well as a lack of mechanistic insight [Black, 2003].

**Table 1**
*Nutrients that may play a role in brain development and cognitive functioning. Source: [Kiefer, 2007].*

| Nutrient | Function | Present in foods |
|---|---|---|
| Carbohydrates | Supply glucose for energy | Whole grains, fruits (especially apples), vegetables |
| Liquids | Stabilise circulation and nutrient transport, among other functions | Water, mineral water, unsweetened herbal and fruit teas |
| Caffeine, in small amounts | Dilates the blood vessels in the brain; increases concentration and memory | Coffee, black tea, green tea |
| Iron | Transports oxygen | Red meats, pumpkin seeds, sesame, soy flour, millet, poppy seeds, pine nuts, wheat germ, oats, dill, parsley, yeast, spinach, watercress, lentils, soybeans, white beans |
| Calcium | Conducts neuronal signals | Milk and milk products, poppy seeds, figs, sesame, soybeans, legumes, nuts, whole grains, wheat germ, oatmeal, broccoli, watercress, green vegetables, parsley |
| Zinc | Aids many chemical reactions in the brain; important for concentration and memory | Wheat germ, poppy seeds, sesame, pumpkin seeds, meat, eggs, milk, cheese, fish, carrots, whole-grain bread, potatoes |
| Phenylalanine, tyrosine | Act as precursors of epinephrine, norepinephrine and dopamine; important for alertness and concentration | Fish (tuna, trout), meat, milk products, soybeans, cheese (cottage cheese), peanuts, wheat germ, almonds |
| Serine, methionine | Act as precursors of acetylcholine; essential for learning and memory formation | Fish, turkey, chicken, soybeans, beef, cashews, wheat germ, broccoli, peas, spinach, whole-grain bread, rice |
| Vitamin B1 (thiamine) | Enables glucose metabolism; aids nerve cell function | Whole grains (wheat, spelt), oatmeal, wheat germ, sunflower seeds, legumes, nuts, pork |
| Unsaturated fatty acids, including omega-3 fatty acids | Build cell membranes | Fish, walnuts, spinach, corn oil, peanut oil, soybean oil, grape seed oil |

**Macronutrients:** Protein is an essential part of our diet and functions both as a source of energy and of amino acids. There are indications that low levels of protein in the diet or poor sources of protein (lacking or very low in amino acid

**Example II**

# Genes determine if breast milk boosts baby's IQ

**The intelligence quotient (IQ) of children who have been breast-fed for several months after birth is higher than that of children who did not have breast milk. However, that is only the case for children who have a specific gene involved in fat metabolism. One out of every eleven children does not have this gene, and does not profit from the beneficial effects of breast milk on IQ.**

Various studies have shown that the difference in IQ between children fed breast milk and those fed infant formula is between three to six points. This difference remains measurable into adulthood, and is independent of social class and related factors. It is one of the reasons health professionals recommend breast-feeding.

The beneficial effect of breast milk on the brain is most likely due to the special fatty acids it contains: long-chain polyunsaturated fatty acids, such as docosahexaenoic acid (DHA) and arachidonic acid (AA). Cow's milk, the basis for infant formula, contains scarcely any of these fatty acids. Nowadays many infant formulas are supplemented with long-chain polyunsaturated fatty acids.

During the first months after birth these special fatty acids accumulate in the baby's brain, and the brains of breast-fed babies contain higher concentrations of them. Animal studies have revealed that long-chain polyunsaturated fatty acids in the diet improve learning and memory processes.

However, not everybody enjoys the good effect of breast milk on IQ, British brain researchers discovered. Only children who were born with a specific variant of the gene *fatty acid desaturase 2* (FADS2) benefit. This gene plays a role in processing DHA and AA in the body.

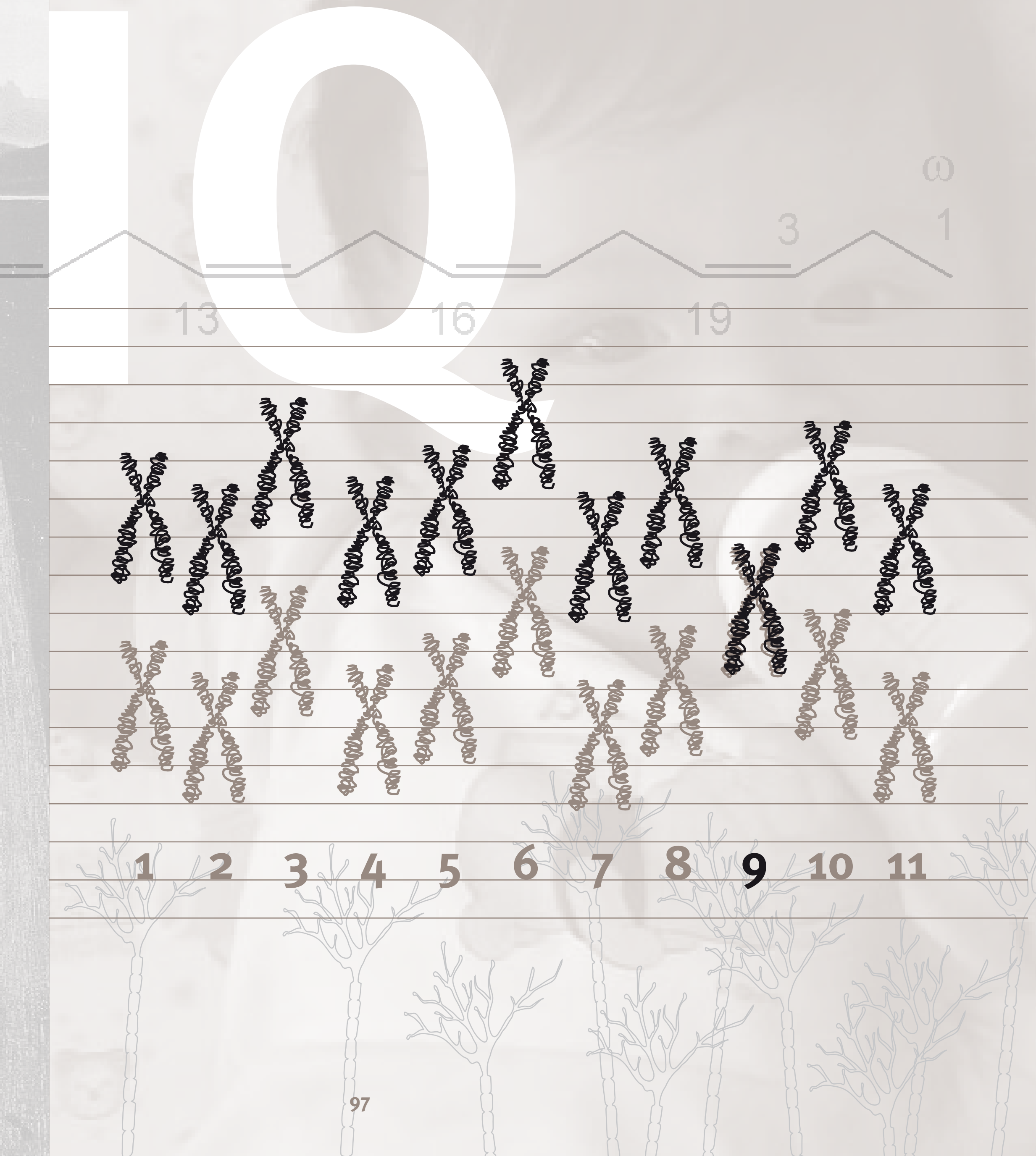
The scientists looked at two variants of the gene: an abundant form and a less abundant form. They screened thousands of children whose IQ had been tested between age four and seven.

Among children with the abundant form of FADS2, the IQ of breast-fed kids was above average, and around seven points higher than that of non-breast-fed children, which was below the average IQ of 100. The type of milk did not affect the IQ score of children with the less-abundant form of the gene. They all had an IQ of around 100. These findings were independent of social class, IQ or FADS2 variant of the mother, and variations in growth.

Original publication: Caspi et al (2007)., *Proc. of the National Acad. of Sciences*, 104, 18860

Even small increments in IQ can have a large impact on the quality of life, studies show. The higher a person's IQ, the greater his or her chance of finishing school, finding a job, and avoiding poverty or crime.

The study shows that food components can affect brain development and function, and that genes can modulate this relationship. Our growing understanding of how genes determine the way individuals benefit from certain nutrients sets the stage for the development of personalised diets or food products.



subgroups) can lead to poor mental development, school performance and behavioural problems [Wachs, 1995]. Carbohydrates are the most important source of energy for the body, with glucose being the brain's only source of fuel (it cannot use fat and/or protein, although some exceptions have been reported, for example ketone bodies (acetoacetate, beta-hydroxybutyrate and acetone)). On the other hand, a high intake of carbohydrates stimulates the synthesis of saturated fatty acids (SAFA) that, when desaturated to oleic acid, can result in a relative deficiency of essential fatty acids and their derivatives [Muskiet, 2006]. Fats are not only a source of energy, but are also required as building blocks for normal growth and development, as they play an important role in the structure and function of cell membranes. Essential fatty acids (those that can not be synthesised by the body and must be supplied by the diet) include members of the omega 3 and 6 family. We look more closely at the specific role these fatty acids play and the evidence and questions associated with this group of nutrients in subsection 2.2.5.

### 2.2.3 The molecular processes in brain development and cognitive performance

The core processes of brain development and cognitive performance — neurogenesis, proliferation, myelination, synapse formation, cell-cell signalling and signal transduction — are covered in detail in numerous papers and textbooks [Siegel et al,. 2005], and there is little point in reviewing them here. Despite the many publications and descriptions, however, we lack evidence linking dietary components on the one hand and the markers of brain development or cognitive performance on the other. In addition, a number of theories concerning key molecular processes in brain development and brain functioning are currently being challenged in the international scientific literature. One example is the work being carried out to unravel the mechanisms regulating the supply, storage and use of energy in the brain. Whereas for a long time it was thought that glucose was the only energy source of the brain and neuronal cells, it is becoming clear that ketone bodies can be used as an energy source, especially during fasts. Further interesting work focuses on the astrocyte-neuron lactate 'shuttle'. The hypothesis is that astrocytes use glucose to produce lactate, which is then transferred to the neurons. The neurons in turn oxidise the lactate to yield adenosine triphosphate (ATP): the molecular currency of intracellular energy transfer [Bonvento et al., 2005].

It was also previously thought that the process of neurogenesis only takes place during the very early phases in life. In recent years, researchers have demonstrated that neurogenesis takes place throughout life, albeit at a lower level. It is in this area in particular that research will not only shed light on the basic principles of adult plasticity, but may also lead to therapeutic strategies for dealing with injuries or combating degenerative neurological diseases [Ming and Song, 2005]. Such research will hence provide us with the kind of breakthroughs we need to combat the growing problem of neurodegenerative conditions in modern society.

### 2.2.4 The indirect effects of nutrition on brain development and cognitive performance

In addition to the developmental and functional impacts of diet and nutrition listed above, we must also consider a couple of other key nutrition-related factors that have a direct or indirect effect on cognitive development and performance. The first of these is the gut. It is not only important that ingredients are released from the food matrix (see subsection 2.2.7); we must also ensure that the gut is healthy and can absorb essential nutrients from the food ingested. Although this is especially relevant in developing countries with a high incidence of gut and intestinal disorders, the problem should not be underestimated even in the developed world. Here, a gut and intestinal dysfunction can lead to poor absorption of essential nutrients and thus result in nutritional deficiencies.

Next, more and more evidence is emerging demonstrating the link between a healthy cardiovascular system and cognitive performance (especially later in life). Since lifestyle (including nutrition) is one of the ways to control the key risk factors for cardiovascular diseases (such as blood pressure and LDL cholesterol), a healthy cardiovascular system also plays a role in ensuring optimal brain function via nutrition.

The last two indirect routes by which diet influences brain development and brain function are related to stimulation and recovery. Here, we can draw a comparison with athletes, whose diet in itself do not result in better performance but rather help them to work harder and longer, thus enabling them to achieve better results in the end. Dietary components that support an active and vital lifestyle and concentration will therefore have a major impact on brain development and cognitive abilities, irrespective of their site of action. The last indirect route, recovery (sleep), influences our ability to concentrate and thus ‘exercise’ our brain.

The relative intensity of the direct and indirect effects of nutrition is a topic of great debate. It has been suggested that the direct effects (building blocks, etc.) are a prerequisite for ‘normal’ development, but that the indirect effects listed in this section are the real differentiating factors that boost development and performance to ‘above baseline’.

### 2.2.5 The case of fatty acids

*Renate de Groot*[21]

Essential fatty acids and their longer-chain polyunsaturated derivatives, the LCPUFAs (long-chain polyunsaturated fatty acids) such as docosahexaenoic acid (DHA) and arachidonic acid (AA), are important structural components of all cell membranes, especially in the central nervous system. A change in the organisation of the essential fatty acids and/or the LCPUFAs in the synaptic membranes can influence brain functioning by altering the neuronal membrane receptors, ion transport and enzymatic processes. In addition it can affect the transmission of intracellular and intercellular signals generated by second messengers derived from precursors of these fatty acids. Optimising the fatty acid status may have beneficial effects for brain functioning; it may optimise normal brain functioning, but also may help to prevent illnesses such as depression, ADHD, Alzheimer's disease and schizophrenia. Whether this is true and in what period of life our brains are most sensitive to fatty acids remains to be seen. We describe the possible role of fatty acids in several critical periods of life below.


**Figure 2**
*Optimising the fatty acid status may have beneficial effects for brain functioning; it may optimise normal brain functioning, but may also help to prevent illnesses such as depression, ADHD, Alzheimer's disease and schizophrenia. Photo of extractions of fatty acids, courtesy of Melanie Bateman, www.flickr.com.*

#### Role of fatty acids in prenatal life

The biochemical essential fatty acid (EFA) status and long-chain polyene (LCP) status of pregnant women is known to decrease during pregnancy [Al et al., 1995]. Since the developing foetus depends on its mother for LCP accretion, the neonatal LCP status may not be optimal under present dietary conditions. Infants born preterm often experience neuro-developmental problems.

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Although a causal relationship with their low LCP status at birth has not been ascertained, it has been suggested by the results of postnatal intervention studies, which generally demonstrate that early LCP supplementation results, at least temporarily, in improved neuro-mental development. LCP supplementation has also been shown to improve neural development in term neonates (which have a higher LCP status than preterm infants), although the results are less convincing than for preterm infants.

The central nervous system experiences a growth spurt in the final trimester of foetal development. Adequate prenatal LCP availability may therefore be of key importance for optimal brain development and function. This view is supported by several scientific findings demonstrating that certain measures of brain maturation during childhood are positively related to the neonatal DHA status at birth.

### Role of fatty acids during pregnancy

Increasing evidence suggests a positive association between DHA and cognitive performance. Research [De Groot et al., 2003] shows that pregnancy, which is marked by a decreased LCPUFA status, is characterised by changes in different cognitive functions. This evidence indicates that an optimal fatty acid status may positively affect cognitive functioning. However, in another study the same researchers showed that at week fourteen of pregnancy and 32 weeks after delivery, higher plasma DHA levels were associated with lower cognitive performance (indicated by longer reaction times in a test measuring selective attention). This indicates that increasing plasma DHA concentrations may decrease attention during early pregnancy or the post-pregnancy period. The question is whether this is a pregnancy-related finding or a more general phenomenon. This rather unexpected result should give rise to further investigations.

### Role of fatty acids in childhood

Research into the role of fatty acids in childhood has been limited to clinical populations, such as children with ADHD and autism. Researchers have been investigating the relationship between ADHD and fatty acid status since the 1980s [Colquhoun and Bunday, 1981]. Many children with ADHD do have lower AA, EPA, and DHA concentrations. In addition, it has been shown that children with a low n-3 fatty acid status have more behavioural, learning and health problems. Supplementation studies have shown only very minor or disappointing effects. All we can say at this point is that the only potentially effective fatty acid supplement for children in a clinical population is a combination of more PUFAs. Larger placebo-controlled studies, however, are required before clear conclusions can be drawn. In addition, research is required to determine the role of PUFAs in the cognitive development of normal healthy children and adolescents.

### Role of fatty acids in adulthood

Very little is known about fatty acid status and cognitive performance in healthy adults aged 20-40 years. Until now, research has focused on babies, adults with illnesses or elderly people. It has been shown that a lower LCPUFA status in adults is associated with depression, post-partum depression and schizophrenia, but there have been almost no studies of healthy adults in this age category. One study [De Groot et al., 2007] looked at the association between plasma phospholipid fatty acid status and objective cognitive performance in healthy women aged 29 on average. The women were administered a test measuring speed of information processing over a 22-week period. It was shown that the fatty acids AA, AdrA, ObA, EPA, DPA, and DHA contributed significantly (26.3%) to the learning effect variance attributed to parity and educational level. In keeping with previous findings in pregnant women [De Groot et al., 2004], these results once again demonstrated that higher DHA concentrations are associated with lower cognitive performance, although a different aspect of cognitive functioning was involved. The unexpected results of these studies demonstrate the need for more research into the role of fatty acids in cognitive functioning during adulthood.

### Role of fatty acids in normal aging

The role of fatty acid status in normal aging is particularly interesting from a primary prevention perspective, although investigations thus far have not been systematic and the results obtained are inconclusive. Unfortunately, all such studies suffer from limitations. They often assessed the fatty acid status on the basis of dietary intake data, which provides only a rough estimate of the actual fatty acid status in the human body. In addition, dietary data collected from subjects who are cognitively impaired may be less reliable, and their food intake may have also changed as a result of their disease. Most of the data suggest a positive association between fish consumption — the primary source of DHA and EPA — and cognitive performance [Van Gelder, 2007], whereas some of the few studies measuring fatty acid in the blood indicate a negative association. The results for a normal aging population are therefore still far from conclusive, and some negative associations have even been reported. Further research into the role of fatty acids during normal adult life is certainly necessary.

### Role of fatty acids in pathological aging

Pathological aging is often characterised by a decline in cognitive functioning. Consumption of fatty fish is known to be inversely related to incident dementia, particularly Alzheimer's disease [Kalmijn, 1997], something that has also been shown for cognitive functioning in a middle-aged population. Patients with Alzheimer's, other dementias, and cognitive impairments (but not dementia) have been shown to have lower plasma phospholipid DHA status than a matched healthy control group. An intervention study has shown improved short-term memory in patients with Alzheimer's who received LA and ALA supplements. This finding suggests that fatty acid status may mitigate the progression of pathological aging and raises the question as to which fatty acids may have a positive (reversing) influence on the cognitive decline of Alzheimer's.

### 2.2.6 Windows of opportunity

*Anne Schaafsma*[22]

Literature indicates that brain growth and brain development take place in standard windows of time. For instance, a study of fifteen post-mortem human brains showed a sharp increase in synapse densities from the prenatal period (week 26), reaching a peak at about seven months for the visual cortex, three and a half years for the auditory cortex and somewhere around seven years for the prefrontal cortex [Huttenlocher and Dabholkar, 1997]. Brain developmental processes are closely related and the combined results determine brain function. Some animal studies even suggest that these windows are *critical* [McNamara and Carlson, 2006], an irreversible process often affecting other windows. Other neuroscientific researchers rather speak of *sensitive* windows [OECD, 2007]. There is still an ongoing discussion on the irreversibility of such windows of opportunity.

The World Health Organisation (WHO) stated back in 1993 that poor preconception nutrition or metabolic status represents a significant risk that may compromise embryonic development, cell commitment and the rate of DNA replication in a manner that cannot be compensated later [FAO, 1994]. Another interesting example of a 'window of opportunity' is pregnancy itself. A follow-up study on maternal fatty acid patterns during normal pregnancy suggests that higher docosahexaenoic acid (DHA) — and not arachidonic acid — status at birth results in lower levels of internalising problem behaviour at the age of seven. Control of childhood behaviour is important, as it decreases the risk for a range of adult psychiatric outcomes. According to the 'early programming' hypothesis (possibly involving epigenetic modifications in the foetus's non-imprinted genes), maternal information prepares the unborn child for the outside world. In the event of a mismatch, e.g. low maternal DHA intake or under-nutrition, the newborn is not adequately programmed, increasing the

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risk of a number of diseases later in life [Krabbedam, 2007]. The non-genomic effects can be transmitted beyond the following generation because richer conditions later in life may increase the degree of mismatch — something that can be expected in societies going through rapid socioeconomic and/or cultural transitions [Godfrey, 2007; Muskiet et al., 2006]. Epigenetic mechanisms, like DNA methylation and histone modification, affect the mediation of precise neural gene regulation and are therefore crucial for higher cognitive functions such as learning and memory [Feng, 2007].

Although a number of sensitive periods in brain development can be identified (see Table 2), there is insufficient information about the length of these periods. Some of the windows are bound to be age-related, others will be limited to a part of the day. An example of the latter may be mealtimes. Breakfast improves performance on several types of cognitive measures (short-term memory, problem-solving), with the type of breakfast determining the magnitude of the effect. Lunch is known to cause a dip in attention and alertness, whereas the afternoon snack alleviates decrements in performance. Finally, the evening meal influences sleep and therefore the processing of information [Mahoney, 2005]. An example of an age-related window has been found in observational studies of the elderly suggesting that a moderate intake of fatty fish (i.e. more than twenty grams a day, about 400 mg DHA and EPA) may postpone cognitive decline [Van Gelder, 2007]. It has also been shown that moderate increases in blood glucose levels improve the declarative memory capabilities of elderly in particular [Benton, 2005].

In considering how to optimise the use of windows in brain development and function, the first step may be to discuss contemporary nutrition. The human diet has changed considerably over the past 200 years [Cordain et al., 2005]. The high intake of carbohydrates and dramatically altered intake of lower-quality fat is particularly worrying, and may be an important factor in the severity of schizophrenia and such problems as ADHD. In addition, nutrition is not the only factor in specific windows. When there is no opportunity to learn — lack of an enriched environment — or when health is impaired, nutrition will have only a slight impact. Finally, we cannot identify the effects of nutrition without adequate measurement tools. So far, most methods are designed to distinguish between good and bad, but we now need tools to measure improvements in the 'good' range. These will preferably be non-invasive methods suitable for infants, adolescents and adults that measure brain activity, development, sleep patterns, etcetera, or animal models with a high predictive value.

So far, studies have involved a limited number of ingredients (mainly long-chain

| Window | Effect | Factor | Reference |
|---|---|---|---|
| Pre-conception-1st month of pregnancy | Storage of nutrients<br>Closure of the neural tube<br>Retinal development | Folic acid<br>LCP | McNamara, 2006 |
| 2nd half of pregnancy | Formation of neurons<br>Brain growth spurt<br>Duration of pregnancy<br>Infant sleep-wake pattern<br>Effect on prevalence of diabetes mellitus, ADHD, schizophrenia | LCP<br>$\alpha$-linolenic acid<br>Iron & selenium | Szajewska, 2006<br>Makrides, 2006<br>Cheruku, 2002<br>Das, 2003<br>McNamara, 2006 |
| First postnatal months | Outgrowth of dendrites in offspring<br>Mother's mood or brain function<br>Prevention of ADHD | LCP<br>Tryptophane | McNamara, 2006 |
| From 3rd postnatal month onward | Development of sleep-wake cycle (brain structuring)<br>Brain function: motor function and behaviour | DHA, tryptophane, folic acid, vitamin B12, carbohydrate,<br>iron & zinc | Black, 2004 |
| Birth to 9 months | Head circumference | Foetal and infant nutrition (e.g. LCP, iodine, selenium) | Gale, 2004 |
| 9 months-9 years | Head circumference<br>Cognitive function measured as full scale IQ | Child nutrition<br>(e.g. LCP, iron, B-vitamins, protein) | Gale, 2004 |
| 10-20 years | Synaptic and axonal pruning | Fatty acids<br>Amino acids | Wainwright and Martin, 2005 |
| Postmenopause | Non-verbal short-term memory<br>Verbal fluency | Phytoestrogens<br>n-3 LCP | File, 2005<br>Beydoun, 2007 |
| Elderly | Protection against several types of dementia, macular degeneration, and age-related hearing loss<br>Inhibition of cognitive decline<br>Verbal memory | DHA / Fish<br>Phosphatidylcholine and B12<br>Phytoestrogens | Arterburn, 2006<br>Bourre, 2004<br>Van Gelder, 2007<br>Kritz, 2003 |

**Table 2**
*Possible windows of opportunity as indicated in the literature.*

polyunsaturated fatty acids, iron and vitamin B12) and products (infant formulae), pregnancy and lactation, and specific disorders, mainly because of commercial reasons — cost price and ease of marketing — and the medical profession's limited interest in the role of nutrition in brain tissue. This lack of interest is undeserved. As Table 2 demonstrates, there have been some interesting studies suggesting that nutrition can affect brain development during certain specific windows of life. These results should trigger follow-up research, for example addressing the following questions:

– What are the most important windows of opportunity for nutrition to affect brain and cognitive development?
– What nutrients are expected to play crucial roles in the different windows of opportunity?
– What are the key parameters of these windows and when can they be measured?
– How are the windows related to one another? Will a 'lost' window have a permanent effect on the next or another window?
– Which windows get a second chance? For example, deficits in neurotransmission in rats caused by prenatal DHA deficiency can only be normalised if dietary DHA fortification is initiated in the first two postnatal weeks.
– Are there differences between populations based on specific window parameters?

### 2.2.7 Delivering functional components on target

*Carina Ponne*[23]

The previous subsections describe the challenge of identifying functional components that have a positive influence on cognitive development. Another, more practical problem is how to deliver these compounds to the right place at the right time. Micronutrients such as minerals, vitamins or fatty acids must also be added to food and remain stable during processing and shelf life[24]. These ingredients should not affect the taste or odour of the product negatively (i.e. add a bitter or metallic taste). After consumption, the bioactive compounds should be released in the body, preferably in a controlled manner. Those compounds that act directly on the brain should be able to pass through the blood-brain barrier.

Several techniques are used to protect the bioactive compound in the food matrix, ranging from the use of chelating agents to micro-encapsulation [Champagne and Fustier, 2007; Prickaerts, 2005]. Encapsulation involves coating or entrapping pure material or a mixture — usually a liquid but also a solid or a gas — in another material (see Figure 3). Encapsulates or microcapsules are particles ranging in size from several tenths of a micron to a few thousand microns. They can be spherical, oblong or irregularly shaped, monolithic or aggregates, and may have single or multiple cell walls. The purpose of micro-encapsulation in this context is to achieve controlled release in the human body and to protect the active ingredient from its matrix. Depending on the physical and chemical nature of the ingredient, this may mean stability vis-à-vis oxygen, moisture, low pH, high temperature, etcetera. One example

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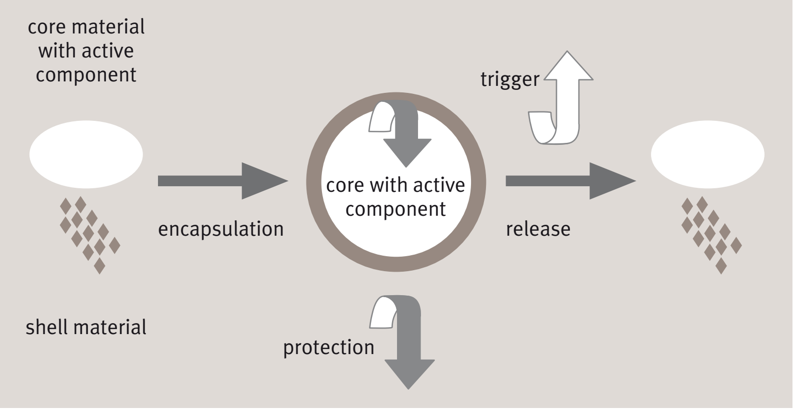
24 Shelf life is the length of time that food, drink and other perishable items are given before they are considered unsuitable for sale or consumption (see www.wikipedia.org).

**Figure 3**
*Schematic representation of encapsulation. Scheme courtesy of Friesland Foods.*




involves protecting unsaturated fatty acids against oxidation (especially if iron is included in the functional mix).

The release of the active compound can be site-specific, stage-specific, or set off by processing triggers. Examples of such triggers are a change in pH or temperature, an osmotic shock, application of shear, or time-dependent solvent activation. Diffusion of the encapsulated components is controlled by using rate-controlling materials or by manipulating the appropriate biological barrier or the fate of the agent once it has passed beyond these barriers.

Examples of encapsulation processes currently used in industry are fluid bed coating, spray drying, co-extrusion, emulsification, and molecular inclusions (e.g. cyclodextrin or liposomes). Edible films and coatings are commonly used as barriers to moisture and oxygen in aromas or oils, thus improving food quality and shelf life. The technology is still far from perfect, however, and has yet to become a standard tool in the food industry.

### Specific challenges in delivering compounds for brain functionality

In its neuroprotective role, the blood-brain barrier impedes the delivery of many potentially important diagnostic and therapeutic agents to the brain. Current drug targeting mechanisms in the brain involve osmotic disruption, the use of vasoactive substances or even localised high-focus ultrasound. Other strategies use endogenous transport systems with transporters such as glucose or amino acid carriers, or they block active efflux transporters. Strategies for drug delivery behind the blood-brain barrier include intra-cerebral implantation.

Researchers are in search of new technologies to aid drug transfer to the brain. Nanotechnology is considered promising in this respect. It was only recently discovered that nanoparticles and liposomes can gain access to the brain, and it is possible that ligands can be used with them to target the blood-brain barrier [Garcia-Gracia et al., 2005]. At the same time, the possibility of these nanoparticles passing through the blood-brain barrier raises questions concerning the safety of these technologies and their use outside of the drugs arena. Not much is known about the potential toxicological side effects of nanoparticles, and it is therefore unlikely that nanotechnology of this kind will be used in the brain food industry in the near future.

### 2.2.8 Future developments in science, industry and government

*Erik van de Linde[25], Ira van Keulen, Paul van der Logt[26], Cor Wever[27]*

The basic premise of this subsection is that there is a right time in life for the right nutrition to optimise brain development and cognitive performance. There was strong qualitative support for this principle within the expert group. At the same time, however, the underpinnings are not entirely stable and require a great deal of additional fundamental and applied research and product and policy development work.

#### Interdisciplinary cooperation

What is the right time? What is the right nutrition? What is optimal brain development? And what is optimal cognitive performance? We can only expect the answers to these questions to emerge gradually, the result of focused cooperation between science, industry, government and non-governmental organisations (NGOs) such as consumer or patient groups. The questions themselves provide common and helpful guidelines for cooperation. They will also require a gradual increase in interdisciplinary teamwork, particularly between food researchers and medical, neurological and clinical researchers. In the Netherlands in particular, food science and technology on the one hand and medical science on the other work separately on opposite ends of the disease-health spectrum [Peppelenbos and De Deugd-Van Kalden, 2007]. It would be far better for the food industry to benefit from medical research exploring the biomarkers of brain and cognitive development. Until now, no significant link has been established between the effect of nutrients on core molecular processes and the markers of brain development and cognitive performance. In the future, brain imaging will help to assess the effectiveness of nutritional interventions in different developmental stages or windows of opportunities. Molecular brain imaging could also help to trace nutrients such as fatty acids to see where precisely they act in the brain.

#### Brain food products

A relationship has already been established between some macronutrients

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26 Principle Scientist, Unilever Foods and Health Research Institute.

27 Policy Coordinator Food Quality, Ministry of Agriculture, Nature and Food Quality.

and micronutrients and brain and cognitive development and function, although the exact nature of this relationship is not always clear. The food industry has started to exploit these insights and has developed different strategies, for example products developed specifically for individual target groups in different geographies. One such strategy is to offer brain food designed to help children in developing and emerging countries to achieve their maximum potential. This is considered a productive strategy in the developing world, as nutritional deficiencies that impede development are common there. Having said that, some experts are questioning the nutritional status of children in the Western world, e.g. malnutrition versus under-nutrition. Consumers are in any event spending more and more on functional food and beverages, especially in the United States and Asia. The growing interest means favourable prospects for the brain food market, but the food industry should be wary of pushing the functionality of such added-value products too far [Datamonitor, 2008].

Brain food products can either be novelty products ('brain bars', etc.) or more traditional value-added products that are optimised during production or processing to naturally contain more of the desired ingredients (omega-3s in dairy products, eggs or meat).[28] A simple strategy of fortifying staple foods (e.g. adding minerals to flour) will probably reach more target consumers in developing countries. In general, however, the expert group expects that current and future functional food products will merely have an optimising effect. If a person's nutrient intake is adequate, supplementation is not expected to enhance or boost brain function above the 'baseline'.


**Figure 4**
*Brain food products can either be novelty products ('brain bars', etc.) or more traditional value-added products that are optimised during production or processing to naturally contain more of the desired ingredients (omega-3s in dairy products, eggs or meat). Photo courtesy of Bifurcafe, www.flickr.com.*

**28** It is possible to create an enriched natural product by feeding farm animals enriched feed, for example, or by using biotechnology (i.e. genomics) in plant reproduction. Such products are relatively inexpensive and can be made available to large groups of consumers, including in developing countries.

### Other market strategies based on the indirect effect of nutrients

It has, however, been suggested that nutrients maintain and possibly enhance cognitive health indirectly, for example because they help to maintain cardiovascular health, optimise glycemic control and make physical and mental exercise possible. The food industry could focus on establishing these indirect effects as well, but that requires another strategy, one that involves promoting lifestyle changes and combining the food product with an activity. Nike's 'Start to Run' initiative is a good example; it is a training programme for people who need a little extra motivation to start running (in a new pair of running shoes). The food industry may also find this an interesting strategy for its brain food sector. For example, as the elderly population in developed countries grows, food companies are starting to see them as an interesting market. It is becoming clear that, although nutrition can play a role, the cognitive performance of seniors depends largely on taking sufficient social, mental and physical exercise. What functional food can do is supply the energy needed for a healthy lifestyle. The food industry could promote similar combination exercise-food programmes. A start-up such as BrainSavers, based in the United States, is a good example. The company website[29] states: *"BrainSavers® is a total lifestyle program that helps people adopt healthier habits through physical and mental exercise, support, education, nutritional guidance, and supplemental nature-based nutritional products"*.

Where markets fail to function, governments and NGOs clearly have a role to play.[30] As a result, we believe that both under-nourishment and over-nourishment and their negative effect on brain development and cognitive function will gradually disappear in various geographical areas.

### Nutritional advice

In addition to new brain foods, we can expect government-funded nutrition consultation centres to use our growing knowledge of the effect of food on the brain to fine-tune their nutritional advice. They will, for example, differentiate between different life stages (such as the elderly or pregnant women) and targets groups (such as subclinical populations, i.e. people who have a genetic predisposition towards stress or mood disorders[31]). Insofar as the relationship can be defined in terms of daily allowances and such, government health councils can advise on the requirements as and when needed and on how to set up interventions. For instance, given the effect of a healthy breakfast and other meals on cognitive development[32], governments may see to it that young children are properly fed, at least in educational settings. At the moment, 10% to 30% of children in the United States and in Europe do not eat breakfast at all [Kiefer, 2007].

**29** See www.brainsavers.com.

**30** For example, the Health Council of the Netherlands will advise the government in 2008 on how food can prevent or postpone diseases and disorders of the elderly.

**31** See the research carried out by Rob Markus at Maastricht University: carbohydrate-rich diets that increase the amount of available trypyophan improve cognitive performance, but only in stress-prone people.

**32** A review of 22 studies has shown that school-age children who do eat breakfast have better memories, test scores and school attendance records [Rampersaud, 2005]. It is also better for children to eat a breakfast with complex carbohydrates that raise the sugar level slowly and moderately, instead of a sugary breakfast [Ingwersen, 2007].

### Evidence-based performance

Another principle that sparked off lively discussion in the expert group was 'evidence-based performance'. Increasingly, countries are prohibiting the publication of unsubstantiated health claims, including cognitive and brain function claims. Certain products — for example those that have direct effects and the ability to pass the blood-brain barrier — will no doubt call for stricter regulation than others, such as those that have indirect effects focusing on a healthy cardiovascular system. We can therefore expect national and supra-national food and drug authorities to be more outspoken with respect to issuing guidelines, thus paving the way for innovative collaboration. They will play an important role in drawing the line between brain food and psychopharmaceuticals. New functional foods, especially those with cleverly wrapped and targeted nutrients, will represent an enormous policy challenge (e.g. in terms of safety regulation).

## 2.3 Influencing food perception and liking

Food perception and food liking are very complex affairs. Whether or not we like a food and to what extent depends on a whole range of sensory, perceptual, emotional and other cognitive factors, each of which has a different neural basis. Subsection 2.3.1 looks at what we know about how our brains represent food stimuli and liking. There are many questions to be answered here, particularly how the different representations are integrated. The next subsection (2.3.2) focuses on sensory preference and how to influence it, in particular cross-modality, i.e. replacing one sensory stimulus by another. Cross-modality may help us to develop compensation strategies, for example to replace the perception of fat by a less fattening flavour. It may also help to intensify consumer food experiences. As we find out more about compensation strategies, the possibility of influencing food perception and liking becomes more likely. It will be a long time before we can predict food preferences, however, even though such predictions are of huge importance to product development in the food industry. Subsection 2.3.3 sheds some light on the problems of predicting food liking and the challenges the food industry faces here. Subsection 2.3.4 deals with three general principles of food preference learning (exposure, post-ingestive consequences and social interactions) and ends with a discussion of food preference stability. It is clear from studies of early food preference acquisition and stability that early conditioning can have long-term consequences. The final subsection (2.3.5) discusses how we may influence food perception and liking in the future.

## 2.3.1 The representation of food stimuli and liking in the brain

*Jan Kroeze*[33]

Food stimuli trigger perceptual, emotional, and other cognitive processes. The perceptual processes create a neural representation in the brain. The emotional reactions to food can be mapped on a hedonic continuum between 'extreme like' and 'extreme dislike', and may initiate approach or avoidance behaviour. Among the many cognitive processes are: activating the name and the conceptual category of the food, generating knowledge about its health implications (both residing in semantic memory), retrieving past eating episodes from episodic memory, and accessing procedural knowledge in long-term memory (how to peel a banana or fillet a fish). The brain processes involved in emotional reactions to a food stimulus are quite distinct from those involved in building the perceptual representation of that stimulus, but in the end the two combine into one integrated experience. The learning and memory effects, as established by food experiences, influence behaviour in subsequent encounters. The memory effects of food may be behavioural as well as cognitive; after many repetitions, they may develop into food habits and enduring food preferences, and even into cultural phenomena like preparation traditions, cuisines and rituals [Prescott and Bell, 1995; Rozin, 1996]. The processes are separate at first, and each is distributed over many different brain locations. In the end, they all converge into the final food experience. An important question — addressed in this subsection — is where and how the perceptual and the hedonic representations of food are integrated.

### Perceptual processing

Food perception results from interactions between the physical-chemical properties of the food and the receptor cells [taste: Sugita, 2006; olfaction (i.e. smell): Ache and Young, 2005; texture: Engelen et al., 2005]. As a complex stimulus, food is captured by several senses simultaneously, such as vision, taste, smell, touch and temperature. Even hearing may play a role, for example the crispness of bakery products, fruit and vegetables [Dogan and Kokini, 2007; Varela et al., 2007]. This complexity means that the brain's neural representation of a food stimulus consists of many fragments, each corresponding to different sensory systems and stimulus features.

### Taste representation of food

The initial taste representation of food is found in the nucleus of the solitary tract (NST), which is the first relay station beyond the tongue's first-order neurons. The neural pattern in the NTS is roughly similar to the pattern in the first-order neurons. Taste fibres project from the NST into the insular cortex and

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adjacent frontal opercular cortex. The latter two constitute the primary taste cortex. This is the location of cells that react specifically to basic taste substances, such as sugar (sweet), sodium chloride (salty), or monosodium glutamate (umami), when applied to the tongue. Other cells in this area serve more than one taste modality. It was also found a few years ago that fatty acids in food trigger activity in the primary taste cortex [Araujo, 2003a], although that study did not show whether the fat was perceived through textural properties such as viscosity or whether there is a gustatory receptor mechanism for fat. Recent studies [Chalé-Rush et al., 2007; Laugerette et al., 2007] have uncovered evidence of a separate oral sensory mechanism for fat. Previous research [Gilbertson, 1998] already suggested a gustatory fat-sensing mechanism in rats. More research emphasising the separation of textural, olfactory and gustatory variables is required. A detailed knowledge of fat perception may be beneficial to our understanding of fat intake.

Based on the available data, it is safe to assume that the activity that takes place in the primary taste cortex is the neural analogue of a taste percept, but without the same emotional and hedonic connotations.

### Smell representation of food

The human nose has about 20 million receptor cells, each of which contains only one of about 450 functional receptors. An odorous food stimulus causes a spatial activation pattern across the olfactory (i.e. smell) tissue, which is transmitted to the olfactory bulb, the first olfactory brain station. All cells containing the same receptor project to the same glomerulus in the olfactory bulb, resulting in a highly converged and unique pattern. The pattern represents the odour quality and is transmitted from the glomeruli to the hippocampus, the amygdale, the piriform and entorhinal cortex. The piriform cortex is considered the primary olfactory cortex. As in taste, the odour message is processed simultaneously in the amygdala (emotional process) and in more denotative structures[34] such as the piriform cortex. Both streams meet again in the orbitofrontal cortex, where olfaction is integrated with other sensory and hedonic features.

### A food percept is the result of integrating many perceptual features

Specific regions in the primary taste cortex have been found to react to food texture and the presence of fatty acids. There are numerous subdivisions within each of these primary sensory areas that receive a large quantity of specific information from the senses. The visual appearance of food is the result of feature analysis and object integration in the primary and higher visual cortices.

34 Denotative structures are structures that only occupy themselves with a direct, explicit representation or reference ('definition' or 'denotation') of the stimulus. This term is more or less the opposite of connotation, which refers to all the other associations, for example the emotional meaning or food images associated with the stimulus.

**Example III**

**The choice between Coca Cola® (Coke) or Pepsi® is not so much a matter of taste. In blind taste tests, both soda drinks score equally well. Nevertheless, many people have a strong preference for one brand or the other. These subconscious preferences, fed by successful marketing campaigns, can now be visualised on brain scans.**

Neuroscientists from Baylor College of Medicine in Texas measured the actual taste preference of 67 people by letting them choose between unlabelled Coke and Pepsi. Then these participants were scanned in a functional magnetic resonance imaging (fMRI) brain scanner while they did the blind test over again. In both blind tests, the preference for the two brands was equally divided over Coke and Pepsi. Tasting either one of the drinks resulted in activation of the reward areas of the brain: the ventromedial prefrontal cortex.

# Coke preference visible in the brain scanner

But when the researchers gave the participants in the scanner information about the fluid they were drinking, by showing a picture of either a Coke can or a Pepsi can, three out of four participants indicated that they preferred Coke.

On their brain scans not only the reward systems were active, but also regions involved in memory: the dorsolateral prefrontal cortex, midbrain, and hippocampus. These brain areas apparently override a person's taste preferences with cultural information. The brand Coca Cola clearly had an added value in the brain over mere taste properties.

In a similar experiment, American neuroscientists from Stanford University measured participants' brain activity while they made purchasing decisions. When they were attracted to a product, a brain area called the nucleus accumbens was active. This brain area plays a role in the expectation of pleasure. If participants judged the price of an item as too high, the scientists saw increased activity in the insula, a brain region involved in anticipating pain. As in the previous study, activation patterns in distinct brain regions can predict whether a consumer will or will not buy.

Market researchers increasingly make use of data derived from brain imaging techniques to determine which aspects of a product persuade consumers to buy it. This new field of consumer research has been named neuromarketing. Information directly from the brain can be more accurate, as consumer's

Original publications: McClure et al. (2005). *Neuron*, 44, 379; Knutson et al. (2007). *Neuron*, 53, 147; Editorial "Brain Scam" (2004). *Nature Neuroscience*, 7, 683 answers to questions about their likings do not always correlate with their actual behaviour. However, some neuroscientists are sceptical about its added value, saying that it is a fad using science to blind corporate clients.

The finished percept of a food item is the result of the neural integration of hundreds of sensory features on the one hand and content already present in long-term episodic and semantic memory on the other hand. We assume that a percept pops into consciousness only after this final integration has taken place. This means that most neural processing takes no more than a few hundred milliseconds.

### The integration of perceptual and hedonic features

Every food stimulus is also associated with a hedonic value. The hedonic value of smell is learned and varies widely between subjects and cultures. Hedonic taste aspects are largely inherited, but may be shaped by experience during development. The available evidence suggests that, although heredity plays some role, food liking is largely learned. A positive hedonic value develops when hedonic brain systems such as the dopaminergic and opioid pathways are activated.

Imaging research in humans and other primates suggests that the amygdala plays a key role in establishing links between the perceptual and hedonic characteristics of food, and that such links are predominantly the result of associative learning. Once established, the perceptual-hedonic complex is represented in the orbitofrontal cortex. There, many single integrative neurons react to several sensory food properties, even if these originate from different sensory systems [Rolls, 2005]. The activity of such integrative cells may be modulated by the hunger-satiety state of the organism [Rolls et al., 1989]. Meta-analysis of numerous studies suggests that the medial orbitofrontal cortex is devoted to processing the reward value of stimuli such as food, whereas the lateral part is concerned with negative stimuli [Kringelbach, 2005; Kringelbach and Rolls, 2004]. The oribitofrontal cortex has a monitoring function, enabling continuous evaluation of the punishing or rewarding properties of stimuli. For example, when a stimulus is no longer rewarding, the orbitofrontal cortex typically sustains a change in food preference. That is why when it is damaged, the patient may be unable to say whether he used to like or dislike a food or another stimulus [Kringelbach and Rolls, 2003]. Taking all the data into account, there is good evidence that the orbitofrontal cortex represents the seat of the percept in the sense that it integrates sensory and hedonic properties.

Many of the relationships that have emerged from research are still uncertain and require further study, in particular the processes involved in linking the hedonic and perceptual aspects of food. Researchers suspect that humans and certain primates may rely more on higher cortical and conscious mechanisms when eating than most other animals. They suspect this because they have failed to find a taste area, present in most animals, in the pons[35] of those primates and humans. Stated in popular terms, most animals probably do not consider food information when driven by hunger but instead seek instant gratification by eating more or less automatically.

### A brain mechanism for food pleasure

Certain behaviours are pleasurable. Olds and Milner were the first to discover a pleasure centre in the brain's striatum [Olds and Milner, 1954; Olds, 1966]. The striatum contains the axons of numerous dopaminergic neurons that in turn are part of the mesolimbic dopamine system and secrete dopamine at the tips of their axons. The system begins in subcortical ventral tegmentum, from where the dopaminergic neurons send axons to the hypothalamus, the amygdala, the hippocampus, the nucleus accumbens and the frontal cortex, including the orbitofrontal cortex. Activating the dopamine receptors in the shell of the neucleus accumbens causes an intense feeling of pleasure. In terms of brain activity, food pleasure is derived from activity in the shell of the nucleus accumbens. This is putting it in extremely simple terms, however. Under normal circumstances, other projection areas of the mesolimbic dopamine system (described above) also play an important role. The hippocampus and the amygdala relate memory to pleasure, the first by consolidating pleasure memories and the second by establishing the reward value of food and food-related stimuli or situations. If a stimulus has reward value, it can serve as a motivator of behaviour, for example food searching and eating.

### Wanting and liking

Activating the mesolimbic dopaminergic system by sensory stimulation or otherwise increases the motivation to eat [Kelley et al., 2002]. The dopamine system must be activated for the subject to be food-motivated and embark on food-related behaviour, in other words 'to go for it' [Berridge, 1995; 2000]. Berridge explains this by distinguishing between wanting and liking. Wanting focuses on the incentive value of food; it is the active motivational component, that which makes the subject pursue the food and eat it. Liking, on the other hand, is passive and evaluative; it focuses on the hedonic value of food. A completely sated subject may be perfectly able to assess the hedonic value of food but not be motivated to eat it. The difference between wanting and liking has been demonstrated in experiments that prevented the breakdown of dopamine in mice, resulting in a hyperdopaminergic brain [Peciña et al., 2003]. The manipulation increased the wanting component only: the animals made a much greater effort to get to the food, but there was no effect on the gusto-facial reflex, indicating the hedonic value of the food.

**35** A structure located in the brain stem.

Wanting and liking are related. The probability that you will want to eat more of a food that has left a hedonically positive impression is greater than when you did not like the food. But first you must recognise the food; the positive hedonic value has to be predictable. Such predictability makes use of perceptual features such as taste, odour, shape and colour. If these features have a hedonically positive value for you, either at birth (e.g. sucrose) or as acquired later in life, they will stimulate your opioid system, another key system related to eating.

The opioid pleasure system is one of several opioid subsystems, each with its own neurotransmitter and receptor type.[36] A stimulus will often excite more than one dopamine subsystem simultaneously, albeit not to the same degree. Sucrose, for example, is not only a pleasure stimulus; it also acts as an analgetic, i.e. a painkiller [Stevens et al., 2004]. Interestingly, when sugar is delivered directly to the stomach, thus bypassing the taste receptors in the mouth, it does not have an analgesic effect [Ramenghi, 1999].

When opioid system neurons are stimulated, they secrete opioid substances known as endorphins, which in turn bind to the receptors of dopaminergic cells. The link between the opioid system and intake-related dopaminergic activity is therefore relayed through the perceptual properties of stimuli, for example the sweet taste of sugar as represented in the primary taste cortex. Once activated through their opioid receptors, the dopamine cells in turn release dopamine, which then stimulates the nucleus accumbens. The nucleus accumbens and the primary taste cortex both project to the orbitofrontal cortex where — as mentioned — hedonic and perceptual pathways converge on integrating cells. It is in this part of the cortex that neurons fire on the sight of favourite foods, but cease doing so when the subject has eaten enough to reach satiety [Araujo et al., 2003b; Rolls, 2005].

## Conclusion

In future, our knowledge of the representations and processes involved in food perception may be used to treat obesity and other eating disorders or to market products. It would be worthwhile to search for ways to influence the brain processes related to food, particularly the hedonic processes, as they are potentially sensitive to pharmacological and conditioning interventions. As we improve our knowledge of brain representations and processes and of all the learned meanings of food (liking, cultural acceptability, healthiness, etc.), opportunities for planned change may increase and become more feasible. The type of research envisaged would involve parallel behavioural observation, functional brain imaging and change-oriented interventions. This means that food-related brain research should focus mainly on brain plasticity and

36 Two well-researched subsystems are the analgetic system, which suppresses pain, and the system that induces flight and hiding behaviour in animals [Carlson, 2004].

behavioural change. More simply stated: how do food-related behaviour or attitude changes translate into structural or representation changes in the brain, and vice versa?

### 2.3.2 Cross-modal compensation strategies

*Carina Ponne*[37]*, Harold Bult*[38]

Wanting is what drives us to (repeatedly) purchase food products. Liking results when we integrate the sensory signals associated with product properties and related experiences. Wanting and liking involve a delicately balanced, complex overall sensory experience, one in which dynamics plays an important role. For example, we like ice chocolate because it combines the perfect melting dynamics of cacao butter or fat at mouth temperature and the sweet taste of sugar counterbalanced by the bitter taste of cacao. We like cheese because of its rich, complex aroma and taste, the way its structure, while initially resistant, softens and melts while we eat it, and its lingering aftertaste.

Food manufacturers are constantly looking for ways to optimise these sensory experiences in order to improve product performance and gain consumer favour. A better understanding of the way in which the senses interact would lead to many new opportunities. For example: they could design a new generation of tasty, healthy products by making clever use of compensation strategies (e.g. replacing fat perception by flavour, etc), or reduce the time to market of food products and improve 'first time right' levels by developing food product design rules.

The food industry is putting a great deal of effort into 'repair mechanisms' these days. There is a large and growing demand for healthier (e.g. lower in fat, sugar and salt, and micronutrient-enriched) food products with a high sensory quality. The holy grail for the food industry is for these foods to taste as good as (or even better than) the foods they are replacing. Product developers struggle with this because food ingredients such as fat, sugar and salt are multifunctional, and the resulting appearance, odour, taste and texture appear to interact. In other words, increasing or reducing the concentration of these ingredients has a multidimensional effect on the product quality. The examples below reflect the current status of food technology and the hurdles the industry is facing when it comes to 'cross-model compensation strategies'.

#### The role of fat in food

Fat is a very important component of many highly favoured foods (e.g. deserts, dairy drinks, cream, baked goods, chocolate, etc.). It is present in small

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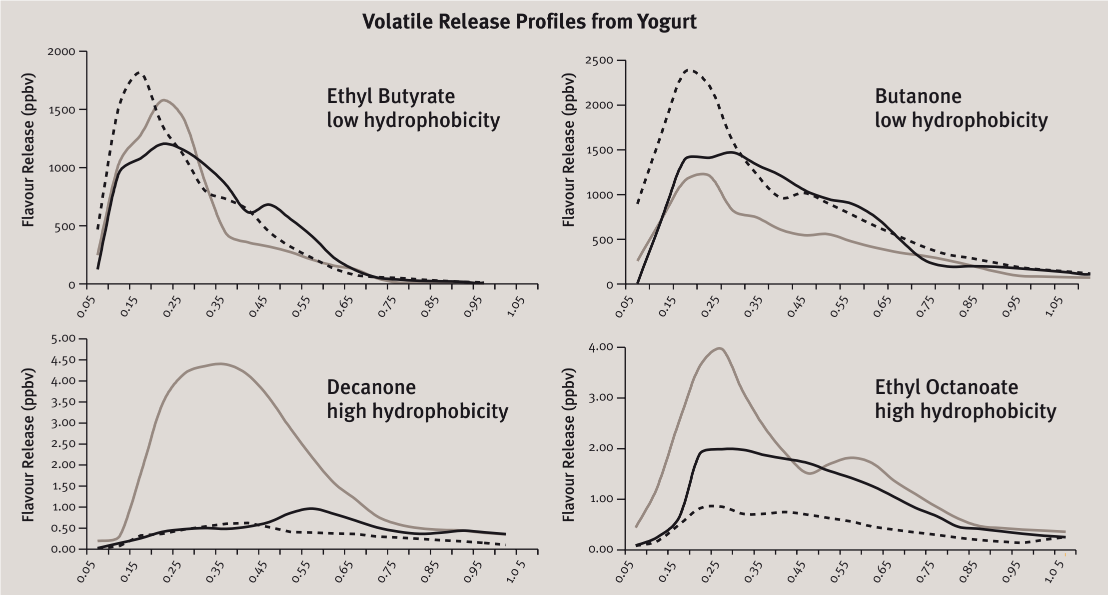



**Figure 5**
*Differences in flavour release pattern in high and low fat yoghurts and effect of addition of ß-cyclodextrin. Source [Taylor, 2006].*

*High fat*
*Low fat*
*Low fat + ß-CD*

globules and is detected by its texture (creaminess and velvet-like feel) and aroma and because it releases a distinct flavour. Fat provides energy but also anti-oxidants and building blocks for tissue synthesis. Humans generally appreciate the contribution of fat to their sensation of foods, which combines visual aspects, mouth feel, taste, smell and — possibly — the perception of the food's heat capacity. Reducing the fat content of a food may therefore reduce appreciation for that food for a complex combination of reasons.

Attempts to reduce the fat content in food products have made it clear that the functionalities of fat cannot be replaced by only one other ingredient. For example, reducing the fat content of Gouda cheese immediately results in a rubbery texture and a bland flavour. Reducing the fat in strawberry yogurt makes it watery with a sharp taste.

The food industry has succeeded in replacing only some of the fat content of foods by adding fat-related aromas combined with other structuralising agents. Figure 5 shows the changes that can be made by adding cyclodextrin to low-fat yoghurt, thereby releasing compounds with a high hydrophobicity.[39] The release patterns of high-fat and low-fat products do not differ as dramatically in the case of low hydrophobic compounds.

Depending on the type of food, it is difficult to reduce fat content below a certain level without compromising too much on sensory quality. The scientific community has suggested a number of strategies to compensate for the sensory effects of lowering fat content, but so far no strategy has proved satisfac-

39 Cyclodextrine consists of a cylinder of glucose rings. Odour molecules inside the cylinder are released with a delay. This way, the aroma release pattern of a low-fat product can imitate the pattern of a high-fat product.

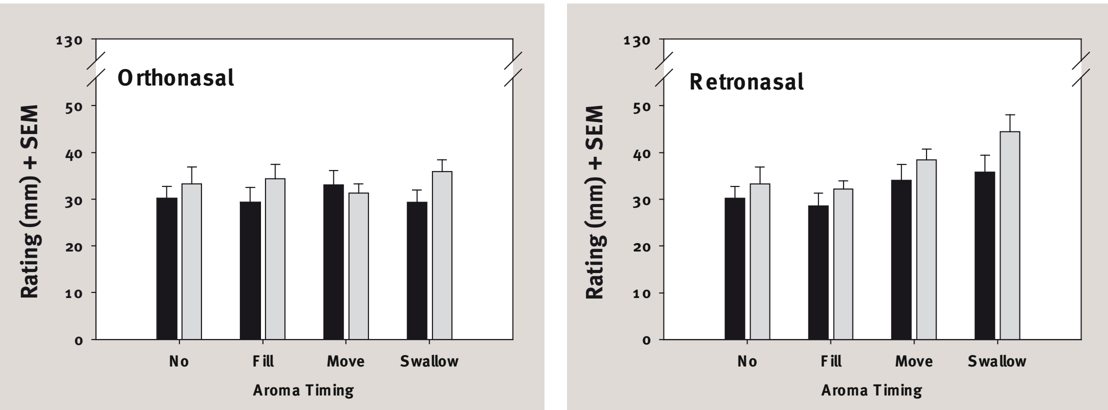
tory. Each one focuses on different parts of total fat perception, but to arrive at a 'total strategy', we need to know more about how the senses interact.

## Odour-based compensation strategies

Food generally release complex mixtures of volatile chemical components that produce aroma sensations when sniffed. If a food contains fats, some of these components may be products of fat degradation. For example, when meat is heated, some of the fat in it will react with oxygen, producing volatile fat oxidation products. At high levels of fat oxidation, the volatiles produce unpleasant warmed-over aromas. However, at moderate levels they make a positive contribution to the sensory evaluation of the meat aroma [Bredie et al., 2000]. Odorants that signal the presence of fat, even when raised by fat oxidation, add to a positive evaluation of the food aroma. Hence, low concentrations of such odorants, as produced by low-fat meats, produce less prototypical meat aromas. The custom of wrapping lean meat in sliced bacon before frying reduces the perceived dryness of the meat and increases the production of fat-signalling odorants while keeping overall fat levels low. This is a good example of a compensation strategy.

**Figure 6**
*Cross-modal effects in thickened milks. Perceived intensity of creaminess with (grey bars) and without (black) stimulation with a creamy aroma in the nose during drinking. Stimulation with the aroma orthonasally (i.e. smelling) does not increase perceived creaminess. Stimulation with the aroma retronasally (i.e. in the mouth or nose cavity) increase perceived creaminess, especially if the aroma is submitted at the moment of swallowing.*

Most odorants are released at lower release rates from fatty media than from watery media. In fact, before ingestion the release rates of most odorants in high-fat foods are fairly low, but exposure to saliva speeds this up. Such changing release patterns may not apply to low-fat foods. The implication is that adding fat-signalling odorants to a low-fat food may not increase fat perception, as the release pattern is not realistic. A recent study evaluated how the timing of a fat indicating aroma in a low-fat (0.07%) milk affected perceived creaminess and thickness [Bult et al., 2007]. It was shown that late presentation of the aroma, i.e. during swallowing, resulted in significantly higher creaminess and thickness perceptions. This suggests that odorants may indeed enhance the perception of typical fat-related aspects such as creaminess and



thickness, provided that their release pattern is realistic (see Figure 6).

### Texture-based compensation strategies

In liquid and semi-solid foods — e.g. custards, dairy drinks and soups — fat may serve as a thickener or it may modulate the structural breakdown properties of other thickening agents. In addition, fat reduces friction on the surface of the tongue. That means that reducing fat content generally increases friction, lowers the food's viscosity and changes the breakdown of gel structures. All these processes seem to affect perceived fatness and related attributes such as creaminess and thickness [Van Aken et al., in press]. Recent developments in food engineering show that optimising other physical properties, such as fat droplet size and interactions with gelling agents, can compensate for the perceptual effects of fat reduction [Sala, 2007].

Lowering the fat content of semi-solid dairy products generally produces a watery sensation and reduces fat-related sensory properties such as creaminess and thickness, lowering appreciation for the product. In these food systems, water retention, perceived creaminess and perceived thickness can be improved to some extent by using thickeners such as polysaccharides (e.g. carrageenan).

### Taste-based compensation strategies

When we refer to the taste of fat, we usually mean the combined textural and olfactory properties of fat. But recent research shows that there are in fact fat-specific oral receptors (see also subsection 2.3.1). The candidate receptor[40], which is found predominantly in the human circumvalate taste buds, is located on the posterior part of the tongue. If such oral receptors are involved in the neural encoding of food fat content, they are not likely to induce any conscious perception of fat taste in humans. Nevertheless, they seem to be essential for learning to associate odours with fat content, perhaps in order to assess whether foods contain sufficient amounts of fatty acids. Recent research by the Wageningen Centre of Food Sciences and the FC Donders Centre tested this hypothesis in a fMRI study involving human subjects. Foods with varying fat content were controlled for textural and taste aspects. In spite of the strict textural and taste control, subjects showed brain activation patterns that correlated with caloric content. The cortical centres involved were the same as had previously been associated with the neural encoding of caloric content [De Araujo and Rolls, 2004].

If fat content information is directly neurally encoded, then strategies compensating for low-fat content cannot rely on the manipulation of modalities such as smell or texture alone. The strategy of choice should then be to deceive the

**40** The receptor is based on the CD-36 fatty acid translocase.

receptor involved, but we do not yet understand the exact mechanism of the CD-36 receptor. Given the growing interest in this field, we will no doubt discover alternative ways to stimulate receptors in the decades ahead.

Summarising, odorants that signal fat under natural conditions may compensate in part for the perceptual implications of fat reduction. However, the release of fat-signalling odorants should be postponed until after oral processing. This requires a sophisticated food engineering methodology that is already available in part but needs to be improved to produce food that has sufficient shelf life. The use of odorants should ideally be combined with textural modifications such as thickening and with enhanced oil droplet coalescence during oral processing. Various food-specific techniques are already being used but need to be optimised for combined odorant and texture modifications.

If CD-36 receptors turn out to be essential fat-signalling receptors, the next step will be to find non-caloric CD-36 stimulants, for instance non-digestible fatty acids. Research groups around the world (Nottingham, Wageningen, Dijon, Sidney) are running programmes aimed at developing compensation strategies for fat reduction. The current approach to reducing fat content is to use multimodal compensatory mechanisms. As research continues to evolve, other applicable techniques are expected to become available in the near future.

### The role of sugar in food

Natural sweeteners such as sucrose, glucose and fructose are important sources of energy. Not surprisingly, human beings show a preference for sweet tastes at birth and that preference persists throughout their lives, regardless of their cultural background (see also subsection 2.3.4 on conditioning food preferences). As in the case of fat, the global obesity epidemic calls for a reduction in the sucrose content of foods while maintaining food appreciation. Sugars such as sucrose are important tastants. Not only do they give products a pleasant sweetness, but they also balance sourness (e.g. in fruit juices, soft drinks, yoghurts) and mask bitter or other strong flavours of specific ingredients. Most current strategies compensating for sugar reduction are either based on known sensory interactions or include specific taste enhancers. A specific combination of aromas (e.g. vanilla, certain fruits, honey, caramel, etc.) and sugary sweetness is known to have synergistic effects on sensory perception. In this case, product developers make use of the learned association between certain aromas and taste. Similar associations are known to exist between colours and tastes. Another strategy is to alter the sweet-sour ratio of a product by applying other types of food acidifiers or by steering fermentation processes towards higher acidity in order to reduce sourness. These methods have their practical limitations, however; because acids also have a preservative function, shelf life stability is affected. Another approach is to use taste enhancers; these small molecules interact directly with the sweetness receptor on the human tongue, enhancing the sweetness signal. In general, the compensation strategies mentioned here do not allow for major reductions in sugar content. That will require a better understanding of perception processes.

### Taste-based compensation strategies

The primary objective when reducing sugar content is to maintain overall sweetness. This requires the unimodal manipulation of foods: reduce sugar content and compensate for the reduced sweetness by adding non-caloric sweeteners. Light drinks are a good example: the sugar is replaced by combinations of intense sweeteners (sodium cyclamate, aspartame and acesulfame K). There is a problem, however: the sweeteners often also introduce metallic or bitter off-tastes that tend to lower consumer appreciation. The general strategy is to combine different sweeteners in ratios that maximise sweetness and minimise off-taste.

### Texture-based compensation strategies

The second problem with using sweeteners is that they change the textural properties of drinks. In terms of weight, soft drinks are typically 10% sucrose. At that concentration, consumers perceive the drink's viscosity as thicker than artificially sweetened soft drinks. In general, consumers tend to prefer the slightly thicker drinks, perhaps because thicker natural products contain more calories and consumers are attracted to the higher calorie option. Similar to fat, the food industry uses the cross-modal compensation strategy of thickening products to make up for reduced sucrose levels. It is not easy to find the ideal combination of artificial sweeteners and thickening agents. Thickening a liquid or semi-solid food suppresses perceived taste and smell intensities [Cook et al., 2003; Weel et al., 2002]. This illustrates the complexity of reducing sucrose levels in foods: by replacing the sucrose with artificial sweeteners (unimodal compensation), the texture changes. Repairing the texture changes (cross-modal compensation) affects taste and odour properties that then also have to be repaired (complex cross-modal compensation).

### Odour-based compensation strategies

Instead of replacing the sucrose in a product with artificial sweeteners, it can also simply be reduced, lowering the caloric content and sweetness at the same time. Reducing sweetness is only possible when done gradually over time, so that consumers do not notice a sharp decline from one day to the next. This strategy, called reduction by stealth, exploits the tendency of humans to habituate to new stimuli, provided that the changes are minor and the intervals between the changes are sufficiently long. This method is already being used to reduce the sodium chloride content in food.

Yet another cross-modal perceptual effect can be used to boost the acceptability of low-sucrose recipes. For example, because taste affects smell and vice versa, adding strawberry aroma to sucrose solutions increases their perceived sweetness (taste) [Frank et al., 1989]. Alternatively, below-threshold saccharin (sweetness) dilutions in water enhance the odour intensity of benzaldehyde [Dalton et al., 2000]. The two examples have something important in common: the combined tastes and odours have perceptual qualities that mimic natural combinations. In other words, the odours used in these experiments are congruent with the tastes. The importance of congruency for taste-odour integration has long been recognised [Schifferstein and Verlegh, 1995]. More recently, research has found a neural basis for these effects. Both hemodynamic neuroimaging experiments, e.g. fMRI, and single-cell recordings of neural activations have shown that odour and taste stimulation will result in supra-additive activation of the relevant brain areas, but only if odour and taste stimuli are congruent [Small et al., 2004]. Activation patterns for non-congruent stimuli will merely show complementary activations. This synergistic merging of senses is not unique for taste and smell combinations. It has also been shown for other combinations of modalities, provided that stimuli are congruent [Verhagen and Engelen, 2006; Gottfried and Dolan, 2003].

Smell-taste enhancement is a candidate compensation strategy. It should be noted, however, that most of the studies cited above involved fairly abstract combinations of taste and smell that only remotely reflected the complexity of real foods. For example, it is easier to boost the sweetness of sucrose alone by administering a strawberry aroma than it would be to boost the sweetness of strawberry-flavoured yogurt. Adding more strawberry odour might even disrupt the optimal taste-odour balance and have a potentially detrimental impact on consumer liking. Careful odorant selection is required here, as the opposite effect is also possible: taste and texture evaluation may also be suppressed by incongruent odours.

### The role of salt in food

Sodium intake is linked to hypertension, coronary heart disease and stroke. Health officials recommend reducing salt consumption to a maximum of six grams a day (minimum is 0.5 and optimum is 1.2). Only 5% to 20% of our salt intake comes from table salt; most of it is from processed foods such as breakfast cereals, bread, cake, meat products, soups and sauces. Salts play an important role in food products; they act as a preservative, deliver taste, enhance flavour and counter ion activity to stabilize structure-building ingredients like proteins. The food industry is actively searching for salt reduction strategies. Current ones include adding taste enhancers (amino acids, glutamates, potassium lactate and yeast extract), compensating for saltiness by adding herbs and spices, and modifying salt dissolution. So far, these various strategies have had only a limited effect. Many of the compensation strategies also have negative side effects, such as a bitter or metallic after-taste. In addition, combining salt, fat and sugar reduction must produce interactions [Kilcast, 2006]. Odour-based compensation strategies for salt reduction are generally the same as for sucrose reduction. Aromas that indicate the presence of salt are the most probable salt compensators.

#### Conclusion

Most of the strategies chosen by product developers to reduce fat, sugar and sodium while maintaining optimal product performance are the result of a highly empirical product development process. Neuro-imaging techniques can help us to understand how sensory cues — evoked by looking, smelling, tasting and touching food — result in a decision to like and to want a product. This type of information cannot be obtained by traditional food research methods, such as surveying consumer preferences and food choices. People are not good at analysing what they perceive and why they choose what they do, nor can they easily explain the rationale behind their behaviour. Neuro-imaging and other neuroscientific techniques offer a promising strategy for obtaining direct, accurate information about how people perceive foods and how they will act on various cues. A better understanding of multi-sensory signal processing will help streamline the product development process and improve the quality of the final product.

### 2.3.3 The difficulty of predicting food preferences

*Rene de Wijk*[41]

'Liking' is a key sensory measure for food product development. New prototypes are usually first tested by in-house sensory panels. Satisfactory liking scores are required before a product moves into the next phases of the product development cycle, perhaps ultimately resulting in its market introduction. Traditionally, overall liking scores of a product are collected along with liking scores for specific textural, aroma, flavour, taste, visual and auditory attributes to identify opportunities for specific product improvements. Statistics can be used to determine the relative contribution of each attribute to overall liking, and product developers may subsequently focus on significant attributes to improve overall product quality. It is often difficult to translate sensory results

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into specific product changes, as attributes typically reflect multiple product properties. An important food attribute such as creaminess combines textural (viscosity), flavour and taste properties, as well as the specific functionality of the food in the mouth, such as the degree of lubrication between the food and oral mucosa [De Wijk et al., 2006]. Hence, any change in the food's flavour or taste properties may have an undesirable impact on the food's creaminess.

Liking as measured in the food laboratory is not the only predictor for purchasing behaviour, however. Indeed, even after extensive laboratory testing, more than 70% of new products disappear from the shop shelves within three months. Liking scores make poor predictors of purchasing behaviour because they are typically measured over a very brief period of time. Research has indicated that liking scores may change during repeated food consumption. Some foods or beverages may receive a low liking score initially, followed by a gradual increase during successive meals or presentations; others may show the opposite pattern, possibly due to product boredom [Koster and Mojet, 2007]. Several of the most popular beverages in the world offer extreme examples of the former. At first, young consumers almost universally dislike coffee and alcoholic beverages. It is only after repeated exposure that their liking for these products increases, and in fact may even become addictive. The fact that they consume these products despite their initial dislike for them demonstrates that actual consumption is determined not only by the sensory properties of the product but also by unrelated factors such as peer pressure, modelling and imitation behaviour.

Liking scores are also poor predictors because they are often measured in testing environments, namely food laboratories. Labs are typically very different from the real-life locations and situations in which the product is consumed. The same meal will receive a different liking score when consumed in a fancy restaurant than it will in a cafeteria. Liking is related not only to the characteristics of food itself but also to the context in which it is consumed [Meiselman et al., 2000] (see also subsection 2.4.3 on situational norms influencing food intake). The Restaurant of the Future was recently opened in Wageningen, the Netherlands, to address this problem; here, it will be possible to study the influences of cultural, situational and social factors on consumer food choice and consumption behaviour in a natural eating environment.

Products are not liked universally among consumers, or we would not have such a huge variety of products on the market. Besides the obvious cultural differences, some of this variation is probably related to physiological differences in people's sensitivities, which in turn may be related to differences in receptor densities. For example, food preferences of smell-sensitive people may depend heavily on the food's odour, whereas for other people it may depend more on the food's taste or texture. Neuro-imaging could help to determine these individual differences in food preferences (see example III).

As mentioned in subsection 2.3.1, the sensory properties of foods are only part of the reason why we like a food product. The other variables bear little relationship to these sensory properties, but are related instead to the cultural, social, and situational context in which the food is consumed. These are factors that should also be taken into account in food product development, something that will require a more interdisciplinary approach involving the social, health and life sciences.

### 2.3.4 Conditioning of food preferences

*Kees de Graaf*[42]

Humans are born with a preference for sweet and a dislike of sour and bitter tastes. A preference for a salty taste develops within the first year of life. It is not clear whether there are inborn preferences for certain odours, although newborn infants do detect and respond to certain odours. Recent research [Marlier and Schaal, 2005] suggests that three to four-day-old newborns prefer the odour of human milk to that of formula milk, irrespective of their exposure to breast milk or formula milk. Except for these few inborn preferences, most human sensory preferences are learned through repeated exposure to particular sensory events and their associated consequences.[43] Basically, when someone is exposed to a certain stimulus associated with positive consequences, his preference will increase; when he is exposed to a certain stimulus associated with negative consequences, his preference will decline.

There are three major operating mechanisms through which preferences are learned: exposure, post-ingestive consequences, and social interactions (for the neural mechanisms behind energy balance and satiety, see subsection 2.3.1). Exposure explains culturally mediated food preferences, for example why many Dutch people like cheese and why Indian children like curry. Positive post-ingestive consequences explain why children quickly learn to like hamburgers but find it difficult to appreciate Brussels sprouts. Modelling and other social interaction explain how family, friends, and commercials influence our liking for specific food products. One important question in this respect is whether we can condition food preferences so that children, for example, learn to like healthy foods such as vegetables. Can we do this, and if we can, is it something that we really want? (See also section 2.6 on social and ethical aspects.)

42 Professor of Eating Behaviour, Division of Human Nutrition, Wageningen University and Research Centre.

43 There has been a lot of research showing that there is little connection to food preferences within families. Rozin [1991] calls this the family paradox, because intuitively the resemblance between parents and children in food preferences is expected to be large based on similarities in genetic and rearing circumstances.

### The powerful role of exposure

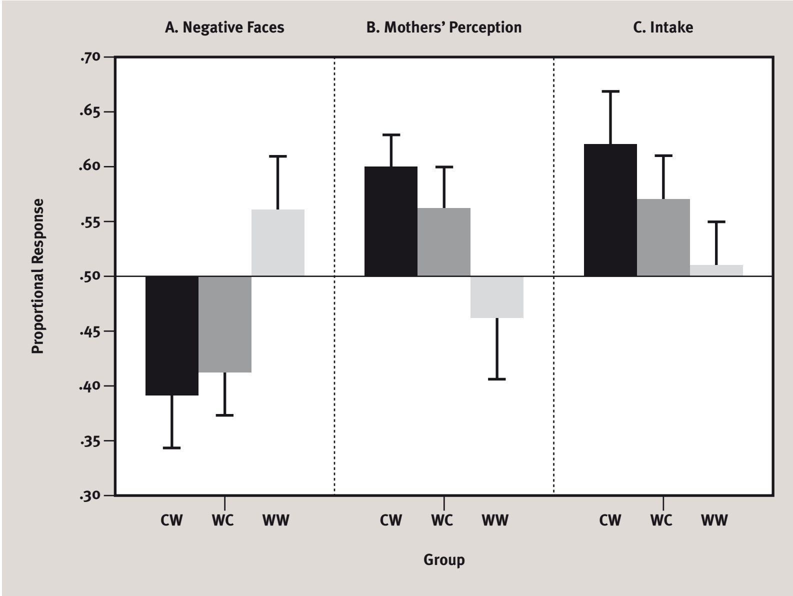
One of the first experimental demonstrations of the effect of exposure on liking was a study in which young adults were exposed to different unfamiliar tropical fruit juices five, ten or twenty times [Pliner, 1982]. The results showed a strong exposure effect; the more frequently a subject tasted a juice, the better he liked it. A later study [Birch et al., 1987] showed that exposure had to involve actually tasting the food; merely looking at it was not enough to produce liking. A more general analysis found that children's food preferences can be described in terms of two main dimensions: sweetness and familiarity [Birch, 1979].

The role of exposure in liking has been confirmed in many other studies. The principle of exposure has also been used to enhance young schoolchildren's liking for fruits and vegetables. A recent study [Hendy et al., 2005] used a combination of exposure and social rewards to increase liking and intake of fruits and vegetables in six to nine year olds. Like other studies [Wardle et al., 2003a; 2003b], the programme succeeded in increasing both liking and intake in all three age groups. However, a six-month follow-up showed that the initial increase in preference had not been sustained. Another recent study found that repeated exposure to spinach resulted in slightly higher liking scores after repeated exposure, but only for subjects who initially disliked the vegetable [Bingham et al., 2005]. These findings suggest that it is hard to produce a strong and long lasting effect through exposure on fruit and vegetable preference or consumption.

Another interesting question with respect to exposure and food preferences is the timing of exposure in the life cycle. One study [Schaal et al., 2000] showed that newborns (three hours old) whose mothers consumed anis-flavoured food during pregnancy responded less negatively to anis odour than newborns whose mothers did not do so. Human foetuses evidently learn odours from their mother's diet. Another study showed that mother's exposure to carrot juice in the third trimester of pregnancy and/or during lactation had a positive effect on weaned infants' liking for carrot flavoured cereals at five months [Menella, 2001] (see Figure 7). Another very early life study [Menella et al., 2004] showed that infants who were exposed to sour-bitter formulas during the first six months of life accepted this formula at seven months, but that infants who had not been exposed to it rejected it at that age. These studies show that the effects of exposure are already apparent very early in life. As will be discussed later, these very early exposures may have long-lasting effects on later preferences.

**Figure 7**

*The infants' relative acceptance of carrot-flavor cereal as indicated by display of negative facial expressions (left panel), mothers' ratings of their infants' enjoyment of the cereals (middle panel), and intake (right panel). There were three different experimental groups; the mothers in group CW drank carrot juice during the third trimester of pregnancy, and water during lactation; the mothers in group WC drank water during pregnancy and carrot juice during lactation. The control group WW drank water during both pregnancy and lactation. Source [Menella et al, 2001].*




Another interesting aspect of the relationship between exposure and food preference is the effect of breast feeding and variety on the acceptance of new flavours. Breastfed infants are more willing to accept a novel vegetable flavour than bottle-fed infants [Sullivan and Birch, 1994]. In an experimental study, newly weaned infants were exposed to either the same food (carrot) or three different foods (carrots, peas, squash) for twelve subsequent days [Gerrish and Mennella, 2001]. In a test session with a novel food (chicken), the infants exposed to a variety of flavours liked the chicken more than the infants who had not been. Both these effects have recently been confirmed [Maier et al., 2005].

## Post-ingestive consequences

Food has powerful reinforcing properties. Humans learn to associate the taste and flavour of a food with its metabolic consequences. Our preference for a food increases or decreases depending on those consequences. There is a difference, however, between learned aversions and learned preferences. Most people have only a few learned taste aversions caused by a single link between exposure to a particular food and subsequent nausea [Rozin and Vollmecke, 1986], for example after food poisoning, cancer radiation, chemotherapy treatment or illnesses causing gastrointestinal discomfort. On the other hand, people have many food preferences that are not formed after a single exposure but after repeated consumption.

It is clear that children learn to like tastes and odours associated with high energy density, i.e. food with carbohydrates and/or fats. Three studies have shown that combining unfamiliar flavours with either carbohydrates or fats eight to twelve times in succession increased the liking for that particular flavour in two to five-year-old children [Birch et al., 1990; Johnson et al., 1991; Kern et al., 1993). Such energy-conditioned flavour preferences are difficult to replicate in adults; studies [Zandstra et al., 2002] demonstrate a clear exposure effect on preference, but no energy conditioning effect. The lack of effect may be due to age or to the more complex stimulation levels in adults. Such complexity makes it more difficult to learn the sensory signal and associated it with the energy signal. Nevertheless, one study has shown that the energy conditioning effect works in everyday life [Appleton et al., 2006]. Energy conditioning had a particularly strong impact on liking when the adult subjects consumed an energy-rich yoghurt drink in a state of hunger. This finding is in line with the Darwinistic view that it makes sense to learn to like those flavours and tastes associated with a high energy density. That is why it is so easy to learn to like the taste of hamburgers or pizzas, but so difficult to learn to like the taste of vegetables. Interestingly enough, repeated exposure usually does not diminish a person's liking for low-energy versions of certain products, for example low-fat or low-sugar products [see e.g. Mela et al., 1994].

### Social effects associated with liking

Social mechanisms may have powerful effects on liking (and therefore on food intake, see subsection 2.4.3). These effects differ per age group. For example, infants are less sensitive to social pressure than adolescents. One of the major social effects on liking and intake is through modelling, imitation, and unconscious conformation to group pressure. Young children learn by observation what other respected people do, and what food they prefer.

Apart from modelling, there are a number of rules that govern how social influences affect food preferences. Using food as a reward for good behaviour will increase a child's preference for it [Birch et al., 1980]. Children will not, however, regard every food as a reward; candy or a high-energy snack will go over better than a vegetable. Another rule is that presenting or giving food to a child while it receives positive attention from respected others (e.g. adults) will increase its preference for that food [Birch, 1980].

The third rule is more controversial: giving someone a reward for eating a particular food may increase his preference for that food, but it may also be counterproductive and decrease his liking for it. For example, the rule 'eat your vegetables and then you can have dessert' may decrease a child's preference for the vegetable and increase his liking for dessert. One important factor may be the extent to which the reward is conceived as a kind of bribery [see also Hendy et al., 2005].

### Stability of food preferences

Preferences are remarkably stable, and those acquired early on in life may have a particularly lasting influence. The foods that a child likes at age two, four and eight are closely associated [Skinner et al., 2002]. Recent work indicates that children who were exposed to bitter-sour tasting protein hydrolisates[44] during their first year of their life had a preference for more sour-tasting stimuli five or six years later [Liem and Mennella, 2002 and 2003]. Some even suggest that preferences established by the age of two or three are predictive for preferences in early adulthood, especially for vegetables, particular cheese varieties, and some types of meat [Nicklaus et al., 2004]. Another interesting finding is that neonatal experience with vanilla odour is associated with a preference for vanilla-flavoured tomato ketchup in adulthood [Haller et al., 1999].

In summary, based on the research so far, the first year of life seems to be a large window of opportunity for developing stable food preferences. Whether and how this window can be used to condition a preference is not clear yet. Determining the neural mechanisms underlying human preference behaviour may well help us design strategies to influence that behaviour. As stated in subsection 2.3.1, future research should focus in particular on the processes involved in the neural linkage between the hedonic (i.e. like versus dislike) and perceptual aspects of food.

## 2.3.5 Future trends in science and industry

*Rene de Wijk[45], Carina Ponne[46], Kees de Graaf[47] and Ira van Keulen*

This final subsection considers how we will influence and predict the perception of natural or engineered food products in future. The expert group believes that the cognitive neurosciences and their imaging methodologies are essential to achieving these aims. At the same time, the more traditional methods of psychological research on food preferences remain important, especially with respect to the social and cultural effects on food liking and preferences. That is particularly relevant now that the food industry and retail are starting to focus on *"what food can be for us instead of what food can do for us"*[48] or: intensifying the eating experience by making the social aspects of eating more important. Research on the setting or ambience in which we eat may be booming business in the future, the point being to design places where consumers not only want to eat but also want to *be*. The new Restaurant of the Future at Wageningen University of Life Sciences may well indicate that in that respect, the future is happening now.

44 Protein hydrolisates are mixtures of amino acids.

45 Senior Sensory Researcher at Agrotechnology & Food Sciences Group (AFSG), Wageningen University and Research Centre.

46 Group Manager Sensory Science, Friesland Foods.

47 Professor of Eating Behaviour, Division of Human Nutrition, Wageningen University and Research Centre.

48 Dick Boer, CEO of Albert Heijn supermarkets, from his lecture at the KIVI conference Future Foods, October 2007.

## Product development

In the future, product developers who wish to design healthier and possibly more experience-intensifying and taste-intensifying products will need a better understanding of the specific sensory functionalities of food ingredients. In particular, they will require groundbreaking insights into how these functionalities (taste, texture, smell, etc.) can be assumed by other (healthier) ingredients. Take the earlier mentioned example of fat: more knowledge on how we sense 'fat content' would make it easier for the food industry to develop fat replacers that mimic the various functionalities more accurately and completely than those currently in use.

In general, the food industry will be looking for food products that induce pleasurable and satiating sensations but without unnecessary calories or other negative side effects. Neuro-imaging may help to determine whether these sensations are present in novel food products (see section 2.4 on food intake). A better understanding of sensory signal processing would be of particular benefit to people who suffer a sensory impairment (either congenital or caused by age, illness or accident). Special food products whose design is based on knowledge of the interchangeability of sensory information would improve the quality of their eating experience and life and prevent undernutrition.

Similarly, a more in-depth knowledge of where ingredients and functionalities are actually sensed (e.g. in the mouth or intestines) will allow industry to develop food structures that increase the concentration of ingredients at those sensitive locations, so that the overall quantity of ingredients can be reduced.

Finally, we should mention an interesting odour-based strategy for the future: molecular gastronomy. Researchers have already identified many different types of smell receptors, about 350 in all. Particular flavour molecules can be used to activate or block each of these receptors, leading to *"an unprecedented level of control over the flavours in our food"*, as the well-known neuroscientist Edmund Rolls stated during a presentation at the New Frontiers of Taste festival.[49]

## Predicting food liking

What else will the future of food product development bring? We may be seeing the emergence of new sensory methodologies that predict not only initial product liking and acceptance, i.e. after one or several encounters with a product, but also long-term acceptance upon repeated consumption. These new sensory methodologies should be observational and reflect the unconscious processing of foods non-invasively, in other words by registering what

49 See www.umamiinfo.com

consumers actually do rather than what they *intend* to do (as in questionnaires). They could be based on neuro-imaging methodologies, with researchers no longer requiring consumers to respond overtly to perceived foods but monitoring their hedonic brain responses directly instead. Different brain regions such as the orbitofrontal cortex are important in liking and craving behaviour. These areas are more active — and thus light up on imaging scans — when, for example, a chocolate lover sees and eats chocolate. According to Edmund Rolls, this means that *"We can tell what people will like from their brain response"* [Farrow, 2007].

Research in Rolls's lab showed that there are indeed individual brain differences for very pleasant food, depending not only on the amount of food eaten — the more you eat, the less you crave a particular food — but on people's particular food liking and craving. Understanding these individual brain differences in relation to food choice and food craving could help us design product development rules for industry and reduce the amount of time spent on trial and error. It can also help the food industry adapt more easily to changes in consumer demand — something that will become more frequent as consumers are increasingly exposed to tastes from other countries and as consumer trends come and go at an ever-faster rate.

### Conditioning food preferences

In the future, we can expect to see food products designed to trigger the areas of children's brains involved in liking and wanting. Children are an especially interesting target group because interventions designed to modify preferences have the biggest and longest-lasting effect when introduced at as early an age as possible. The first year of life appears to be a large window of opportunity when it comes to developing stable food preferences. However, it is not clear whether this window of opportunity can be used to condition a preference for healthy foods such as vegetables. One possible option is to flavour formula milk with vegetable flavours, but we do not know whether this will actually make vegetables more acceptable to children later on. The early programming of food preferences is also an issue with ethical considerations (see section 2.6 on social and ethical aspects).

Other research topics related to the conditioning of food preferences are the timing of nutrient delivery to the gut in relation to sensory exposure in the mouth. More accurate timing may help to reinforce the association between the flavour and its physiological consequences. Precise knowledge of timing could help us to develop foods with lower energy densities and positive energy-taste conditioning.

## 2.4 Influencing the mechanisms of food intake

This section focuses on food intake from a range of different perspectives. The first subsection (see 2.4.1) focuses on neuro-imaging studies: Which neural mechanisms are involved in maintaining our energy balance and feeling of satiety? We pay particular attention to the role of the hypothalamus.
The second subsection (see 2.4.2) concentrates on the current state of knowledge in food research, i.e. epidemiological and intervention studies. The main questions there are: How do our food patterns influence satiety? In other words: Which specific food properties make us feel 'full'? The third subsection (see 2.4.3) looks at the external cues that influence food intake, for example the ambiance and portion size. Each subsection considers future research and interventions for controlling body weight. The final subsection (see 2.4.4) goes into some of these ideas in more detail.

### 2.4.1 Neural mechanisms behind energy balance and satiety

*Jeroen van der Grond*[50]

The brain plays a crucial role in the decision to eat, integrating multiple hormonal and neural signals. Over the last ten years, functional neuro-imaging techniques, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), have enabled us to search for regions in the brain involved in regulating eating behaviour, hunger, taste and satiation. Several studies have revealed the complexity of the human brain mechanisms related to eating behaviour. The challenge over the next decade is to understand that complexity.

When food reaches our mouth, we smell and taste it before ingesting it. The neuro-anatomical correlates of taste and smell are known to be primary reinforcers of food intake. They have been described in a fair amount of detail and are potent elicitors of brain activity in limbic and paralimbic regions such as the amygdala, insula, orbitofrontal cortex, cingulate cortex and basal forebrain [Small et al., 2001]. What is still unclear, however, is where in the brain taste and olfaction interact. Since eating is often driven by the hedonic value of food, there is likely to be a considerable overlap between the neural substrates of the sensory perception of food and the brain's representation of reward. Besides hedonic values and caloric intake, the body's nutritional status also affects the level of brain stimulation. There are also many supplementary stimuli involved in the digestive tract, ranging from motor cortex stimulation (chewing, swallowing) to effects related to satiation. On top of this, the release of hormones and gut-peptides before (e.g. CCK, PYY or GLP-1), during

50 Principal Scientist Radiology, Leiden University Medical Center.

or after food intake not only underlies these brain responses but also interferes with them (see also subsections 2.3.1 and 2.5.2).

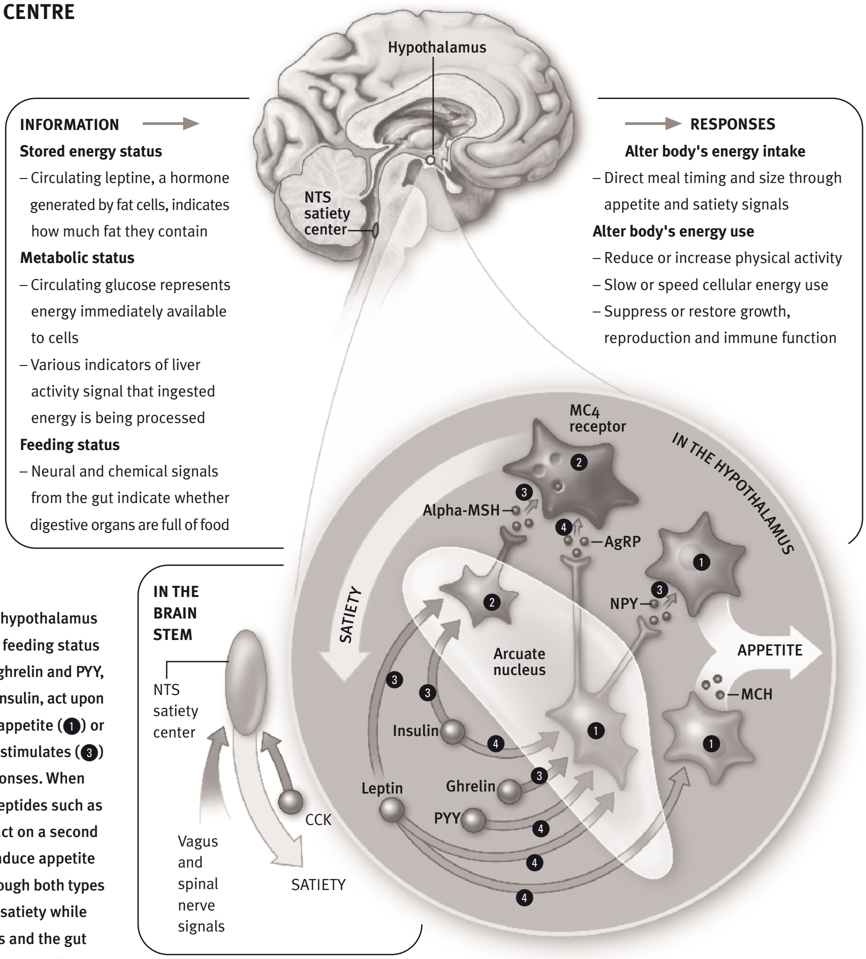
### The hypothalamus

The role of the hypothalamus in regulating energy homeostasis has been well established. Researchers have made remarkable progress in recent years in understanding of the neurobiological complexity of the hypothalamic pathways involved in the regulation of satiation and body weight [Tatarinni and DelParigi, 2003]. There are some technical problems involved in using functional neuro-imaging techniques to study the human hypothalamus, mostly related to spatial resolution: it is an organ located deep in the midbrain, lining

**Figure 8**
*The brain as command center.*
*Source: [Popkin, 2007].*

**THE BRAIN AS COMMAND CENTRE**

The human brain regulates weight by integrating information about the body's energy needs and the status of its stores, then initiating changes in behaviour and energy processing in response. Specialized brain areas stimulate feelings of appetite or satiety to cause more energy, in the form of food, to be taken in or to terminate a meal. Over time, the brain can also raise or lower the body's overall energy use and reallocate energy away from systems, such as reproduction, that are not essential for short-term survival.




**Appetite Control**
In the arcuate nucleus (ARC) of the hypothalamus (far right), indicators of energy and feeding status in the form of gut peptides such as ghrelin and PYY, and hormones including leptin and insulin, act upon groups of neurons associated with appetite (❶) or satiety (❷). Each substance either stimulates (❸) or dampens (❹) the neurons' responses. When stimulated, the ARC cells release peptides such as NPY, AgRP and alpha-MSH, which act on a second set of hypothalamic neurons that induce appetite or satiety. Leptin and insulin act through both types of cells simultaneously to promote satiety while suppressing appetite. Nerve signals and the gut peptide cholecystokinin (CCK) also communicate feeding status directly to the nucleus tractus solitarus (NTS), a satiety centre (right) in the brain stem.

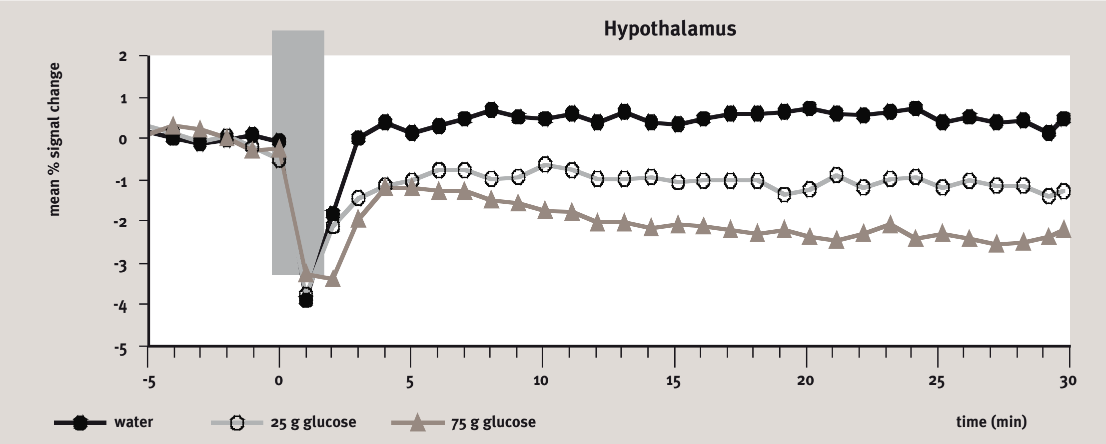



**Figure 9**
*Decrease in hypothalamic BOLD signal after oral ingestion of a glucose load. Shaded area indicates the drinking period. Adapted from [Smeets et al., 2005a].*

the lateral walls of the third ventricle and surrounded by a very rich vascular network. Despite these limitations, a number of studies have used functional imaging to study the hypothalamic response to a meal. It is known now that the responses of the neurons in the caudolateral orbitofrontal cortex taste area and in the lateral hypothalamus are modulated by satiety, and that neural activity may be related to whether a food tastes pleasant and should be eaten [Rolls, 2006]. Other research reports that seven to twelve minutes after administering a glucose load, fMRI detected a profound and sustained (approximately ten minutes) decrease in neural activity in two distinct regions of the hypothalamus (possibly corresponding to the ventromedial nucleus and paraventricular nucleus) [Liu et al., 2000]. Furthermore, the BOLD signal response[51] in the hypothalamus — once again after administering a glucose load — lasts at least thirty minutes and the level of response is dose dependent (see Figure 9).

These findings concur with a similar decrease in neural activity in the hypothalamic region in response to a liquid formula meal, observed by PET measurements of local neural activity [Tataranni et al., 1999]. The exact neurophysiological mechanisms underlying this finding are unclear. However, the decrease in BOLD signal after administration of a glucose load indicates a decline in neural activity in the hypothalamus. It is possible that administering glucose directly inhibits hypothalamic neural activity, which may be elevated in a state of hunger. Alternatively, the glucose may activate inhibitory pathways (i.e. prefrontocortical hypothalamic pathways), which in turn suppress the neural activity of the hypothalamus. It is also unclear which direct physiological process or response associated with the intake of glucose (i.e. insulin, gut hormones or autonomic nervous system afferent signals) mediates the hypothalamic response observed. Caloric intake or sweet taste alone do not inhibit hypothalamic neural activity [Smeets et al., 2005b]. At present, no specific

51 BOLD (Blood Oxygen Level Dependant) is the signal response measured in fMRI to observe which areas in the brain are active at any given time.

hypothalamic data are available on the pleasantness or taste of food or on sensory-specific satiation.

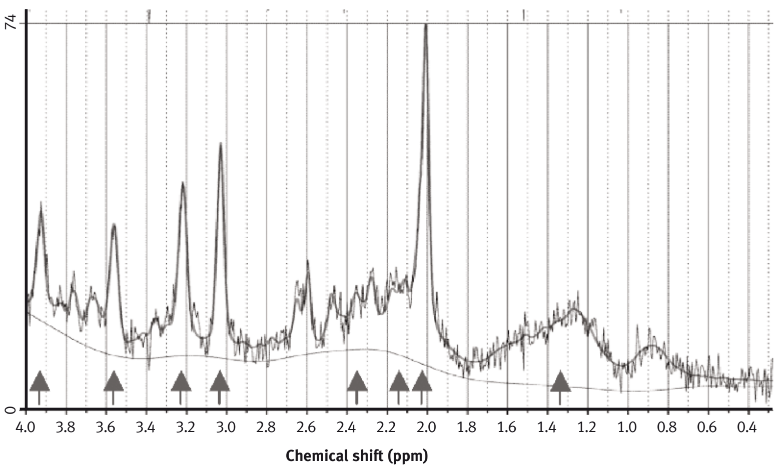
We can expect to see growing interest in the hypothalamus in the next decade, as both fMRI and PET studies have also shown that hypothalamic activity in obese individuals decreases significantly after a meal, compared with lean individuals [Gautier et al., 2000; Matsuda et al., 1999]. This may indicate that the hypothalamus plays a role as biomarker for satiation, suggesting a new target for research on the neurofunctional features of normal and abnormal eating behaviour.

New imaging techniques such as magnetic resonance spectroscopy (MRS) may become important in this respect. MRS provides information about metabolic processes in the living human brain, such as the concentration of N-acetyl aspartic acid (a putative marker of viable neurons), glucose transport in the grey and white matter, the neural tricarboxylic acid cycle (TCA), and the release of neurotransmitters (i.e. glutamate, glutamine, gamma-aminobutyric acid (GABA)) in the living brain. MRS has only a limited ability to detect processes that occur in small concentrations and does not have the spatial resolution required to distinguish subtle changes from noise. Nevertheless, recent studies have indicated its usefulness in monitoring changes in hypothalamic neurotransmitter release (i.e. glutamate, NAA-glutamate) in real time after administration of a glucose load. An example of a hypothalamic MR spectrum is shown in Figure 10. The advantage of MRS is that it exposes mechanisms that are related more directly to the neural response than PET or fMRI.

## Future challenges

Most studies investigating the effect of food processing on the brain have applied whole-brain fMRI or whole-brain PET. The fundamental advantage of

**Figure 10**
*MR spectrum of the hypothalamus. The arrows at the bottom of the spectrum (X-axis) refer to the specific MRS visible metabolites indicated in the table at the right. Y-axis illustrates relative metabolite concentrations.*




| | |
|---|---|
| 1.33 ppm: | Lactate |
| 2.00 ppm: | NAA |
| 2.10 ppm: | NAAG |
| 2.35 ppm: | Glu/Gln |
| 3.05 ppm: | Choline |
| 3.22 ppm: | Creatine |
| 3.55 ppm: | Myoinositol |
| 3.95 ppm: | Creatine |

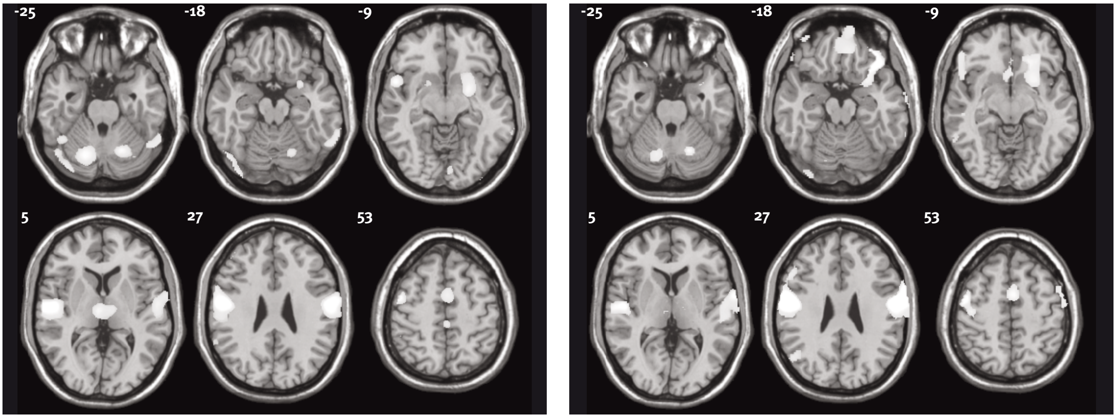



**Figure 11**
*Brain response (in white) to the taste of chocolate in hungry subjects (left) and subjects satiated with chocolate (right). Adapted from [Smeets et al., 2006].*

this approach is that we can study the entire system rather than restricting our investigation to pre-selected regions of interest. An fMRI of differences in sensory-specific brain response is shown in Figure 11. This figure shows the brain response to the taste of chocolate of hungry subjects and of subjects satiated with chocolate. The brain responses of the hungry subjects were located in the cerebellum, whereas in the satiated subjects the specific signals were located in the frontal parts of the brain.

The whole-brain approach does have one disadvantage: the multifactorial effects of eating may produce inexplicable responses. In terms of whole-brain fMRI or PET, the challenge facing scientists in the next decade is to develop controlled study designs in which only a very limited number of food or eating-related variables are modified.

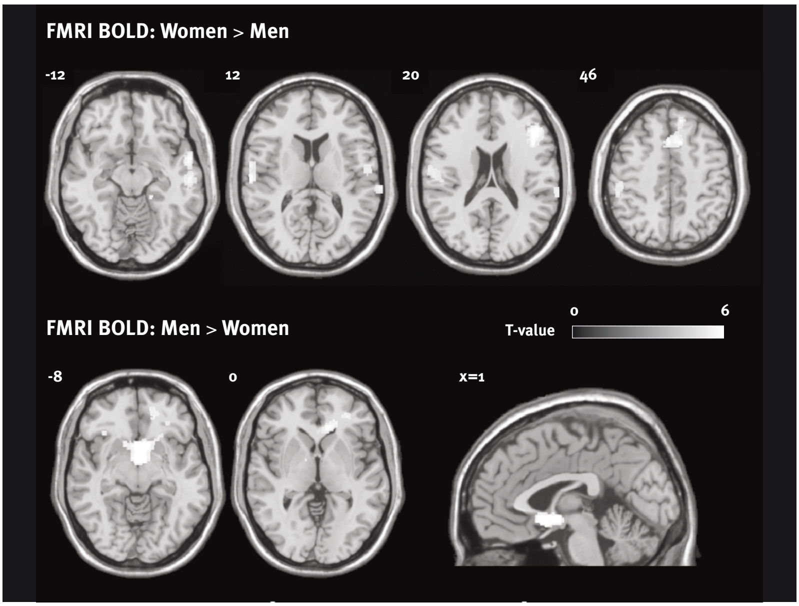



**Figure 12**
*Differences in brain response to the taste of chocolate between men and women (in white). Adapted from [Smeets et al., 2006].*

Another factor that must be considered in future is that men and women differ in their neural response to food. Figure 12 shows the fMRI BOLD response to the taste of chocolate by gender. Any research into the neural correlates of obesity or eating disorders must take hormonal differences between men and women and the phase of menstrual cycle into account.

### 2.4.2 Adjusting food patterns to influence satiety or food intake

*Kees de Graaf*[52]

Certain food patterns obviously have a strong impact on satiation and satiety, i.e. the regulation of food intake. It is easier to overeat some foods — i.e. take in more calories — than others, for example chocolate versus spinach. In general people will ingest more calories from a high energy-density diet than from a low energy-density diet. A vast amount of work has been done in the last twenty years to determine the effect of different properties of food on satiation and satiety.

Individual food patterns develop from metabolic processes that drive hunger, and from sensory processes involved in food selection (see Figure 13). We get hungry every couple of hours. The feeling of hunger is unpleasant and this creates a strong drive to search and ingest food. The processes leading to hunger are responsible for the energy balance; in general, human beings have enough of an appetite to maintain their energy balance. Humans are more sensitive to energy deficits than to energy surpluses.

Sensory factors are responsible for food selection. We select the foods that we 'want' or 'like' most. However, repeated exposure to any particular food reduc-

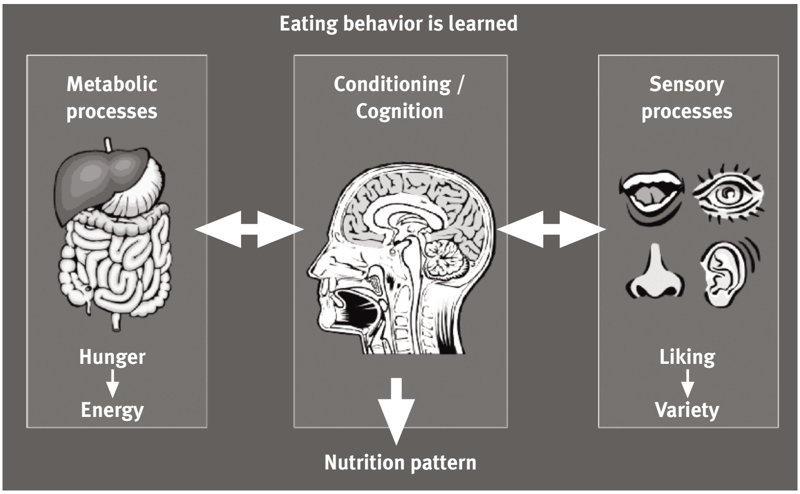



**Figure 13**
*Three different factors (i.e. metabolic and sensory processes and food conditioning) influence our eating behaviour.*

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es its reward value. For example, we truly enjoy our first cup of coffee in the morning, we like the second cup less, and after our third cup, most of us say no to more coffee. This phenomenon, sensory-specific satiety, is not caused by the energy content of food but by its sensory properties (see also subsection 2.3.3). Sensory-specific satiety is the driver behind variety in the diet.

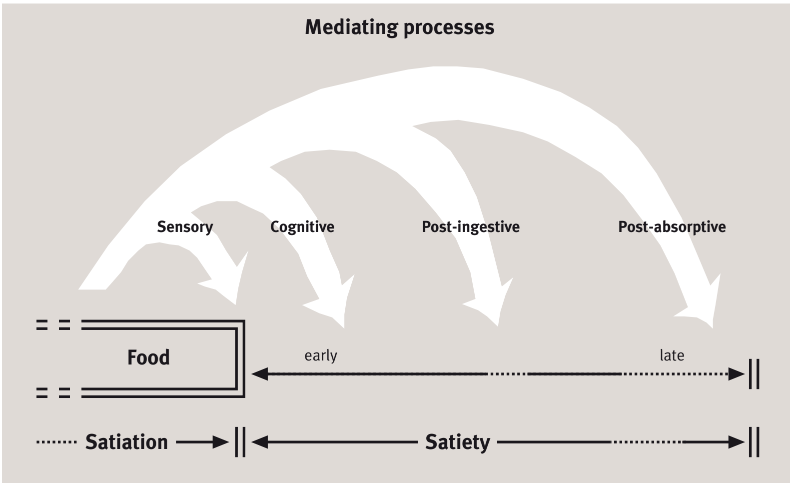
The sensory properties of the food we are eating are linked to their metabolic impact on the brain (see also subsection 2.3.1). This is how we learn that certain foods with certain sensory properties have particular satiating properties, e.g. we know that we should eat two cheese sandwiches for breakfast if we want to remain satiated until lunch. These learning mechanisms form the basis of our food and nutrition pattern.

A food pattern consists of eating occasions.[53] Within the context of energy intake, we can distinguish between the factors that determine meal termination (satiation) and the factors that determine meal initiation. This idea is nicely reflected in Blundell's satiety cascade (see Figure 14). Total energy intake is determined by eating frequency and the amounts eaten on every eating occasion. Before dealing with the effect of the separate properties of food on food intake and meal termination and initiation, it is worthwhile to consider the effect of specific eating patterns on food and energy intake.

### Eating frequency, snack intake and body weight

The popular media is fond of noting that industrialisation has brought on a food pattern of grazing, with meals becoming less important and snacks more important. The rising incidence of obesity has at times also been attributed to more frequent snacking, especially high energy-density snacks such as crisps, chocolate and sugared soft drinks. Most of these ideas are not supported by

**Figure 14**
*Overview of mediating processes involved in the regulation energy intake, satiation (meal termination) and satiety. Adapted from [Blundell et al., 1987].*




53 Eating occasions are moments when someone eats a meal or a snack.

actual scientific data, however. The percentage of energy derived from snacking has been relatively constant in the past few decades. In the Netherlands, for example, energy intake from snacking in young adults was about 32% in 1987/1988 and 33% in 2003. Data derived from large food consumption surveys in the USA confirm this finding [Kant and Graubard, 2006].

Cross-sectional epidemiological data offer a mixed picture regarding the effects of eating frequency on body weight. There are few prospective studies on snack intake and body weight changes. One seven-year follow-up study [Philips et al., 2004] showed no effect of energy-dense snack consumption in pubertal girls. With regard to soft-drink consumption, the situation is different. A recent review [Malik et al., 2006] suggests a positive relationship between sugared soft-drink consumption and body weight.

The picture that emerges from controlled intervention studies is that snacking does not lead to weight gain per se. It is the nature of the snacks that plays a role here. Mandatory snack consumption did not lead to weight gain [Kirk, 1997; Whybrow et al., 2007], but snacks consumed as liquid calories, for example in soft drinks, do lead to a positive energy balance [Raben et al., 2002].

In summary, there is no clear trend in the energy derived from snacks. The effects of snacking on the energy balance depends on the energy density and liquid-solid state of the snack. Liquid calories may lead to weight gain.

### The satiating effect of food properties

Foods differ in their physical-chemical composition, and such properties have a major impact on a food's satiating capacity; for example, we feel fuller after eating half a kilo of apples than after drinking the same amount of apple juice. A large number of short-term and long-term studies have highlighted a number of important properties in this respect. These are: energy density (including weight and volume), macronutrient content, fibre content, and texture. Researchers are exploring a more detailed classification in term of different types of carbohydrates (e.g. low and high glycemic), proteins, and fats.

Other research is focusing on the satiating efficiency of particular functional ingredients that are added in smaller quantities to foods. There is a whole range of dietary supplements on the grey market that contain a variety of such substances as CLA (conjugated linoleic acid), hydroxy citric acid with chromium, and products such as guar gum pills, tea extracts, etcetera. Until now, there has been little scientific evidence supporting the efficacy claims of any of these ingredients.

Calorie for calorie, high energy-dense foods are less likely to satiate than low energy-dense foods [Ledwike et al., 2006]. This observation is based on the observation that short-term food intake — when someone is hungry — is regulated mainly by weight and volume cues, and not by energy cues. Many studies have shown that people feel equally satiated after preloads[54] with equal weights and covert variations in energy content [e.g. De Graaf, and Hulshof, 1996]. Energy intake compensation is also far from perfect. All this implies that people are not good at detecting covert energy differences between various foods.

With respect to the four macronutrients, studies have demonstrated a hierarchy in their satiating efficiency: protein is more satiating than carbohydrates, carbohydrates are more satiating than fats, and fats are more satiating than alcohol. The low satiating efficiency of fat may be related to its high energy density. Alcohol has the lowest satiating efficiency; meals taken with alcohol have higher energy levels than meals taken without alcohol. After alcohol is ingested, energy intake during a later test meal does not decline. Alcohol hence acts as an appetizer. Fibre has a positive effect on satiety. Foods with a high fibre content are more satiating than foods with a low fibre content, although it is not yet clear precisely why that is so.

Solid foods have a higher satiating efficiency than liquid foods. This finding has been confirmed by many studies. Solid foods also lead to a better energy intake compensation than liquids. The literature suggests that humans are better equipped to 'sense' calories in solid product than in liquid products. One possible explanation for the difference between liquid and solid food is that solid foods are generally eaten much more slowly than liquids. For example, eating 500 grams of apples takes an average of seventeen minutes, whereas consuming 500 grams of apple juice takes only one and a half minutes [Haber et al., 1977]. Oral sensory exposure while consuming a solid is higher than while consuming a liquid. Longer sensory exposure may facilitate a learning process between sensory signals and metabolic consequences.

In summary, foods with a higher satiating efficiency generally have a lower energy density, a higher weight or volume, and a high fibre content. Future research will focus on designing foods that produce a higher satiating efficiency per calorie.

### Food properties involved in meal termination and satiation

As defined earlier, satiation is the process that brings a meal to an end. Satiation determines the size of an eating occasion. Verbal reports on the processes that bring a meal to an end indicate that 'fullness' and 'boredom with taste' are two major reasons to stop eating [Hetherington, 1996; Mook

54 Food or beverages taken before a meal.

and Votaw, 1992; Tuomisto et al., 1998]. These reasons may vary depending on whether we are dealing with a single food or a composite meal. Boredom is more likely when a single food is involved; fullness may be more important for composite meals.

Satiation is important because it determines meal size. Within the context of energy balance and obesity, it is instructive to note that there is no close relationship between eating frequency and body weight [e.g. Bellisle et al., 1997; Whybrow et al., 2007]. As obese people ingest more energy than non-obese people, the implication is that meal size may be the key factor in the over-consumption of energy in obese people.

Before focusing on the food properties that affect satiation, we should remind ourselves that in real life, most eating occasions end owing to environmental factors or cues. For example, food consumption increases with portion size, and in most cases we finish our plates (see subsection 2.4.3).[55]

Researchers measure satiation by analysing the 'ad libitum'[56] food consumption of particular experimental foods under standardised conditions. The ad libitum consumption of foods can vary hugely. For example, in a study on sensory-specific satiety [Weenen et al., 2005], the subjects were observed to eat an average of seventy to eighty grams of savoury cheese cookies, whereas they ate about five times as much weight in pears in slightly sugared syrup. This was not due to differences in liking, as they liked the pears and biscuits about the same.

It is clear that sensory factors play a major role in satiation. Many studies have shown that palatability (i.e. sufficiently agreeable in flavour to be eaten) has a strong impact on ad libitum food intake. This finding emerged in both controlled experimental studies [De Graaf et al., 1999] and more real life studies [De Graaf et al., 2005]. Higher palatability scores resulted in higher food intakes.

The satiety cascade also shows that cognitive factors may play an important role in meal termination. After consuming thousands upon thousands of different foods throughout our lives, we gradually learn to estimate the satiating effects of what we eat. We 'know' that we need to consume two slices of bread and cheese for breakfast to keep us going until lunch. These learning mechanisms determine our expectations about the satiating properties of foods, and probably also determine how much we put on our plate [Brunstrom, 2007].

A crucial factor in this learned response (i.e. expectation) is the energy den-

55 A study in which US soldiers consumed about 5700 main meals and 8800 snacks revealed that they ate 100% of their portion 80-90% of the time. Even when they were indifferent to the food (giving it a five on a nine-point hedonic scale), they still ate 87% of their meal on average [De Graaf et al., 2005].

56 Ad libitum means providing a subject free access to food, so he can self-regulate intake according to his needs.

sity of the product. In the example give above, where the subjects consumed five times more pears than cheese biscuits, the energy density of the savoury biscuits (2268 kJ/100 g) was about eight times higher than the energy density of the pears (272 kJ/100 g). At first glance, it seems that the standard portion sizes of energy-diluted foods (e.g. many liquids) are much larger than the standard portion sizes of energy-dense foods (e.g. chocolate, cheese, peanuts, etc.). No systematic data has been found linking standard portions sizes to energy-density values, however.

Experimental data on the effect of varying energy density on ad libitum food intake (with matched sensory properties) suggest that people are slow to respond to covert changes in energy density [Blundell et al., 1996; Kendall et al., 1991; Lissner et al., 1987]. This may be particularly true of liquid foods and fast foods that do not induce strong sensory cues [Ebbeling et al., 2004; DiMeglio and Mattes, 2000; Raben et al., 2002]. The absence of clear sensory cues may prevent people from learning to associate oral sensory cues during eating with post-ingestive metabolic consequences (see Figure 13).

The texture of foods is also important in satiation. As stated earlier, in an ad libitum setting, people consume more liquids than solids. This is because they can consume liquids more rapidly than solids and semi-solids [Zijlstra et al., 2008], probably because the swallow size is larger with liquids than with solids and semi-solids. These observations imply that research into the effects of food properties on meal termination should control for texture.

People have certain ideas about the satiating effect of particular foods. These learned responses generally concur with other sensory or environmental cues. For example, when we empty a bottle of soft drink, the weight of the bottle gives us a clear cue of how much we have already consumed. In the following subsection we look more closely at these external cues.

In summary, the amount that we eat of a particular product is influenced by a variety of factors related to the properties of the food and the context in which it is consumed. In general, the ad libitum consumption of food is a learned response based on associations between the sensory properties of a food and its metabolic consequences after ingestion. Researching the effect of properties on meal termination requires us to vary one factor while keeping other important factors constant. When studying satiation, we need to consider the palatability, energy density, and texture of foods, the motivational state (hungry versus satiated) of the subjects, potentially important environmental cues (e.g. visual cues, plate size, effort involved) and cognitive factors such as learning effects.

### 2.4.3 Situational norms influencing food intake

*René de Wijk*[57]

As stated in the previous subsection, the amount of food we must consume to feel satiated is related not only to the energy content of the food in question but also to the way the food is presented and the ambience in which it is consumed. Behavioural research has led some researchers to assume that hunger and satiety in humans play a relatively small role in everyday eating in modern Western countries. Instead, eating behaviour is driven primarily by personalized and situational norms. Personalized norms are rules that individuals develop to help themselves determine how much is appropriate to eat in a given situation. Situational norms are derived from the situation in which one eats, and include, for example, portion size and social influence (e.g. does one eat alone or with others?), both of which exert a powerful influence on food intake [Herman and Polivy, 2005]. This subsection focuses on these various situational norms.

#### Situational norms derived from the food itself ('food norms')

As we found out in the previous subsection, liquids are less satiating than solids. Calories derived from beverages have even been implicated as important contributors to obesity [DiMeglio and Mattes, 2000]. When asked, consumers indicate that liquids are less satiating than semi-solid food, even prior to ingestion. This suggests that consumers derive expectations of the food's satiating properties based on visual and perhaps olfactory and auditory cues. Foods also become more satiating when their volume increases, for example when air is mixed into a semi-solid food like yoghurt [Rolls et al., 2000]. Single foods are typically more satiating than a variety of foods (the well-known 'dinner buffet' phenomenon), an effect known as sensory-specific satiety [Rolls, 1986].

#### Situational norms derived from the way the food is served ('serving norms')

The amount of food people consume before reaching satiety depends on plate size: the larger the plate, the more they eat [Wansink, 2006]. Similarly, the amount of liquid they consume depends on the size and shape of the glass. In other words, food consumption increases with portion size (the well-known 'super-size' effect of McDonalds). Consumers also use cues on the amount of food left to regulate their food intake. A very clever study showed the importance of such concurrent visual cues in meal satiation [Wansink et al., 2005]. It demonstrated that the ad libitum consumption of soup was influenced by visual cues indicating how much soup was left in the subject's bowl. In one

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condition, researchers partly refilled the bowl through an invisible tube. These subjects ate about 73% more than the control group, even though their perceived consumption was about the same. The study illustrates that people use many environmental (instead of internal) cues to decide whether or not to continue eating.

### Situational norms derived from the social context ('social norms')

The amount of food someone consumes typically increases dramatically with the number of people sharing the table [Stroebele and De Castro, 2004]. Eating is social behaviour and an individual's eating behaviour is modelled on that of others. This is especially true of children, who learn their eating behaviour by observing their parents, siblings and peers (which may explain the close correlation between parental and off-spring obesity [Johnson, 2000]). Modelling remains important throughout adulthood. How fast we eat and how much depends on how fast other people at the table are eating, especially if they are sexually attractive [Pliner and Chaiken, 1990]. Whether our table companion is on a diet is important [Polivy and Herman, 1979], but apparently not his or her body weight [Rosenthal and McSweeney, 1979]. Modelling behaviour not only affects the amount consumed and the rate of consumption but also the choice of foods. Neophilic or neophobic behaviour on the part of others, i.e. whether they love or hate novelty, has been shown to affect the subject's choice behaviour, irrespective of whether the subject himself is neophilic or neophobic [Hobden and Pliner, 1995].

### Situation norms derived from the ambience ('ambience norms')

The amount of food we eat depends on the location in which it is consumed. Food intake in a fast-food restaurant differs considerably from food intake in a regular restaurant. Moreover, when we eat food in front of the television or popcorn while watching a movie, we typically consume larger quantities than we would if we ate elsewhere. Watching television or a movie distracts us from the act of eating, suggesting that attention plays a role in food intake.

In short, these results demonstrate that the amount of food consumed, and the way it is consumed, are partly determined by situational factors and not by the actual nutritional needs of the consumer. This means that we may be able to alter consumption behaviour by changing the situational factors. That may not be as easy as it sounds, given that situational factors determine our modern lifestyle and behaviour to a considerable extent. In order to change food consumption behaviour, we will probably need to change the interaction between the consumer and his environment.

**Example IV**

**Older adults who took folic acid supplements for three years had a sharper memory and processed information faster than people who did not take this supplement. Folic acid appears to slow down the normal age-related decline of these cognitive functions.**

# Folic acid keeps the aging mind sharp

Along with vitamin B6 and vitamin B12, folate – the natural form of folic acid – lowers the concentration of a compound called homocysteine in the bloodstream by converting it into harmless molecules. Homocysteine damages the lining of blood vessels, promotes blood clotting and reduces blood vessel flexibility, leaving blood vessels more vulnerable to atherosclerosis. Previous studies have indicated that lowering blood homocysteine levels may have beneficial effects on cardiovascular health. This, in turn, may positively affect cognitive performance.

People with low folate levels and raised concentrations of homocysteine are more prone to cognitive deterioration. Whether this is caused by the abnormal levels of these compounds in the blood has not yet been determined. In fact, several studies have shown that increased folic acid intake has no effect or even an adverse effect on cognitive performance. These were mostly short-term or small-scale trials, however, and the tests were not sensitive enough to pick up cognitive changes.

Scientists from Wageningen University and Research Center and Maastricht University randomised 819 men and women of fifty to seventy years of age. They all had raised blood homocysteine levels and normal vitamin B12 levels. Half of them were given a daily dose of 800 micrograms of folic acid, for three years. The other half were given a placebo pill. At the beginning and end of the study, research assistants who did not know which treatment the participants had received, assessed their word learning performance, selective attention, information processing speed, word fluency, and how quickly the participants could switch between concepts.

At the start of the study, the placebo group and the folic acid group scored the same on the various tests. After three years, the folate concentration of the folic acid group was around six times higher than that of the placebo group. The blood homocysteine levels had decreased by 25 percent. Memory performance in word learning and information processing speed were significantly better in the folic acid group than in the placebo group. The folic acid group

Original publication: Durga et al. (2007). *Lancet*, 369, 208 could recall more of the fifteen words they had learned than the placebo group, both immediately after the learning phase and twenty minutes later. They could also name more animals within one minute, indicating that their verbal fluency was better than the placebo group's.

Long-term folic acid supplementation improves various domains of cognitive function in people with raised homocysteine levels in their blood. Whether this effect will be as profound in the normal population remains to be seen.

## 2.4.4 Future trends in science, industry and policy

*Ira van Keulen, Kees de Graaf*[58]*, Jeroen van der Grond*[59]

Our current food environment offers us a huge variety of palatable, readily available, high energy-density foods that are furthermore designed for rapid consumption. Inevitably, that environment is conducive to a positive energy balance or weight gain. The wish to change consumption behaviour and increase mobility in order to prevent overweight is widespread, including in the food and health industry. A recent survey by the American Grocery Manufacturers Association (GMA) indicated that 92% of American food companies are reformulating and introducing new products with reduced fat or sugar. In the past five years they have introduced more than 10,000 healthy, nutritionally improved food products. Besides healthier traditional products, there is also a huge market for weight management supplements, worth 3.93 billion US-dollars in the United States alone — not surprising when one considers that 40% of the American population claims to be on a diet. A survey commissioned by DSM recently revealed that consumers were especially interested in products that 'reduce your appetite'. It is highly likely that the food industry will take a more proactive approach to the weight control trend in future.

### Product development

Some foods are more satiating than others because they have a lower energy density, a higher weight or volume, or a high fibre content. In future, more and more products will be designed for higher satiation per calorie; in other words, they will increase the sense of being full after eating and help consumers avoid feeling hungry and 'grazing' between meals. The main strategies for creating satiating products are to add fibre or protein. Fibre is particularly interesting in this respect; it may be more satiating because it slows down the rate at which the stomach empties, thereby allowing sustained absorption of the nutrients (carbohydrates, protein or fats) involved in satiety. It may also work because it increases the bulk in the gastrointestinal tact (or gut) by absorbing water. Most of the research on satiety has focused on people of normal weight thus far, but future research and development will probably also study overweight and obese people. Neuro-imaging research may shed some light on how obese consumers respond to satiating products.

Satiating food products are clearly not the only solution to the problem of overweight and obesity. Lifestyle factors, such as too little exercise and too much food, also play a crucial role. A reductionist approach that focuses on functional food alone is unlikely to succeed. Furthermore, as with brain food

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(see section 2.2), the guiding principle behind the development of value added food designed to have a satiating effect must be evidence-based performance. Functional food developers must balance appropriate and relevant research with the necessary marketing. Randomised clinical trials will therefore be important, especially if the food industry wants its hunger management products to be taken seriously. Unfortunately, the US is less stringent about product claims and marketing than the EU, posing a problem for many international food companies.

### Interdisciplinary cooperation in research and product development

This section has shown that the physiological, psychological and social mechanisms behind food intake are quite complex. It will not be easy to develop interventions that keep the Body Mass Index (BMI) of the developed and developing world under control. Success will depend on closer cooperation between various parties (science, industry and government, including regulatory bodies) and on interdisciplinary research and development strategies.

Cooperation between nutritional science and neuroscience looks particularly promising. For example, nutritional studies carried out in the past ten to twenty years have shown that various food properties have a major effect on food intake. Today researchers are increasingly exploring the biological mechanisms through which hunger and satiety are influenced. Research and product development focuses on the food properties that bring meals to an end and postpone subsequent eating times. The cognitive neurosciences have made only a minimal contribution to this research so far, but work on the satiating effect of foods could benefit enormously from imaging research into the brain's responses to food. As mentioned in the first subsection, such techniques can help to identify the effects of food on those parts of the central nervous system involved in food intake regulation. There is still a lot we do not know about the mechanisms behind these processes, in particular why they vary so much between individuals.

Much of our eating behaviour is unconscious. More traditional research methods rely on subjective measures, for example asking respondents how hungry they feel at a given moment or watching how much they eat. The advantage of neuro-imaging techniques is that they measure directly how the brain is involved in eating, and are therefore more objective.

### Future challenges for neuro-imaging

The main challenge for PET and fMRI studies of the future is that food intake has a multifactorial effect on the brain and that out of that mass of neural signals, those signals have to be isolated that are specifically related to the

process under investigation. Three lines of research can be envisaged:
- Investigating the neural correlates of hunger and satiation.
- Investigating differences in the way normal individuals and those with a specific disorder (for example obesity) respond to food.
- Investigating and unravelling the brain mechanisms underlying the pleasantness and reward of food in various aspects, like taste, odor, look or texture.

The first two lines of food-related neuroresearch are relatively straightforward in terms of their design. The stimuli and conditions are kept constant while the physiological states such as hunger and satiation or the type of subject are varied. This approach will soon make it possible to study differences in food response not only in obese subjects but also in subjects with eating disorders such as anorexia nervosa or bulimia nervosa. Untangling the complex neural response of eating will require much more effort in the next decade.

#### Nutritional advice

With research and development focusing on functional food products designed to give consumers a feeling of fullness, governmental bodies may offer special nutritional advice on the satiating effect of regular food. Such bodies could also help to dispel myths about overweight, for example the myth that high energy-dense snacking is behind the prevalence of obesity today (see subsection 2.4.2).

More difficult and complicated, but just as important, is to advise on the influence of situational norms on eating behaviour. There has already been a great deal of research in this area, but many of the findings — for example on portion size, tablescape, distracting circumstances and the other psychological mechanisms mentioned in subsection 2.4.3 — have not filtered through to the general public.

## 2.5 The case of obesity

*Bram Felius[60], Henriette Delemarre–van de Waal[61]*

The previous section focused mainly on the food intake of people at a 'normal' weight. The neural mechanisms involved in excessive food intake or food addiction appear to be somewhat different, and we have therefore included a separate section on obesity in this chapter. The first subsection explains what obesity is (prevalence, classification and consequences). The second subsection describes some of the neuro-endocrine mechanisms behind overweight

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and obesity. Interestingly, while the brain steers our eating behaviour, our food patterns influence our brain in turn. Subsection 2.5.3 describes the negative effects of overeating on the brain and cognition. The following subsection looks at how pharmacological and other brain-based interventions such as electrical stimulation and neurofeedback are used to treat obesity. The section once again ends by considering future trends in science, industry and policy.

### 2.5.1 Features of obesity

Obesity has now become the most prevalent nutritional disease in the developed world. And it is a disease that is spreading; in developing countries, where underweight is still a major problem, the transition to a Western behavioural and dietary lifestyle appears to be replacing the problems of undernutrition with those of over-nutrition.

Both in the United States and the Netherlands, the greatest increase in body weight has occurred in children and adolescents who are in the upper half of the Body Mass Index (BMI) distribution[62], with the BMI mean increasing more than the median. This suggests at least two possibilities: either the genes that predispose toward obesity only occur in approximately 50% of the population, or the factors that influence the occurrence of obesity are discrete and act on only half of the population. To find out which possibility is correct, we need to know more about the genetic and environmental mechanisms of obesity.

In the past, the onset of obesity tended to occur in late puberty and young adulthood. Today, however, children are already becoming overweight and obese at a very young age, even in infancy. Eating behaviour, satiety and other behavioural components are programmed in early childhood, as the brain is developing. We need to know more about the relationship between these programming processes and brain development during periods of weight increase. Another important issue is to develop a classification system for obesity, so that underlying defects can be properly diagnosed and effective treatment strategies developed. Some types of obesity can already be distinguished, i.e. early versus late onset, pubertal onset, familiar or genetic forms and others, but more research is needed.

Obesity is a multisystem disease with potentially devastating consequences (for example cardiovascular risks and insulin resistance syndrome), even for young children. Type 2 diabetes — one of the most common complications of obesity and formerly unrecognised in children — accounts for as many as half of all new diagnoses of diabetes in some populations [Fagot-Campagna, 2000]. Glucose intolerance and insulin resistance is particularly common in severely obese children, irrespective of ethnic group. Other related disorders

62 The Body Mass Index is a statistical measure of an individual's weight scaled according to their height. A low BMI (<18.5) indicates underweight and a high BMI (>25) overweight or obesity.

**Figure 15**
*In Western countries people live in an 'obese society'. Food intake is driven not by our need for energy, but by abundance and the desire for food. Photo courtesy of Colin Rose, flickr.com.*

include pulmonary, hepatic, renal, muscoskeletal and neurological complications. All this results in a poor physical quality of life in obese adolescents. In addition to these somatic consequences, obesity is also associated with depression and dementia in adolescents [Goodman, 2002] (see subsection 2.5.3).

Eating behaviour and dieting history seem to play an important role in the pathophysiology of obesity, and may even indicate an eating pathology. Family habits associated with having breakfast and eating at the table with other family members without simultaneously watching television all influence the course of the body weight. Even in children, such eating disorders as binge eating[63] and night eating (formerly unrecognised) may be part of the problem.

Given the undesirable health consequences of obesity, it is important to understand why some people are unable to resist excessive eating. The theory is that impulsivity underlies the inability to control eating behaviour to some extent: an impulsive person may find it more difficult to resist food intake. Impulsivity appears to play a role in both the onset and the persistence of obesity. For example, obese children have weaker response inhibitions in stop-signal tasks and are more sensitive to rewards in gamble tasks than lean children. Not only do obese children generally appear to be more impulsive, but within a group of obese children, a high level of impulsivity is related to less weight loss during treatment. Treatment programmes might improve if impulsivity and inhibition control are taken into account.

Functional neuro-imaging provides an increasingly important tool for investigating how different regions of the brain work together to orchestrate normal

63 Binge eating is defined as recurrent episodes of binging without the compensatory behaviours to avoid weight gain as seen in bulimia nervosa.

eating behaviours, and in particular how they conspire to produce obesity and eating disorders [Jagust, 2007; Tataranni and DelParigi, 2003]. The following subsection briefly reviews what we know about the neural mechanisms behind excessive eating.

### 2.5.2 Neuroregulation of excessive food intake

Neurotransmitter and peptide signalling pathways play an important role in controlling food intake and body weight, so a more detailed understanding of the pathogenesis of obesity could ultimately guide the related treatment. These peptides and neurotransmitters are linked to the energy balance and fall into two categories. The first group increases energy expenditure and decreases food intake, and is therefore called catabolic.[64] The second anabolic group does the opposite: these peptides and neurotransmitters increase food intake and decrease energy expenditure.[65] This implies a feedback system designed to maintain a relatively constant level of adipose mass, i.e. fat tissue. These pathways are involved in normal eating behaviour, but may go awry and result in excessive eating and obesity.

It is not only these peptides and neurotransmitters that influence food intake; receptor expression and post-receptor signalling pathways are also of utmost importance. Neurons located in the hypothalamus — specifically the arcuate nucleus — and expressing the precursor molecule pro-opiomelanocortin (POMC) may play a key role in energy homeostasis. POMC is a precursor for endorphins and melanocortins. The latter play a dominant role in the suppression of appetite, suggesting that the melanocortin system is an interesting therapeutic opportunity.

POMC gene expression is diminished by leptin and insulin. Obese children may have high to very high leptin and insulin levels, indicating resistance to these hormones. The presence of concentrations of the leptin and neuropeptide Y (NPY) provides evidence that obesity is associated with neuroendocrine dysfunction and a high leptin and NPY ratio, which could be a useful marker for central obesity (i.e. 'apple-shaped' or 'masculine' obesity).

#### Food addiction

Some studies have supported the idea that the brain has the same response to stimuli related to eating as it does to other addictive stimuli such as drugs or alcohol. To understand food addiction, we should thus be taking research on drug and other addictions into account.

Addiction can generally be conceptualised as a disorder that progresses from impulsivity to compulsivity, with tension and arousal being displaced by anxiety

64 Classified as catabolic are $\alpha$-melanocyte stimulating hormone ($\alpha$-MSH), $\beta$-MSH, brain derived neurotrofic factor, corticotrophin releasing hormone (CRH), glucagons-like peptide 1 and 2, insulin, leptin, interleukin-1 (IL-1), interleukin-2 (IL-2), and many others.

65 Anabolic peptides and neurotransmitters include agouti-related protein, $\beta$-endorphin, dopamine, endocannabinoids, ghrelin, and neuropeptide Y.

and stress under prolonged exposure to the addictive substances. The neuroanatomical substrate for addiction is represented by the extended amygdala.[66] One interesting hypothesis is that many of the neuropharmacological effects of drugs, including their reinforcing effects, may be mediated by this circuitry.

The process of addiction also has a lot in common with the neural plasticity associated with natural reward learning and memory. Dopamine and glutamate appear to play a key integrative role in motivation, learning and memory and therefore model adaptive behaviour. In addition to the availability of the dopamine D2 receptor (DRD2), the polymorphism of the DRD2 gene also appears to play an important role in the pathophysiology of addiction. Changes in the neural pathways of reinforcement learning may therefore also play a role in obesity. The availability of DRD2 decreases in obese individuals in proportion to their BMI. Dopamine deficiency in obese individuals may therefore perpetuate pathological eating to compensate for the weaker activation of these circuits [Wang, 2001]. In other words, overweight persons constantly seek new rewards in food because they suffer from a dopamine shortage. At the same time, their brain compensates for the flow of dopamine after excessive eating by reducing the number of dopamine receptors. Whether treating obese individuals actually changes their neurological response is questionable. The abnormal response to meals may persist even in post-obese individuals [DelParigi, 2004].

Another important insight into addiction, one that is also related to the neural pathways and mechanisms behind reinforcement learning, is called 'incentive sensitisation'. This theory states that addiction sensitises the brain systems involved in the process of incentive motivation and reward for drugs and drug-associated stimuli. The sensitised systems do not mediate the pleasurable or euphoric effects of drugs (drug 'liking'); instead, they mediate a subcomponent of reward, known as incentive salience (drug 'wanting'). Incentive salience occurs when addictive stimuli begin to reinforce themselves and make people crave drugs, food, alcohol, etcetera. Incentive salience determines the value of incentives, and thus the associated control-seeking and instrumental behaviour. When neural systems that mediate incentive salience become sensitised, and when the incentive salience attributed to drug-taking and to associated stimuli becomes pathological amplified, then compulsive drug-seeking and drug-taking behaviour may ensue. Once again, the powerful effects of dopamine neurotransmission on motivated behaviour appear to play an important role [Berridge and Robinson, 1998; McClure, 2003].

Addiction research has focused on the construct of craving for the past few decades. Researchers have recently used imaging techniques such as fMRI

**66** The extended amygdala is a component of the amygdala which is part of the limbic system and responsible for memory and emotional reactions.

and PET in combination with the technique of cue-reactivity to detect brain regions involved in the pathogenesis of craving [Wilson, 2004]. Cue-reactivity involves exposing addicted individuals to stimuli designed to elicit craving while assessing associated changes in one or more response systems. Several brain regions have been linked to cue-elicited craving: once again, the amygdala, the anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC), and the dorsolateral prefrontal cortex (DLPFC). Activation of these regions has been reported frequently, but unfortunately the data are not consistent. In active drug users, cue-reactivity was found in two areas of the prefrontal cortex, i.e. the OFC and DLPFC, while in studies involving treatment-seeking users, no significant activation of the OFC and DLPFC was found. The OFC is a control centre that monitors our behaviour. People who have suffered damage to their orbitofrontal cortex are often unable to control themselves and act more impulsively than others who do not have this brain damage.

Decreased dopamine availability is associated with decreased metabolic activity in the prefrontal cortex, orbitofrontal cortex and cingulated gyrus. In active cocaine abusers who report craving, the orbitofrontal cortex and striatum are hypermetabolic, i.e. show an increased rate of activity. The same research postulates that increase of dopamine facilitates activation of these brain regions and therefore leads to craving. It turned out that subjects who experienced intense craving had increased absolute and relative metabolism in the right striatum and right orbitofrontal cortex, but this was not found in subjects who did not experience intense craving. This indicates that increasing the level of dopamine is not enough by itself to activate these frontal brain regions.

### 2.5.3 Possible effects of obesity on neural development and cognitive functions

Various brain mechanisms are involved in pathological food behaviour, but like undernutrition, obesity also has an impact on brain development and cognition. There has been some research on the direct or primary consequences of obesity for brain and cognitive development, and especially for IQ. Obesity is furthermore closely related to disorders such as depression or dementia, known as secondary consequences.

#### Primary consequences related to obesity

The British National Child Development Study, which commenced in the late 1950s, showed that a lower IQ in childhood is associated with obesity and weight gain in adulthood. This association remains after adjusting for childhood characteristics, including socio-economic factors. More worrisome is the reciprocal relationship: obesity may produce cognitive decline and is even linked to Alzheimer's disease and changes in brain structure.

Some studies [Ong, 2006] have shown an association between accelerated infant growth and a high risk of obesity, combined with insulin resistance during childhood. Early catch-up growth may interfere with the growth of other organs, including the brain. Another interesting study found that the level of compensatory growth following a period of undernutrition at a young age in zebra finches was associated with long-term negative consequences for cognitive function [Fisher, 2006]. In human twins, the early postnatal compensatory growth period (up to one year of age) correlates negatively with IQ [Estourgie et al., in press]. This effect of postnatal growth on childhood cognition was also found to persist beyond the age of nine years when adjusted for socio-economic factors [Pearce, 2005]. In summary, we have a lot to learn about the influence of growth (weight and height) on brain and cognitive development. One way to do so is to monitor brain development during different patterns of growth.

### Secondary consequences related to obesity

Many obese children exhibit depressive behaviour and appear to have a lower quality of life. The depression suffered by obese adolescents appears to be induced mainly by parent distress and peer victimisation. It is important to teach children how to cope with these factors in order to prevent or minimise depressive behaviour.

Obesity is also associated with an increased risk of dementia. Research has found that programming for obesity during pregnancy may contribute to the potential risk of developing Alzheimer's disease [Ross, 2007]. It appears that the more organ fat an individual has, the higher his risk of dementia (as a result of neurodegenerative, vascular or metabolic processes affecting the brain structures underlying cognitive decline and dementia).

### Neural synchronisation and obesity

One interesting finding that merits closer investigation is that neural synchronisation is altered in obese adolescents [Olde Dubbelink et al., in press].[67] Neural synchronisation is related to the communication between neurons. Oscillations are a prominent feature of neuronal activity, and the synchronisation of oscillations, which reflects the temporally precise interaction of neural activities, is a generally accepted mechanism for neural communication [Schnitzler and Gross, 2005].[68] The synchronisation of neural oscillations is thought to change when the communication between neuronal networks changes. For example, various studies on Parkinson's and Alzheimer's report significant changes in synchronisation, implying that changes in oscillatory brain communication may underlie neurological disturbances [Stam, 2006].

**67** We still do not know where in the brain neural synchronisation changes in obese people, nor do we have a precise denotation of this change.

**68** Synchronisation can be studied best by means of magnetoencephalography (MEG). This non-invasive technique provides highly accurate measures of the magnetic fields generated by electrical activity in the brain. These can then be used to study both the normal and pathological communication processes of the human brain.

## 2.5.4 Pharmacological and other interventions to treat obesity

So far two drugs, orlistat and sibutramine, have been approved for clinical use in adolescents of twelve years and older. Orlistat's primary function is to prevent the absorption of fats from food, which reduces caloric intake. Five out of six clinical trials have shown statistically significant reductions in BMI from baseline, ranging from 0.5 to 4 kg/m². In the United States, Orlistat is also offered in an over-the-counter form under the brand name Alli®.

Sibutramine prolongs the exposure of neurons in the brain to the neurotransmitters norepinephrine and serotonin, which reduces appetite. It has also been evaluated in six trials that demonstrated a statistically significant reduction in BMI up to 5.5 kg/m² (from baseline). Its side effects are more worrisome than with Orlistat: elevated blood pressure, increased pulse rate and depression. Another drug used in diabetes type 2, Metformin, has recently been evaluated for its effect on obesity. In small, short-term trials it produced only a modest reduction in weight and BMI.

Cannabis sativa (marijuana) increases hunger and food intake, especially for sweet and palatable (i.e. tasty) food. This process is mediated by the cannabinoid receptors. Cannabinoid receptors type 1 (CB1) are abundantly expressed in several areas of the brain (basal ganglia, cerebellum, hippocampus and cortex), and type 2 (CB2) in peripheral tissues.[69] Cannabinoid receptors (and their endogenous ligands[70]) seem to act as a neuromodulatory system that influences not only the central nervous system but also the endocrine and immune system. This neuromodulatory or endocannabinoid system may play an important role in regulating drug reward processes and in modulating cue reactivity. Blocking the receptor represents a novel approach to drug abuse treatment.

In animal models, CB1 mediates the reinforcing and motivational effects of heroin and heroin-associated cues, which can be influenced by a receptor antagonist such as SR141716A (i.e. rimonabant). CB1 antagonists generally appear to offer promising medications for drug dependence. For example, twice the number of motivated smokers treated with rimonabant quit smoking in a clinical trial than the placebo-treated subjects. In addition, subjects showed a marked reduction in weight during treatment. In a study of overweight adults, subjects treated with twenty milligrams of rimonabant over the course of one year showed a significantly greater improvement than the placebo group in terms of weight loss, waist circumference, HDL-cholesterol, triglycerides, insulin resistance and the prevalence of the metabolic syndrome. But rimonabant has not been approved by the American Food and Drug Administration (FDA) because there are concerns about the quality of the

69 Recent research has made it plausible that other receptors play a role [Begg, 2005].

70 Endogenous ligands are chemical substances produced by the body itself and capable of stimulating specific receptors.

safety data and psychiatric side effects such as depression and anxiety. Data has revealed a doubling of the risk of depression in the subgroup of patients who did not even have a history of psychiatric illness. Animal studies have shown that other receptor antagonists appear to have the same properties as rimonabant with respect to decreased food intake.

In short, new drug strategies are required that focus on regulating food intake. None of the drugs currently available produce more than a modest reduction in body weight, and behavioural programmes are only effective in the short term. Another approach to reulate food intake is the electrical stimulation of specific areas of the nervous system or the brain. High-frequency stimulation (HFS) — also known as deep-brain stimulation (DBS)[71] — has been used since 1997 as an alternative to lesions in functional neurosurgery for movement disorders. More recently, it has been used to treat obesity, but there are no clinical data as yet confirming that long-term HFS resets neural networks or induces profound modifications of functional organisation or synaptic connectivity. Vagus nerve stimulation (VNS) may be used to regulate satiety signals transmitted to the central nervous system by the vagus nerve. VNS uses a stimulator that sends electrical impulses to the vagus nerve in the neck through an electrode lead implanted under the skin. In theory — no clinical data are available — it should be possible to alter the vagus signal and modify eating behaviour.

Another interesting strategy in treating patients with eating disorders or obesity is neurofeedback. Neuro-endocrine regulation of food intake appears to be important in learning preferences, inducing hunger and satiety. These regulatory mechanisms could prove to be a powerful tool for treating patients with abnormal eating patterns, with neurofeedback methods being used to learn to control food intake. Neuro-imaging techniques such as EEG or fMRI visualise active parts of the brain, giving patients the opportunity to train and control them. The relevant brain area in this case may be the insula, which has been implicated in food and drug cravings.

### 2.5.5 Future trends in science, industry and policy

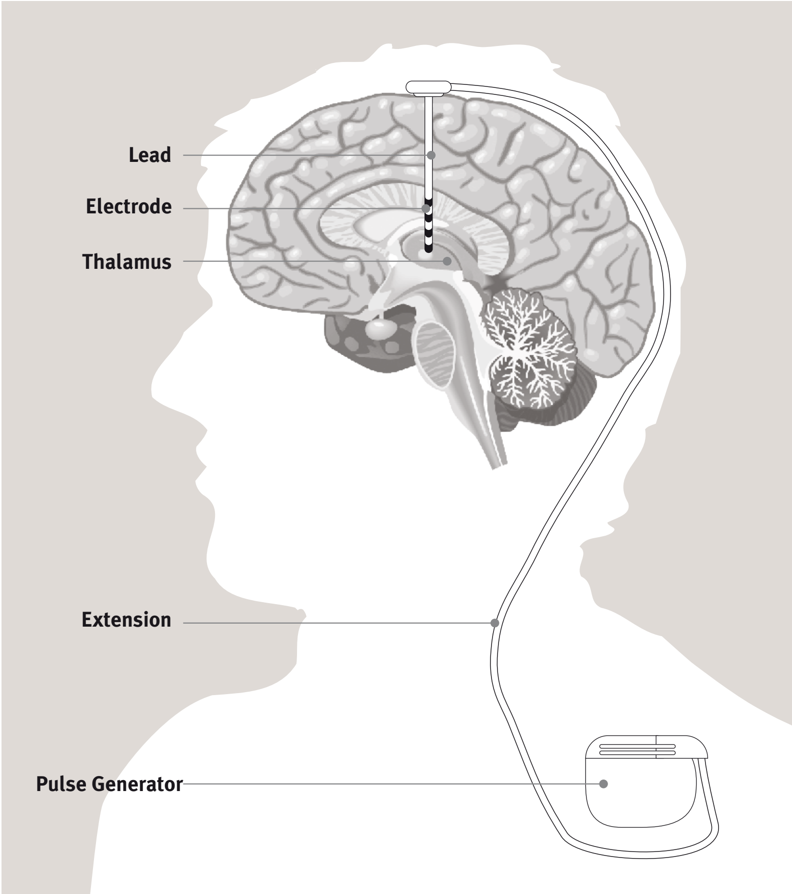
*Ira van Keulen, Bram Felius*[72]

Evolution designed our bodies to stockpile energy for future use. This was useful in times when food was scarce, but now, in a world with plenty of food, this mechanism is causing health problems for a growing number of people all around the world. The worldwide, rapid increase in the population of obesity patients and the multilateral health effects of obesity should make the disease

71 This technique involves placing electrodes inside the brain to stimulate the relevant neurons.

72 Paediatrician, VU University Medical Center.

**Figure 16**
*In deep brain stimulation (DBS), a device similar to a pacemaker is implanted in the chest and connected to electrodes placed in the brain. The technique has been approved as a treatment for Parkinson's disease and its being tested for a variety of other uses, like (morbid) obesity.*




a major priority on the research agenda, in the health care system, and in future political decision-making.

### Future research questions

Three closely related domains of research could play an important role in the study of obesity: nutrition research, metabolic pathways, and the neuro-endocrine regulation of food intake. One important aim of nutrition research is to establish healthy food preferences and nutrition behaviour early in life that will last into adulthood. What are the metabolic and neuro-endocrine mechanisms for achieving healthy preferences? There is a lot of work to be done in this area (see subsection 2.3.4). Another question is how food consumption is and can be influenced by situational factors, and not just in the short term (see subsection 2.4.3). The first domain of nutrition research is closely related to the second domain of research on the metabolic pathways. The various properties of food have a strong impact on food intake (see subsection 2.4.2). What characteristics of food have an effect on the biological mechanisms of hunger and satiety? How can this knowledge be used to diminish food intake?

Neuro-endocrine regulation of food intake appears to play a significant role in learning preferences, inducing hunger and satiety, as well as in normal circumstances and pathological eating patterns. Understanding this regulation mechanism is important for the development of pharmacological interventions, but also for other brain-based interventions. In the future, drugs and psychotherapy are likely to be supplemented by other intervention methods. Applied neuroscience is gaining ground and is also taking other therapies such as neurostimulation and neurofeedback into account [Desain et al., 2007]. Both interventions may be beneficial for people with severe obesity. In the end, however, the treatment of food addiction and obesity would benefit most from a multifaceted strategy: pharmaceuticals, neurofeedback and group therapy all have their place [Volkow, 2007].

Another neuroscientific challenge is to gain a better understanding of the genetic and environmental mechanisms of becoming obese. We need a better classification system for obesity in order to properly diagnose the underlying defects and develop effective treatment strategies. We also need to know more about the brain development of children and adults during periods of increasing body weight. The effects of overeating on the brain and cognitive functions have been neglected in the discussion of the co-morbidity of obesity, i.e. conditions that are either caused or exacerbated by obesity. This is partly because we know so little about the subject, although research has demonstrated the positive relationship between obesity and depression and obesity, dementia and cognitive decline. Research on obesity and neurological or psychiatric disorders could increase exponentially in future, based on the neuroimaging technology currently available.

### Policy measures

No country so far has successfully reduced the number of overweight people in its population [Popkin, 2007], although policy makers are considering and testing a range of different strategies. One important incentive for governments to search for successful interventions is a financial one. In the United States, for example, annual expenditure on overweight and obese people represents 9.1% of the national health budget [Grimm, 2008].

What will current and future neuroscientific research on obesity signify for government policy? Subsection 2.4.4 offered a few ideas concerning nutritional advice. Neuroscientific research is producing evidence showing why it is so hard for obese people to lose weight. Food and drug addiction, for example, turn out to be opposite sides of the same coin. Imaging research has demonstrated that obese people are more sensitive to reward. This means that external cues such as food advertisements will induce intense food cravings in them, unlike people who are less sensitive to reward (see example I). This is evidence supporting the idea of banning advertisements for sweetened food products and beverages from children's television or from all media, as policy-makers have frequently proposed. Such measures fit in with a public health policy based on environmental interventions, rather than the individual strategies more popular nowadays. Although historically speaking, measures targeting the collective (and social) determinants of disease and health have proven to be more successful [Stronks, 2007][73], public debate often portrays obesity as an individual problem [Lawrence, 2008]. Neuroscientific evidence appears to contradict this assertion and might in future lead to policy strategies becoming less individually directed and more collective in nature. That does not mean, of course, that obese or overweight individuals should not bear their own share of the responsibility.

## 2.6 Social and ethical aspects of nutricognition

*Suzanne van de Vathorst*[74]

The brain develops over a much longer period than we traditionally thought, and we now know more about how nutrition influences its development. The interventions suggested in this chapter involve:

- influencing the brain by influencing nutrition (both qualitatively and quantitatively);
- influencing food intake (eating behaviour) through direct and indirect interventions in the brain.

Both interventions raise separate ethical and social questions. The first intervention, influencing the brain through food, mainly gives rise to questions of social justice. Who is going to benefit from the new knowledge? Will it lead to a widening gap between the 'haves' and the 'have-nots'? Will the new insights and new food products be available to those who need them most? Are the new functional foods something that everyone has a right to, or should we view them as luxury items, to be sold on the open market? What are the responsibilities of the consumers, industry and government in these matters?

The second intervention could also lead to social inequity, but the more interesting ethical issue here is that of autonomy. Does an intervention that influences our food choice toward a more balanced diet free us from unwanted cravings, or does it restrict us in our choice? Are there circumstances in which people (e.g. obese children) should be forced to submit to such a 'treatment'? How autonomous are food preferences established in early childhood?

73 Examples of successful collective measures are sewering and vaccination programmes.

74 Ethicist, Erasmus Medical Centre.

**Figure 17**
*Influencing the brain through food mainly gives rise to questions of social justice. Influencing food intake through direct and indirect interventions in the brain could lead to social inequity, but also to ethical issues on autonomy. Photo of brain gummies courtesy of Lisa Ruokis, www.flickr.com.*

### 2.6.1 Influencing the brain by influencing nutrition

There are numerous examples of how nutrition may influence the brain, including the levels of omega-3 essential fatty acids (DHAs) in food and the right infant formula. Optimising our nutrition (the right quality, quantity and timing) may help the brain to achieve its full potential (or to retain that potential, e.g. by slowing down neurodegeneration or dementia). Even though there is always a genetically determined limit to an individual brain's development, all brains are better with optimal nutrition than without it. In that sense, everyone can benefit from this knowledge, and most certainly all children.

For this knowledge to be beneficial, however, it must be widely accessible, reliable and offer feasible options. This means developing practical guidelines and useful and readily available products. There are some social issues at stake here.

First of all, there is the risk associated with disseminating the information. Much of what we are learning about the impact of nutrition and the application of research findings in new products comes from commercial parties, for example the producers of nutritional products. Infant formula, cookies, pasta, soups, sauces — many of our foods are made in factories by manufacturers whose aim is to sell. One of the ways in which they promote their products is by attaching a health claim to it. But how do we know that this claim is true, or even reasonable? Every day we read advertisements for new products claiming that they will improve our health or even our cognitive performance. The protein in yoghurt makes us smarter, the DHA in margarine helps our children concentrate better, etcetera. How can the public be sure about these claims? Various governments in Europe, Asia and America have set rules for producers concerning the quality of their information, and that gives the public a minimum standard. On top of that, consumer organisations are in a good position to test the reliability and validity of the product information, but their countervailing power depends on their financial means. In terms of advertising budget, industry can outspend consumer organisations by a wide margin. So the question remains: is it possible to ensure that all consumers are provided with reliable information?

In terms of corporate responsibility, there is a need to adequately inform the new groups of consumers in developing countries who are being targeted by food companies selling brain food. The transition from a traditional food culture to a 'modern' Westernised culture is leading to specific problems in some countries. In the Philippines, overweight is now as much of an issue as underweight, but not for the same social groups. How are we to assess the introduction of new brain food in such a society? Can these new consumers rely solely on the information provided by the producers? How can we guarantee that people do not focus exclusively on the 'healthy' ingredients but keep an eye on maintaining a well-balanced overall diet as well?

Secondly, there are issues concerning access to knowledge. New knowledge, developed on the cutting edge of research, does not enter society by osmosis, unfortunately. It has to be made public. This entails making it comprehensible to a wider audience, *and* making it available. Higher-educated people have an advantage in this respect, as they are the first to grasp and implement new knowledge. Indeed, research shows that men in uppermost socio-economic groups live an average of almost five years longer than men from the lowest socio-economic group [Van Herten et al., 2002]. This difference can be explained in part by life-style factors, such as smoking, alcohol consumption and nutrition [Schrijvers, 1999]. Any advice on taking high doses of folic acid or using margarine with DHA will reach the groups that are already advantaged first. They will be more prepared to follow the new recommendations, better able to understand why, and more motivated to do so, as they are more likely to take a long-term perspective. There is hence a risk that new interventions in nutrition, for example new strategies for ameliorating cognitive performance, will only be undertaken by the upper socio-economic groups, leading to sharper distinctions between their cognitive health and performance and that of the lowest socio-economic class. Inequity between social groups will therefore increase. Whether such inequity should be considered an injustice depends entirely on our views of justice, something that is beyond the remit of this section. If, however, growing inequity is viewed as undesirable, then these issues must be considered.

Another issue related to new knowledge and nutrition is that of freedom and social pressure. If it is true that people become smarter by eating the right bread, with the right margarine in the right quantities, how free are we to *not* eat the bread or margarine? Adults are considered autonomous beings unless proven otherwise, and their autonomy grants them the right to injure their own health. But what about their children? Should people who refuse to feed their child the best possible formula, enriched milk or the right margarine be considered bad parents? As long as the effects are relatively minor, that is unlikely to happen. However, the larger the effect, the greater the likelihood that they will indeed be expected, or even forced, to give their child the best.

One more point is that the development of nutraceuticals, i.e. nutritional products with explicit medicinal claims, may lead to the medicalisation of food. That would mean neglecting the social and psychological value of food — the fun of sharing meals, the hedonistic experience of a delicious dinner, or even of gorging yourself on chocolate — in favour of their medicinal properties. We could view this as a loss, for food can be a genuine source of pleasure. In public health context, however, (protein) rich food is regarded almost exclusively as a sin. Developing more products with health claims could increase society's pre-occupation with health.

Finally, if we really believe that these new products enhance our health and/or brain function, should we not be reimbursed by our insurance companies for purchasing them? Some insurance companies already reimburse high-risk policy-holders for cholesterol-lowering margarine. Should other products also be reimbursed? Or should people who want to drink anti-Alzheimer's milk pay for it themselves? And can we rely on market mechanisms to answer such questions?

### 2.6.2 Influencing food intake by direct interventions in the brain

So far, it has been proven difficult to intervene directly in the brain. It is hard to design pharmaceuticals that pass the blood-brain barrier, and until recently other intervention methods simply did not exist. Now, however, it has become feasible to influence the brain directly by means of deep brain stimulation (DBS). Previously, interventions used to target the brain in a general sense. With DBS, we can be fairly precise in getting the effects we seek. It may also become possible, within the foreseeable future, to influence the brain directly by new pharmaceuticals means. There is no cure without side effects, of course, and such interventions are no exception (e.g. behavioural and emotional side effects, risk of infection and haemorrhage), but let us assume, for the sake of argument, that such side effects are virtually non-existent, or at least acceptable.

In terms of nutrition, either intervention could prove useful in three food-related conditions: anorexia nervosa, bulimia and obesity. One of the questions at stake is whether the use of 'artificial means' — pharmaceutical or physical — undermines or enhances the patient's autonomy.

Anorexia nervosa may be the easiest case here, since the severely anorectic patient cannot be considered autonomous with respect to his or her food preferences [Giordano, 2005]. Any intervention that frees the patient from the inability to eat enhances, not undermines, his or her autonomy. A similar argument may apply in the case of bulimia, as sufferers do not feel that they are in control of their binging. Obesity is a more difficult case, however. It should be seen as distinct from overweight, since both the causes and the consequences may be different. There is no scientific need to intervene in cases of mild overweight, but there is reason to prevent or cure obesity. Not all obese people are disabled in their autonomy. Obesity may be the result of a very conscious choice to enjoy life and good food. It may also be the result of unwanted, but hard-to-ignore cravings. These cravings, or even the experience of hunger, are also likely to be related to genetic factors [Farooqi and O'Rahilly, 2006]. Fat people tend to feel hungrier than lean people [O'Rahilly, 2007]. This hunger can be deemed dysfunctional, since it would be better for their health not to indulge in food whenever they are hungry. Whether these people experience their hunger as a burden is uncertain — maybe they do, and maybe they do not.

Anyone who takes a pill or has a chip implanted to rid himself of these unwanted cravings or of dysfunctional and burdensome hunger will have his autonomy enhanced. The main issue is clearly the extent to which the urge to eat feels alien to the person, something they wish to rid themselves of. People who undergo stomach surgery are not blamed for diminishing their autonomy.

Some people argue that any intervention, whether surgical or medicinal, is a morally weak solution, because the goal could also be achieved through 'willpower'. Some even see it as a disgrace that any of these interventions are paid for by insurance, because it would be much cheaper if these people simply ate less. These arguments are too simplistic, however. Although most people do manage to lose weight, only few manage to do so long term. It is evidently very difficult to keep the weight off. We can only hope that future research will show us why that is the case, but for now, it is simply unrealistic to say that people should 'simply lose weight'. For all practical purposes, obesity should be regarded as extremely difficult to treat.

If we argue that people who voluntarily undergo interventions to free themselves from 'unwanted cravings' are exercising their autonomy, forcing an intervention on someone is then detrimental to his or her autonomy. Even if it is in their own best interests, forcing people to accept an intervention against their will is a paternalistic strategy. Although paternalistic interventions may be justified at times, in most cases they are not. The question is whether we will end up classifying obese persons as patients, as we now do with people who suffer from anorexia nervosa. Will we come to believe that most of them are simply not autonomous in their food choice, and should therefore be compelled to undergo therapy? We would need to make a very good case to justify such a position. Their autonomy should extend beyond their desire to eat to include their decision to choose (or not choose) a safe and effective treatment.

Since the aim of any intervention is to free people from the inclination to overeat, there is no 'moral hazard'. That would be the case if knowing there is a remedy made them more risk-prone, or if they were insured against the consequences. There is no moral issue, however, for interventions designed to free people from their risk-proneness (by freeing them from their wish to overeat).

### 2.6.3 Influencing food intake by indirect interventions in the brain

The conditioning of food preferences could be viewed as indirect interventions in the brain. Subsection 2.4.5 explained that food preferences can be conditioned at any stage of development. Preferences established early in life are especially powerful. It may therefore be feasible to condition young children to develop food preferences according to what we believe are the 'right' preferences. One of the problems is how to establish what the 'right' preference is. If we accustom young children to bitterness, for instance, will it turn out to be a healthy choice when they grow up? Will they prefer Brussels sprouts or will they develop an unhealthy preference for Campari?

Another question is whether willingly shaping children's food preferences challenges their autonomy. It would be difficult to argue that it undermines their autonomy, as their preferences are always shaped, whether or not we manipulate this process. If we do not intervene, they will adjust to whatever their parents feed them. We would need to argue that it would harm them to shape their preferences not according to the whims of their parents, but according to a plan drawn up by some third party (i.e. government or industry). But even if we do not think it is harmful to prefer sprouts over custard pudding, it may undermine public trust to effect such a plan in secret. Parents should be warned that giving their child formula A may lead to a preference for bitterness, whereas formula B may lead to a preference for vanilla. But unless data can be produced showing that one or the other is harmful, parents should be given an informed choice. That way we harm neither the autonomy of the child nor that of the parent.

In conclusion, we can say that the ethical and social issues involved in developing nutritional products that enhance brain function are mainly associated with equality, whereas interventions in the brain altering people's behaviour mainly evoke autonomy issues.

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# 3

# Neuro-centred Design

## 3.1 Introduction

*Jan van Erp*[1], *Ira van Keulen*[2], *Maurits Kreijveld*[3]

The aim of man-machine interfaces (MMI) is to optimise the interaction between users and a system or environment, for example the menu on your mobile phone or complex aircraft cockpit systems. Technological advances are leading to systems with more functionalities but less visible and more intangible underlying mechanisms. The commercial success of such systems depends increasingly on their accessibility and user-friendliness, in short on the user interface. One of the authors of this chapter, MMI scientist Huib de Ridder, foresees that MMI will be more user-centric in the future. Such user-centric design will go beyond the current trend of user-friendliness by trying to understand and even anticipate user intentions. The slogan used by Philips, 'Sense and Simplicity', articulates this to some extent. The same goes for Apple's user-friendly touchpad. The international trend towards self-learning systems expresses a similar preference for user-centred design.

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MMI researchers and developers will be trying to tackle human-centred design by bringing together system functionalities and user capacities: how can we make these increasingly advanced functionalities comprehensible and manageable for the user? Knowing the user is thus essential. Nowadays, such knowledge is derived mainly from cognitive studies, for example to determine how well human beings perceive certain things, how many numbers they can remember, or what information people use to make decisions. So far the traditional cognitive sciences, such as psychology, have made major contributions to MMI, mainly by providing models of cognitive and human functions (perception, memory, movement, etc.) that help optimise user-interface design. For example, models of the human sensory system and cognition have greatly influenced such aspects as colour use, symbol size, menu structures, telephone frequency range and button size.

The contribution of the cognitive sciences to the the turbulent field of MMI is clear, but how can the neurosciences contribute? This brief introduction lists four different ways, which we will return to in greater detail later on in the chapter.

### Improving interfaces by offering better models of cognitive functions

Because of the close cooperation of the cognitive sciences with the neurosciences, we now have the opportunity to expand existing models of cognitive functions — for example attention or memory — to improve interfaces and systems. Cognitive neuroscience, with its neuro-imaging techniques, is already making a substantial contribution to our understanding of the human — and

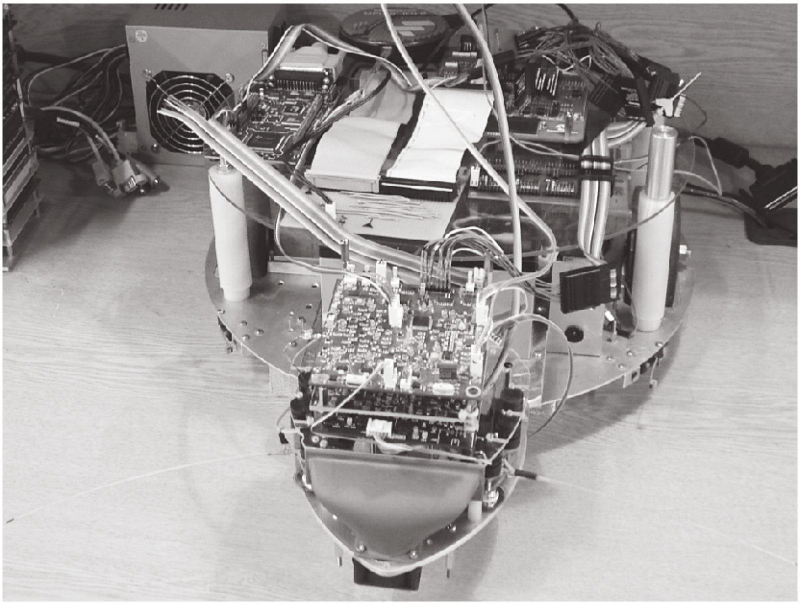


**Figure 1**
*The whiskerbot: a small mobile robot with whiskers to assess surroundings like pipe-lines or collapsed buildings. The design is based on computational models of whisker-related brain areas in the rat brain. Source: www.whiskerbot.org.*

therefore the user's — brain and mind. This new knowledge is expected to strengthen the basis of man-machine interaction theory and practices. For example: our knowledge of the elderly brain can help us design user interfaces for an ageing population, and knowing how to fool the brain into thinking that the limbs of our avatar are our own, will make virtual reality (VR) much more engaging than it already is.

At the same time, our growing knowledge of the brain's mechanisms can be used as a source of inspiration for designing MMI. Using the analogy of bio-mimicry, we can call the imitation of neural mechanisms in novel interfaces or systems 'neuro-mimicry'. An example would be the whiskerbot, a small mobile robot that has whiskers to assess its environment. The design is based on computational models of whisker-related neural circuitry in the rat brain (see Figure 1 and example VI).

### Improving user interfaces through neural evaluation of their effectiveness

Besides improving on current models and theories, neuroscientific research tools can also be used to evaluate user interfaces by testing the extent to which various known brain areas and signals are involved while the interface is being used. Neuro-imaging may therefore help determine whether and to what extent interfaces stimulate those brain regions that are involved in a particular task, enabling us to design the most effective man-machine interaction that takes the least amount of effort. For example, cognitive workload is an important factor in designing a good user interface, but it is very difficult to measure. Workload measurement is currently based on a combination of performance, subjective assessment and physiological variables. If we could determine the neural correlates of cognitive workload, we might be able to evaluate such interfaces faster and more easily and reliably on criteria of effectiveness. The gaming industry already evaluates new games in terms of engagement. The American company EmSense, for example, uses electro-encephalography (EEG; see Appendix 1) (and skin response and heart rate) to measure levels of arousal during games.[4] Many other possible applications come to mind. One example is the neurocognitive evaluation of possible information overload in traffic situations or health care technology, the ultimate goal being an information optimum: enough relevant information for users to make a quick and goal-oriented decision.

### Optimising user interfaces by feeding back neural information

In future, neural information might also be fed back directly into an adaptive system. The system can then adapt to the present state of the specific user, for example his visual attention, task engagement, surprise and, again, cognitive overload. In the latter case, the adaptive system could take over some of

4 See www.emsense.com.

the user's tasks or postpone certain messages to the user. Another possibility is that we will be able to measure brain signals indicating spatial disorientation before a pilot even becomes aware of this threatening situation.

The great advantage of neuroscientific measuring methods is that they help us understand variables that cannot be determined by behavioural measurement, either because the variables take place on a subconscious level or because they depend on subjective judgments that are not reflected in behaviour. In future, brain signals may possibly give valuable and objective information on cognitive states such as surprise, absorption, disgust, empathy, etcetera that is not easy to access by other techniques such as questionnaires or trained panels. Another major advantage of neural measures is that they can add vital information to — sometimes less reliable — behavioural measures. For example, we can use eye movement technology to determine what someone is looking at, but not what that person is actually seeing or, more accurately, perceiving. By measuring brain signals in the visual cortex, we might be able to determine the focus of someone's visual attention.

### Controlling systems by measuring and interpreting brain activity

Neural information or brain signals can also be used to control a computer or other system, in lieu of a keyboard or mouse. One such example is the communication prosthesis for patients with ALS (amyothrophe lateral sclerosis), who cannot move or communicate at all in the final stage of this disease

**Figure 2**
*"The Emotiv neuroheadset makes it possible for games to be controlled and influenced by the player's mind." Source: www.emotiv.com.*

(see subsection 3.2.3 on the limitations of brain-machine interfaces for ALS patients). Applications for healthy users are foreseen as well. For example, the American company EmotivSystems has developed a computer game that includes a wireless 'neuroheadset' with sixteen sensors (see Figure 2). The neuroheadset enables the user to move objects on the screen with his thoughts, for example 'I want to lift this stone'. The Emotiv neuroheadset has not yet been introduced to the market though. This gives room for speculation of some neuroscientists who think the Emotiv headset with 'dry' in stead of the usual 'wet' electrodes is more sensitive to muscle strains in the forehead of the user than to its brain activity. Some therefore dismiss the Emotiv system as a frown machine interface in stead of a brain machine interface. In short, it remains to be seen to what extent such devices will in fact work and be sold.

The first two applications of neuroscientific knowledge — better models of cognitive functions and neural evaluation of effectiveness — are nowadays also known under the designation, neuro-ergonomics. This is an emerging field which combines neuroscience with man-machine interaction studies in order to evaluate how well a technology matches human capabilities and limitations. The term neuro-ergonomics was first coined by Raja Parasuraman [2006] who edited a handbook on the subject. In that book he explains the aim of the field in the following words: *"To use the discoveries of human brain and physiological functioning both to inform the design of technologies in the workplace and home, and to provide new training methods that enhance performance, expand capabilities, and optimize the fit between people and technology"*. An illustrative example is the recent brain-imaging research on cell phone use during driving that indicates that even the hands-free or voice activated use of a mobile phone is as dangerous as being under the influence of alcohol during driving. The listening-and-drive mode produced a 37% decrease in activity in the parietal lobe, which is associated with spatial processing, critical for navigation. Activity also decreased in the occipital lobe, which processes visual information [Just et al., 2008].

The latter two applications — neural signals for feedback or control — are examples of brain-machine interfaces (BMIs).[5] The field of BMI, which can in fact be seen as a branch of MMI, is still in its infancy, and BMIs are still unreliable and suffer from low neural information transfer rates. The basic problem is that we do not have a good understanding of the communication system of the brain yet (see subsection 3.2.3). We do know that only the most fundamental brain functions (i.e. motor and sensory functions) are localised in specific areas in the brain. Other brain functions are regulated by networks of nodes that are activated to various degrees. This explains partly why the underlying neural representation of various mental processes — the code

5 Some people use BMI in reference only to artificial sensory systems such as cochlear implant. Others never use BMI, but employ the term BCI, brain-computer interfaces. In this chapter we will use the term BMI for every application: artifical sensory systems as well as invasive and non-invasive interfaces using brain activity to command and control external devices.

— is difficult to understand. Progress is being made, however. For example, an functional magnetic resonance imaging (fMRI; see Appendix 1) experiment was able to predict whether or not a respondent would remember a specific word, and neurocognitive researchers have been able to accurately identify which of two objects a respondent had been looking at, for instance a horse or a cow, a bird or a butterfly, based on twenty seconds of fMRI data (see example XIII). EEG (a much more manageable technique in day-to-day use than the large MRI scanners) makes it possible to detect whether or not a user is imagining moving his hand, although it cannot detect whether he is imagining a circular or a linear movement. BMIs would apply in many more instances if we understood the coding for: place-related and face-related memory, access to the mental lexicon, and selective attention with respect to spatial locations or auditory sources. Besides the challenge of understanding the neural codes behind mental processes, there is the equally big challenge of adapting neuro-imaging technologies to suit the daily routines of users or consumers.[6] Subsection 3.2.4 will look at how engineers are working to make BMIs portable, wireless and non-invasive.

This chapter does not look in detail at applications such as neurofeedback[7] and neurostimulation[8] (see also box 1). These techniques influence the user's brain signals by means of self-control (i.e. neurofeedback) by electrical stimulation.

Finally, we also need to consider the research tools that MMI technologies such as VR can offer the neurosciences. Virtual environments can be powerful tools for studying (by manipulation) the workings of the brain in general and the brain mechanisms behind self-perception and self-representation in particular. That will be even more the case if the next-generation VR includes the possibility of fooling the brain of the user into perceiving the virtual body of an avatar as his own physical body. Virtual reality techniques are already being used to study out-of-body experiences [Lenggenhager et al., 2007; Miller, 2007; Henrik Ehrsson, 2007].

In short, the symbiosis between the neurosciences and cognitive sciences on the one hand and MMI research and development on the other goes beyond brain-machine interfaces. Neuro-mimicry, neuro-imaging-based evaluation and improved models of cognitive functions are equally significant methods for improving even the more traditional interfaces or interactions between man and machine. A broad view of how MMI might exploit neuroscientific knowledge could lead to a new area of research and development: the neuro-centred design of interfaces.

6 The American company Neurosky is looking at applications of BMIs for healthy users in a very broad way: control of electronic toys, mood based song selection, meditation, mind improvement games, sleep and distraction detection, attention training, advertisement effectiveness, etcetera. It is questionable whether all of these applications will be desirable and attainable in the future. See also www.neurosky.com.

7 Neurofeedback is a therapy technique that presents the user with real-time feedback on brainwave activity, as measured by sensors on the scalp, typically in the form of a video display, sound or vibration. See www.wikipedia.org.

8 Neurostimulation makes use of an implanted pulse generator (IPG) designed to deliver electrical stimulation to specific parts of the brain. The IPG is an integral component of surgically implanted systems such as deep brain stimulation and vagus nerve stimulation, designed to treat such neurological disorders as Parkinson or the Tourette syndrome. See www.wikipedia.org.

**Box 1: The Dutch BrainGain consortium**

The Radboud University in Nijmegen, the universities of Maastricht and Twente, the Netherlands Organisation for Applied Scientific Research (TNO), and several industrial partners and patient organisations are combining their expertise in brain-computer and computer-brain interfacing in the BrainGain consortium. Their mission is to apply recent advances with respect to analysing and influencing brain activity to improve the quality of life and performance for both patients and healthy users. The consortium focuses on three elements. The first is the development of brain-computer interfaces, i.e. a direct connection between the brain and a computer, for patients with ALS (amyothrophe lateral sclerosis) and spinal chord injury. The second is neurostimulation, an area that makes it possible to treat disorders in which, for instance, an excess of activity in certain brain regions causes someone to be anxious or hear voices. Implanted electrodes can be used to detect natural brain signals but can also stimulate nerve cells directly. This technique has been used to spectacular effect to reduce tremors in Parkinson patients. Other important issues in this area include learning to reduce chronic pain and epileptic seizures. The consortium's third focus area is neurofeedback training. Recent studies claim that learning to control simple aspects of one's own brain signals treats a broad range of disorders such as ADHD. Researchers tend to be critical about these claims, however. The consortium partners will cooperate with patient organisations on in-depth studies into the mechanism and efficiency of these simple systems in order to evaluate the use of neurofeedback.
The consortium also aims to investigate whether neurofeedback can also be used to meet the health, performance, or quality of life needs of healthy users. Stress exacts a high price on society, and brain-computer interfaces (BCIs) could help teach healthy users to relax, concentrate or meditate. Other possible applications include entertainment, such as computer games driven by brain signals, or the presentation of information on computer screens only when visual attention is detected, for example for air traffic controllers or customs officials checking scanned luggage. Together with industrial and non-governmental (like patient) organisations, researchers are recognising that analysing and influencing brain activity patterns can yield many opportunities for commercial and social innovation.

*Source: www.braingain.nl*

### 3.1.1 Social and economic relevance of researching neuro-designed interfaces

The advantages of neuro-designed man-machine interfaces will be manifold. They will be more *efficient*, as the design will take the pros and cons of the human brain as an information-processing machine into account. They will be more *effective*, as the interfaces will be evaluated according to how the relevant brain areas are activated. The interfaces, in particular the BMIs, will also function *faster*, thanks to a higher bandwith interface between the human brain and the digital computer (although at the moment the neural information transfer rates are still slow). Most importantly, the interface will be able to 'read' the intentions of the user much more accurately. Man-machine interaction is still hampered by fundamental limitations, e.g. the computer cannot react properly to the user's unexpected utterances. This problem will be solved in future when information about the user (i.e. cognitive workload, task, engagement, frustration, surprise and even intention) is fed back into the interaction. In general, anything that allows the interpretation of verbal or non-verbal messages from the user or from the machine — sometimes known as the 'cognition of communication' — will help improve MMI, and this is a domain to which the neurosciences can contribute in many different ways.

Such improved neuro-centred and at the same time user-centred interfaces could have a huge impact on many domains (education, health care and entertainment), although some social issues are more relevant than others.

### Ageing population

The number of elderly people is growing. In 2030, four million people in the Netherlands will be over 65 years of age, nearly a quarter of the total Dutch population. Many of them would like to live on their own for as long as possible. Indeed, it is important for the elderly to remain self-reliant, as a labour shortage in the elderly care sector is likely, with fewer professionals taking care of more people requiring help. Assistive technology — ranging from medical monitoring systems to automated fall detection or service robots[9] — will play an increasingly important role in elderly care and improve the autonomy, safety and quality of life of the elderly at home. Post-war generation elderly are likely to be more willing to adopt technologies that will help them age well in their homes, but this does not mean that interfaces do not have to be improved significantly. Research has shown that elderly-specific needs, for example with respect to presenting and customising health information services, often go unmet [Marschollek, 2007]. Knowledge of cognitive decline can also help us develop interfaces based on the specific characteristics of the elderly brain.

### Online communities

Internet use continues to increase. In the Netherlands, 83% of households were online in 2005. Besides being a source of news and information, the internet is also increasingly used for social purposes, or, as the PEW Internet organisation states: *"Many-to-many is elemental to the online experience"*

9 For example Robosoft's home-centred Robuter or Sony's companion robot dog Aibo.

[Horrigan, 2007]. For example, in 2005 Dutch teenagers spend 60% of their time online on chatting and instant messaging. And in the United States, 23 million Americans (i.e. 20% of the online users) actively participated already in 2001 in online communities. It is therefore safe to say that online networks are increasingly important in the lives of many people and will continue to be so as mobile access to the internet grows. Some people use online communities to share their lives (i.e. blogging, posting photographs or video content) [Lenhart, 2007], while others look for help with a variety of problems or decisions. As the real world merges with the virtual world, it is becoming more acceptable to replace offline meetings between colleagues, friends and family by online ones (at least in part). Such a trend might have an enormous positive impact on the mobility issue in the Netherlands. In 2006, for example, there were more than 41,000 kilometres of traffic congestion in the Netherlands, causing 500 million euros of economic losses. This illustrates the importance of neuroscientific and cognitive research on the cues that make the experience of an online or virtual meeting comparable to a real-life one. And in fact there are several cognitive studies being carried out on virtual group interaction and 'telepresence', i.e. the subjective experience of 'being there' in a mediated environment.

### Gaming

Nearly half of the Dutch population (43%) regularly plays games online or offline (with game consoles).[10] The creative industry and, in particular, the gaming industry are the key innovation areas within Dutch economic policy. There is a substantial market for gaming and simulation applications, not only in the entertainment sector but also in other relevant domains such as education (see also the chapter on Personalised Learning), mobility, security and health care. Latter applications are also known under the header of 'serious gaming' [Te Velde et al., 2007].

When it comes to BMIs for healthy users, gamers are the first target group developers think of. The success of Nintendo's Wii has shown that people are ready for novel ways to interact with games. Nintendo has even accessed new user groups with the Wii and with its brain training software for the Nintendo DS. The current market is less interested in finding new game genres than in looking for new hardware to enhance the game experience [Graham-Rowe, 2008]. An example is the earlier mentioned Emotiv Systems' neuroheadset. Researchers at Keio University developed a BMI that enables the user to walk through Second Life by thinking about it. And then there is the game Mindball, in which the user wears a headband with sensors measuring brain waves and in which the user wins by remaining as focused and relaxed as possible. One feature that must be considered for the next generation of games is the level

10 See www.gamingonderzoek.nl.

of immersion. Users like to experience being immersed in a gaming environment. Understanding the neural mechanisms behind physical ownership and self-representation will help turn virtual reality into ‘real virtuality’ in future. Such VR applications may be very sustainable, as they will reduce the need for mobility and the production of physical products.

#### National security

National security has been one of the most prominent political issues since the terrorist attack of 9/11, resulting in what some call a ‘screening society’. In the fight against crime and terror, officials are collecting more and more data, using everything from surveillance cameras and DNA material to phone taps. Identification or biometric technology has expanded enormously. One interesting option is to use brain-machine interfaces as a biometric device. Researchers at Carleton University plan to use the unique response of the individual brain to stimuli such as sounds or images as an authentication method. The most intriguing problem of the ‘screening society’, however, is that it is generating large and complex datasets. Unlike the human brain, computers are very bad at recognising visual patterns, a skill that is absolutely necessary in order to analyse video datasets of conspicuous events. Once again, brain-machine interfaces can offer a solution. At Columbia University, researchers are attempting to determine recognition patterns in human brain activity while a person — not a computer — watches accelerated images of surveillance datasets (see example VIII).

In general, improved MMI is likely to be economically relevant in multiple sectors. One such sector is new consumer products related to ambient intelligence, in which gaming, entertainment, education and communication inside and outside the home environment are blended. Another is the high-tech industry, in which the Netherlands has a strong position in equipment manufacturing for which the improved neuro-centred design of interfaces is essential, for example medical and industrial scanners, sensors, and machine control.

### 3.1.2 How to read this chapter

The STT expert group on MMI — the authors of this chapter — is an interdisciplinary group whose members work in MMI research and development, in academia, in industry, in neuroscientific and cognitive research, and in government. Its members met five times to discuss the need for cooperation between the two disciplines. The field of MMI and the neurosciences and cognitive sciences generally do not communicate regularly. Consequently they are not up to date on the progress made on the other side. As indicated in the introduction, it became clear during the meetings that there are many ways

**Example V**

**Just by thought alone 25-year old Matthew Nagle, paralysed from the neck down by a spinal cord injury, could open an e-mail program, play a computer game and direct an artificial hand. He could do this via a chip implanted in his brain that converts electrical brain signals into computer commands. Users of such neuroprosthetic devices may one day be able to control wheelchairs and computers with their thoughts.**

Nagle had been stabbed in the back during a street fight, leaving him unable to move his arms or legs. Three years after the dramatic event, American brain scientists surgically implanted a silicon chip on the surface of the brain area controlling voluntary movement, the primary motor cortex. The chip, measuring just half a centimetre across, contained 96 microelectrodes, each thinner than a human hair, that detected the electrical activity of dozens of brain cells. Via a large bundle of wires under Nagle's skin, the brain signals were led to an external computer in real time to control external devices.

# Brain implant converts thought into action

Over a period of nine months, Nagle took part in 57 sessions to test the BrainGate device, which was developed by Cyberkinetics Neurotechnology Systems, Inc. in collaboration with several universities. He was able to perform simple actions in computer e-mail and game programs, and he could change the volume of a television set, all while having a conversation at the same time. He could also pick up candy with a prosthetic hand and place it in the hand of a researcher.
One important aspect the pilot trial makes clear is that the motor cortex can remain functional even years after a spinal cord injury.

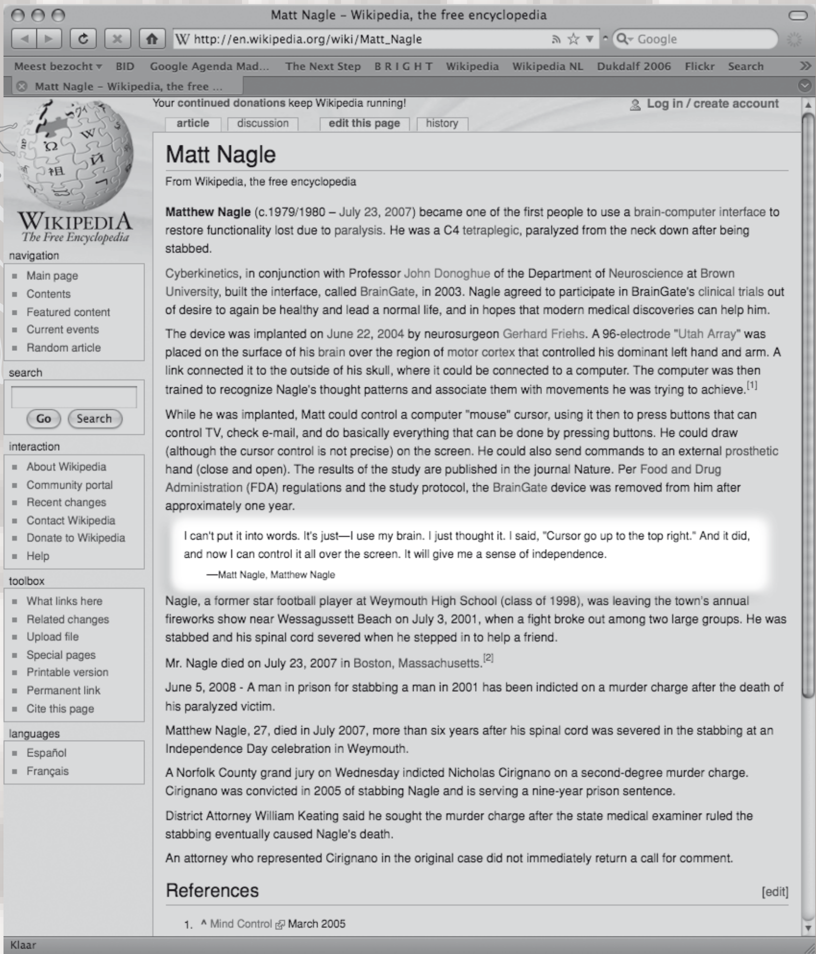
When it comes to converting brain activity into action, invasive brain implants offer advantages over non-invasive techniques such as electroencephalogram (EEG) recordings, because they have a higher resolution and can be functional within minutes instead of weeks.

Many problems have to be addressed before invasive brain implants can be used outside the laboratory. Two of those are the high risk of infection and the relatively low durability of the implant. It is encouraging that these risks have been overcome in the most widely used neuroprosthetic device: the cochlear implant. Over 100,000 deaf people have currently been implanted with an

Original publication: Hochberg LR et al. (2006). *Nature*, 442, pp. 164-171 array of electrodes in their ear that stimulate their acoustic nerve cells when sounds are detected by an external headpiece and processor.

People can become paralysed after severe neurological damage due to stroke, spinal cord injury or neuromuscular disease. Brain-controlled technologies would allow such persons to lead a more independent life. The ultimate goal is to create brain-machine interfaces (BMI's) that are safe, fast, effective and reliably controlled by the thoughts of paralysed people. In future the technology may even be used to restore brain-to-muscle control, allowing injured people to use their brain signals to activate limb muscles, to control breathing, bladder or bowel movement.

Matthew Nagle died in 2007 of a blood infection.


Matt Nagle – Wikipedia, the free encyclopedia

http://en.wikipedia.org/wiki/Matt_Nagle

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# Matt Nagle

From Wikipedia, the free encyclopedia

**Matthew Nagle** (c.1979/1980 – July 23, 2007) became one of the first people to use a brain-computer interface to restore functionality lost due to paralysis. He was a C4 tetraplegic, paralyzed from the neck down after being stabbed.

Cyberkinetics, in conjunction with Professor John Donoghue of the Department of Neuroscience at Brown University, built the interface, called BrainGate, in 2003. Nagle agreed to participate in BrainGate's clinical trials out of desire to again be healthy and lead a normal life, and in hopes that modern medical discoveries can help him.

The device was implanted on June 22, 2004 by neurosurgeon Gerhard Friehs. A 96-electrode "Utah Array" was placed on the surface of his brain over the region of motor cortex that controlled his dominant left hand and arm. A link connected it to the outside of his skull, where it could be connected to a computer. The computer was then trained to recognize Nagle's thought patterns and associate them with movements he was trying to achieve.[1]

While he was implanted, Matt could control a computer "mouse" cursor, using it then to press buttons that can control TV, check e-mail, and do basically everything that can be done by pressing buttons. He could draw (although the cursor control is not precise) on the screen. He could also send commands to an external prosthetic hand (close and open). The results of the study are published in the journal Nature. Per Food and Drug Administration (FDA) regulations and the study protocol, the BrainGate device was removed from him after approximately one year.

> I can't put it into words. It's just—I use my brain. I just thought it. I said, "Cursor go up to the top right." And it did, and now I can control it all over the screen. It will give me a sense of independence.
>
> —Matt Nagle, Matthew Nagle

Nagle, a former star football player at Weymouth High School (class of 1998), was leaving the town's annual fireworks show near Wessagussett Beach on July 3, 2001, when a fight broke out among two large groups. He was stabbed and his spinal cord severed when he stepped in to help a friend.

Mr. Nagle died on July 23, 2007 in Boston, Massachusetts.[2]

June 5, 2008 - A man in prison for stabbing a man in 2001 has been indicted on a murder charge after the death of his paralyzed victim.

Matthew Nagle, 27, died in July 2007, more than six years after his spinal cord was severed in the stabbing at an Independence Day celebration in Weymouth.

A Norfolk County grand jury on Wednesday indicted Nicholas Cirignano on a second-degree murder charge. Cirignano was convicted in 2005 of stabbing Nagle and is serving a nine-year prison sentence.

District Attorney William Keating said he sought the murder charge after the state medical examiner ruled the stabbing eventually caused Nagle's death.

An attorney who represented Cirignano in the original case did not immediately return a call for comment.

## References [edit]

1. ^ Mind Control March 2005

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in which both fields can benefit from each other's R&D. At the same time, the demand for knowledge appears to exceed the supply: MMI scientists have more questions than can yet be answered by neuroscientists and cognitive scientists, especially when it comes to detecting the neural code for different mental activities (e.g. creativity, intuition, automatism, perception of fiction or reality, etc.). But regardless of our limited understanding of the workings of the brain, the expert group still believes that it is possible, and also important, to think about applying neuroscientific knowledge in the field of MMI. Or, as one expert in one of the MMI meetings stated: *"While the car was being developed, a horse was still the faster mode of transport"*.

This chapter explores the neuro-centred design of interfaces in greater depth, based on:
– Trends and opportunities in MMI (see subsection 3.2.1). Certain trends in the field of MMI — for example ambient intelligence — are of particular interest to the neurosciences, e.g. when it comes to understanding and anticipating user intentions.
– Trends, opportunities and challenges in the neurosciences and neuroimaging technology (see subsections 3.2.2, 3.2.3 and 3.2.4). Although we do not yet have a grand theory of the brain, small nuggets of neuroscientific knowledge can be used to improve interfaces or systems. At the same time, R&D in brain-machine interfaces still face many challenges: performance variability, a low level of detail in neurophysiological recording, and numerous problems in engineering wireless, non-invasive, portable BMIs.
– Possible future applications of neuroscientific knowledge in different fields of cognitive functioning relevant for MMI: perception and interpretation, learning, motivation and reward, and attention and alertness (see section 3.3). These applications are shown in a table that links current findings in the neurosciences to urgent MMI issues, resulting in some initial application proposals. Some of these potential applications are discussed in the final section (3.6), which describes various fictional scenarios developed by individual members of the expert group based on their specific expertise.

The chapter concludes with a discussion of the differences and similarities between the two disciplines, the need and opportunities for cooperation, clusters of important R&D questions for the future, and the ethical and social implications of the neuro-centred design of interfaces.

One final point needs to be raised before we begin. Although this chapter focuses mainly on the contribution of the neurosciences — and especially the cognitive neurosciences — to the field of MMI, this does not mean that the expert group believes that the cognitive sciences will no longer have anything to offer MMI in the future. On the contrary, it is the close cooperation between the neurosciences and cognitive sciences which will eventually make a difference.

## 3.2 Trends, opportunities and challenges in MMI and the neurosciences

This section begins by outlining the most important trend in MMI, e.g. ambient intelligence. At the same time, the author identifies related questions that pose a challenge to the neurosciences (subsection 3.2.1). The chapter continues with an overview of the most relevant findings in the neurosciences and cognitive sciences in relation to man-machine interaction (subsection 3.2.2), including suggestions on how to improve MMI based on the latest neuroscientific findings. The last two subsections (3.2.3 en 3.2.4) consider the neuroscientific and engineering challenges associated with research and development in brain-machine interfaces.

### 3.2.1 Trends in man-machine interaction, technology and user perspective

*Huib de Ridder*[11]

We live in dynamic times — a claim that must be taken literally, as our environments and the products inhabiting them become increasingly dynamic and interactive. The main reason for this trend is that a growing variety of consumer and professional products are being equipped with sensors, data storage capacity, information processing technology, actuators and new display technologies. Advances in network and wireless communication technology will also allow us to connect such products to smart environments that can sense and reason about user intentions in a natural setting and react and anticipate accordingly. Humans will be continuously connected to one another in such smart environments, and information will be available anytime and everywhere [Aarts and Marzano, 2003]. There is a growing awareness that these developments will have a major impact on everyday life in near future, for example in health care [Schuurman et al., 2007], our working lives, our leisure time, and mobility. It is therefore important to take a careful look at these trends and explore how such new technologies can be geared to the needs and wishes of humans. We should focus not only on the technology, but also on its consequences for man-machine interaction and the changing role of humans as individuals and community members. Such an analysis will simultaneously help clarify how the neurosciences can help improve future man-machine interaction.

11 Professor of Information Ergonomics, Delft University of Technology.

**Figure 3**
*Ambient intelligence as envisaged by Philips: humans will be continuously connected to one another in smart environments, and information will be available anytime and everywhere. Source: www.philips.com.*


## Trends in technology: Ambient Intelligence

The technological trend referred to above was first identified in 1991 by Marc Weiser of Xerox PARC and is known under various names. Probably the most familiar is the one introduced by Aarts and Marzano [2003] at the beginning of this century: Ambient Intelligence (AmI). The concept of Ambient Intelligence poses the following challenges:

- Embedding: how can we integrate networked devices into the environment?
- Context awareness: how can these devices recognise you and your context?
- Personalisation: how can they be tailored to your needs?
- Adaptivity: how can they change in response to you?
- Anticipation: how can they anticipate your desires without conscious mediation?

These challenges have a number of interesting implications for the way humans will interact with their environments and products. First, there will be a broad spectrum of different environments, ranging from natural environments to completely virtual ones, with different varieties of mixed and augmented realities in between.[12] Secondly, the challenges suggest an important change in the way we think about man-machine interaction. Until now, we analysed these interactions by focusing mainly on the following questions: *what* do you like to do (functionality), *how* do you like to accomplish this (interaction style) and *with what* (available input or output devices)? These questions now have to be extended by the following: *when* and *where* will the interaction take place and (the most challenging one) *why*? Thirdly, the list of challenges

12 Mixed reality involves overlaying the real environment with virtual entities. For example, by projecting an arrow on to the front window of a car indicating which direction the driver has to go next, we generate a mixture between a virtual object and the real environment. If the arrow is projected in such a way that it fits in naturally with the environment, e.g. on the road ahead pointing in the right direction, the real environment is said to have been augmented.

indicates a growing need to understand the user in the man-machine interaction. Interestingly, this sense of urgency comes from the technology itself. While the first challenge is clearly technology-oriented (e.g. miniaturization, connectivity between different materials), the others depend increasingly on a thorough understanding of human behaviour. The greatest challenge by far is to develop technology to anticipate human intentions: a perfect illustration of a technology push for human-centred design.

### Man-machine interaction: from user-friendliness to human-centred design

These technological developments will have a major impact on man-machine interaction. Some even claim that the revolution in information technology is bringing about a paradigm shift in the field of human factors[13] and ergonomics [Boff, 2006]. Until now, the focus has been on respecting human physical and cognitive capabilities and limitations and adapting the equipment accordingly [Norman, 2002]. Nowadays, however, the focus is shifting increasingly to how products can collaborate symbiotically with humans to enhance human capabilities *"…well outside the range of normal biological variation thereby altering traditional boundary constraints on the adaptability of humans in complex system design…"* [Boff, 2006]. This may be accomplished by means of a tightly coupled neural fit between equipment or computing devices and the central nervous system. Cochlear implants are a good initial indication of the direction in which this will evolve. Symbiotic collaborations amplifying human capabilities imply a shift from user-friendliness to a human-centred design approach, with user context playing a key role. The latter implies that we should not consider the interaction between a user and a product in isolation, as so often occurs in laboratory settings. The natural situation in which the interaction takes place, both in space and time (including the mental state of the user), has to be taken into account. The human-centred design approach requires in-depth knowledge of the way humans perceive and reason about their environments. Moreover, we also need to understand how humans accept and appreciate smart products and environments [Rijsdijk, 2006].

### Transparent interfaces

The introduction of new technologies has inevitably led to a range of consumer and professional products with complex and embedded functionality. Increasingly, products are being designed to handle a number of complex tasks and offer growing amounts of information to the user. Such products incorporate an increasing number of functionalities with which users can only interact via a complex, menu-structured interface instead of a simple, straightforward one where each function has its own unique input device (e.g. a button). As a result, users often struggle with the complexity of the interface instead of interacting with the content. Ideally, the user interface should be

13 Human factors involves the study of all aspects of the way humans relate to the world around them, with the aim of improving operational performance and safety of systems and services. See www.wikipedia.org.

invisible. In other words, the focus should be on interacting *through* the interface instead of interacting *with* the interface per se. This means finding ways of making the interface as transparent or unobtrusive as possible, thereby allowing the user to engage in the task or content at hand rather than be bothered by how to control or interact with the product.

One important assumption — and one that may also be interesting when it comes to incorporating insights from the neurosciences — is that we can improve transparency by equipping products with technology such as BMIs to collect (preferably instantaneously) information about the user. The product can use such information, for instance on what the user is doing, feeling or looking at, to adapt itself to the needs and wishes of the user. Current research on how products can increase transparency, in particular by reducing ambiguity, focuses on two areas. First, researchers are looking to identify the features of human behaviour that may help products guess and track user intentions, detect intentions not reflected in overt behaviour, or ignore overt behaviour that does not reflect user intentions. Secondly, researchers are trying to present functionalities in a way that corresponds with how humans experience their environment, preferably based on a knowledge of the user's intentions.

Methods for tracking user intentions in a smart environment are only acceptable if they are non-obtrusive. For example, using smart cameras to derive user intentions from gestures should not involve using special gloves to identify the position and shape of the hands.

### User perspective

Smart products and environments have two main implications for users. In the first place and most importantly, the interface no longer needs to be confined to a single display. This is often referred to as 'the interface goes beyond the desktop'. This introduces a possible new element to user interfaces, namely the experience of near-immersion. In the field of virtual and augmented reality, the subjective experience of 'presence' is closely linked to the phenomenon of immersion[14]. In the second place, it will become increasingly common for groups of individuals to be immersed in and interacting with the same environment simultaneously, both physically (e.g. smart rooms, smart homes) and virtually (e.g. Second Life, MySpace). More broadly speaking, the trend of going beyond the desktop indicates that user interfaces can no longer be evaluated merely on their usability (effectiveness, efficiency and ease of use). It clearly underlines the importance of understanding the user experience and the underlying emotional dimensions. This is nicely reflected in recent developments in evaluation methodology, which is starting to focus on other,

14 Presence refers to the degree a person feels immersed in the mediated world while believing this world to be non-mediated, i.e. real [IJsselsteijn et al., 2000].

emotional criteria such as enjoyment, fun, engagement, beauty and hedonic quality [Quesenbery, 2002; Hassenzahl, 2002; Hassenzahl, 2004].

Note that this trend does not imply that the traditional usability elements should be forgotten. More than ever, it is crucial to assess the user's mental model about the current or future situation. But it *does* imply that all aspects of human behaviour (needs, desires, beliefs, emotions, knowledge, skills, experiences, perceptions and reactions) should be taken into account and translated into workable variables. Additionally, it is important to understand group processes and the role individuals play in groups, as described by James Surowiecki [2004] in 'The Wisdom of Crowds'. This means considering such topics as how to induce human cooperation in sharing and distributing content in decentralised peer-to-peer television systems [Fokker et al., 2007].

The usefulness of understanding user experiences and emotions was shown in a study on engagement [De Ridder and Rozendaal, 2008]. Engagement is the intrinsic readiness to put more effort into exploring and/or using a product than strictly required. The study involved game-like user interfaces in which the richness of the interface was varied by manipulating its appearance (colours, contrast, sound effects) and the number of possible actions. It was found that engagement depends on the richness of a user interface via perceived challenge and sense of control. Users appreciate the challenges evoked by the richness of an interface, provided that they still have the feeling that they are in control. This sense of control can be threatened in two ways: firstly, if the system is too simple (in that it does not provide enough means to fulfil one's goals), and secondly, if the interface is too complex and so confuses the user. In other words, developing successful user-centred interfaces is a delicate balance requiring a thorough knowledge of human beings. Any means of acquiring this knowledge, for example from the neurosciences, is welcome.

### User understanding and neurosciences

Panasonic's futuristic system known as LifeWall was recently demonstrated at the 2008 Consumer Electronics Show[15]. LifeWall is literally a wall created by a high-definition projection system acting like a hypersensitive computer screen that can recognise faces, gestures and a person's motions (see Figure 4). This makes new ways of interaction possible; for example, the wall can track the viewer's movement through the room, detecting the distance between the image and the viewer and optimising the size of the image accordingly. Or it will automatically recognise a person's face and display a customised table of contents. Whether LifeWall will succeed in *"enhancing the human experience by bringing people together around a whole new kind of digital hearth, one that goes far beyond the boundaries of our living rooms. A place that*

15 See www.panasonic.com/cesshow/

**Figure 4**
*Panasonic's LifeWall aims to "enhance the human experience by bringing people together around a whole new kind of digital hearth, one that goes far beyond the boundaries of our living rooms. A place that enables new ways to learn, communicate and interact, not just with friends and family, but with new friends around the world". Photo is taken at the 2008 Consumer Electronics Show.*


*enables new ways to learn, communicate and interact, not just with friends and family, but with new friends all around the world..."*[16] is not clear yet. But what it clearly illustrates is the growing dependence of new technologies on fast and accurate interpretations of human behaviour. At the same time, there is a growing awareness that the complexity of human behaviour cannot be captured just by looking at overt actions [Norman, 2004]. New insights into and measures of human behaviour are needed, e.g. for continuous monitoring. Neuroscience is one of the upcoming disciplines that might provide such insights, contributing in this way to the development of truly human-centric interactive products and environments.

### 3.2.2 Trends and opportunities in the neurosciences potentially relevant to MMI

*Frans W. Cornelissen*[17]

This chapter reviews a number of neuroscientific findings about the human brain that may be relevant to the human-centric design of products and smart environments. The list is not intended to be exhaustive but serves as a guide to the type of information that the neurosciences could provide to those working in the field of MMI. Most of the neuroscientific findings mentioned here

**16** Quote by Panasonic's president, Toshihiro Sakamoto, at CES2008.

**17** Associate Professor, Laboratory for Experimental Ophthalmology and BCN NeuroImaging Center, University Medical Center Groningen, University of Groningen.

are potentially important when evaluating the effectiveness of interfaces (i.e. do the interfaces stimulate the relevant brain regions or functions?), including in relation to the user's perception and emotions. The following five topics will be touched on:

- Quick and flexible information processing using a modular brain.
- Measuring attention and emotion: beyond the fixation map.
- Measuring obtrusiveness and immersion using network analysis.
- Learning, understanding and anticipating using mirror neurons.
- Dealing with ambiguous and multi-source information using neural population codes.

Each neuroscientific finding is explained briefly, with its possible relevance to MMI being indicated.

### A guide to quick and flexible information processing: modular information processing in the brain

The human brain is a highly modular, parallel system, something that is relatively well understood for the visual system. It contains functionally specialised modules (i.e. brain areas) for colour vision, motion vision, stereovision, form vision, texture vision, object representation, face recognition, and so on [Livingstone and Hubel, 1987; 1988]. Separate neural pathways (i.e. circuits of anatomically and functionally connected brain areas) encode visual information specifically for localising objects in the environment, for recognising and performing actions, for recognising objects, and for recognising the surface properties of objects. In fact, most of these pathways originate in the retina (in the case of sighted people, but not in the case of blind people).

In many real-world tasks more than one of these pathways is activated. For example, when we look at tools, not only are our object recognition areas active, but also regions of the action pathways. This suggests that tools also activate areas in the action pathway related to reaching and grasping, presumably in order to prepare us to use the tools. We do not even need to be fully aware that we are observing tools for this kind of activation to happen [Fang and He, 2005].

'Pre-activation' of this kind may constitute an important part of what makes an MMI 'intuitive' and 'self-explanatory'. It implies that to be successful, interfaces need to specifically stimulate those brain regions involved in the task they are designed for. In turn, this suggests that relatively simple, task-geared interfaces may often be the best choice. This would avoid competition between multiple pre-activated brain areas. Neurocognitive methods and neuro-imaging techniques could be used to evaluate the effectiveness of an interface by verifying the presence and specificity of activation in relevant brain areas. An example: in certain cases sign interfaces (non-touch) may be a very useful means for communicating with a computer. As we all know, in certain emotional situations — for example in traffic — humans (too) easily use and learn to use sign language to communicate very simple messages. However, a sign language that can be used to communicate more complex information — as used by deaf people — requires a long time to learn. Neuro-imaging might assist in finding ways of signing that are both easy to learn and intuitive, and can convey relatively complex information to a computer.

### Measuring attention and emotional responses: beyond the fixation map

Current methods of evaluating web pages often involve gaze tracking, i.e. determining where on the web page the eye has dwelled. The measurements are plotted as fixation maps, which show what parts of a page viewers have looked at most. While such maps may indicate the items salient to the observer, the measurement cannot tell whether the viewer has actually processed the information, consciously perceived it, or had an emotional or aesthetic response to it. Neuro-imaging techniques could provide more data on the degree to which the viewer actually absorbed the information. Indeed, current efforts are underway to measure emotional and expert response to visual material using a variety of imaging techniques. The idea is that such neuro-imaging information can be used to create visualisations of a person's emotional and attentional state. Synchronising these measures with the viewer's gaze direction could produce an 'interpretation map'. For example, such information could constitute a 'beauty' map indicating what aspects of a painting were considered most attractive.[18] Other efforts aim to objectively measure, model and predict the psychological effects of colour and texture.[19] At present, such information can only be measured reliably for groups of research participants, as much averaging of the neuro-imaging data is required before subtle differences in brain response can be detected. Yet the ability to do so could already have a substantial impact on product design in its most general sense. Designers of buildings, consumer products, novel food, and computer program, web page and game interfaces could benefit from the ability to communicate information predictably. For example, neuro-imaging research showing that specific colours or textures are related to specific brain activity — which in its turn is related to a certain kind of emotion — can be used to achieve intended psychological effects.

These novel measuring methods will result in the emergence of 'neuro-centered design', the use of neuro-imaging to evaluate and optimise designs. Instead of filling in a questionnaire, research participants will view many different variations on, for example, the design of a web page. Measurements

18 See www.nest-percept.eu.

19 See www.syntex.or.at.

of their brain responses will tell researchers which one they liked best. It may be a while before such techniques make it into mainstream web page evaluation tools, however. After all, it took well over forty years for eye-tracking to become a standard tool in advertising.

### Measuring obtrusiveness and immersion: about networks and connectivity

Neuro-imaging started out largely as a modern form of phrenology[20]. The presence of a nicely coloured blob on top of a high-resolution brain image provided evidence for the presence of a brain 'function' in that region. This 'where', or localisation question, dominated the cognitive neurosciences in its early years. Over time, scientists realised that localisation alone would never tell them how the brain actually works and how it performs all of its computations. More elaborate paradigms and methods of analysis, as well as more powerful imaging tools, have allowed the neurosciences to move from the 'where' to the 'how' question, with varying degrees of success.

The current trend is to not only consider brain areas or regions, but to specifically examine connectivity. Brains are thought to consist of networks of nodes that are activated to various degrees depending on the task at hand. The strength of the connection and the relative node activation may vary depending on task, intention or goal. Again, new developments in analysis and paradigms have enabled this conceptual transition. Although measuring network activity in itself is more complicated, it will most likely help improve any future man-machine or brain-machine interface, as more specific and selective activation patterns can be measured that are easier to interpret in terms of mental activity.

Interesting in this context is that neuro-imaging and network analyses may help determine when an interface becomes 'obtrusive' rather than helpful (e.g. because certain brain networks become overstimulated, shown by a loss in response specificity or interference between networks). We may then also be able to say whether it is actually possible to stimulate all the human sensors in order to evoke a feeling of immersion (see subsection 3.1.1 and 3.2.1). Or will this only cause the human brain to adapt or even shut down certain information gates (as we do when we go to sleep in a noisy environment)? Will such highly stimulating environments actually be effective? It is interesting to compare this with the use of colour. Sparse use of colour helps improve an interface by highlighting important aspects of it. Colouring everything causes crowding, attenuates colour signals in the brain, and in the end is only confusing. Neuro-imaging could help determine whether certain information channels are sufficiently independent to allow them to be used effectively in parallel.

**20** Phrenology was an 18th and 19th-century pseudoscience based on the belief that each bump and depression in the human skull stands for certain personality traits, for example benevolence, imitation, wonder, wit, idealism, etcetera.

## Learning, understanding and anticipating: using mirror neurons to observe and understand the actions of others

Research shows that people feel more positively towards robot workers when they cooperate with them than when they take over certain tasks [Takayama et al., 2008]. Yet one of the main issues associated with robots — and interfaces in general — is that they are still very clumsy when dealing with people. They do not understand humans properly and are not very social. This is where robotics and domotics (i.e. comfort and convenience improving technologies at home) could learn a great deal from the neurosciences. For example, the human brain appears to use the brain areas involved in action performance to observe and understand the actions of others as well. These areas contain 'mirror neurons' (see Figure 5): neurons responding both when an individual acts himself and when he observes someone else acting [Rizzolatti et al., 2001]. Current research indicates that humans use the neural systems for initiating their own actions to understand the actions of others. This action recognition system is broadly tuned; the human brain tends to treat robots that perform simple actions similarly to humans that perform these actions [Gazzola et al., 2007a]. Even people without arms and hands who have learned to perform actions with their feet nevertheless activate the same regions of the brain as people with hands when observing other people perform actions [Gazzola et al., 2007b]. This implies that at least part of the coding of information in the brain is in terms of action goals, rather than specific actions. Determining goals might also make it easier to anticipate the intentions of others.[21] Indeed, some researchers claim that the mirror neuron system (MSN) is aimed at response preparation and therefore anticipation [Newman-Norlund et al., 2007].

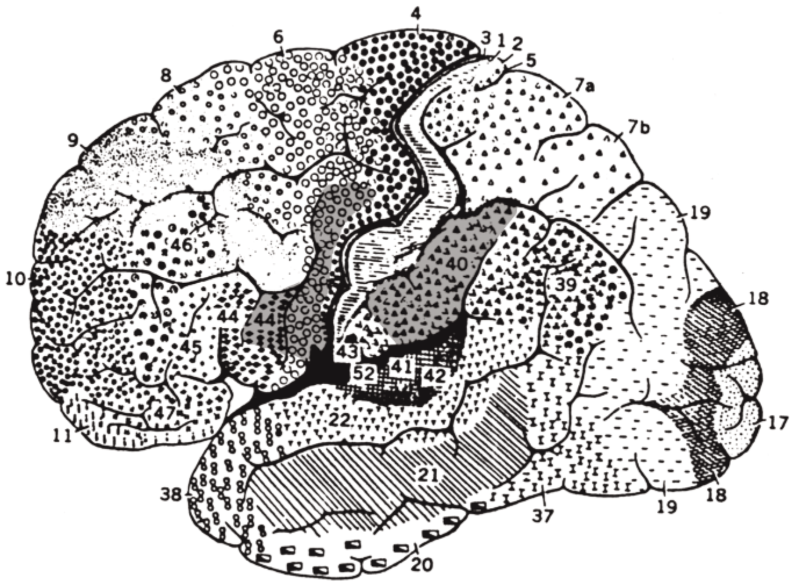



**Figure 5**
*The mirror neuron system in humans. This view of the human brain is showing the areas (grey) that form the mirror neuron system. Source: www.scolarpedia.org*

**21** It is the difference between noting that someone is moving his hand (i.e. momentarily useful information) and predicting that he is going to pick up a cup (i.e. predictive information).

One of the implications of this is that robotic systems or even interfaces need not *look* very human-like in order to be effective. In order to be ‘understood’, the system or interface should, however, activate the brain areas that encode the relevant behaviour. Presumably, however, *acting* human-like may facilitate the recognition processes, e.g. recognising the aim of a particular action. Moreover, natural interfacing through imitation and learning by observation could make MMI very intuitive. Robots could use their own action machinery to interpret the actions of others. This would be particularly successful if they used somewhat similar action systems, but such similarities may not be necessary. According to the Hebbian hypothesis [Keysers and Perret, 2004], we develop mirror neurons because we see ourselves act. Robots could be programmed to do the same: observe the consequences of their own motor programs, and then reactivate these motor programs while they observe others (even humans) perform similar actions in order to understand these actions.[22]

### Combining information to reliably sense the world around us: dealing with ambiguous and multi-source information using neuron population codes

In many regions of the brain, information is represented by patterns of activity occurring over populations of neurons. In general, these populations consist of neurons that sense similar aspects of the environment (e.g. the orientation of a line element). Although all neurons in the population may encode orientation, each of them will have a slightly different tuning function. In this example of orientation tuning, some neurons respond more to horizontal lines, others to vertical lines, and yet others to oblique lines. In this way, the population as a whole is able to detect lines regardless of orientation, even though individual neurons cannot.

Individual neurons are also noisy, in the sense that one and the same neuron may respond somewhat differently when confronted with the same line orientation multiple times. By pooling the information over a large number of neurons, the brain may nevertheless obtain accurate estimates of environmental properties (e.g. the actual orientation of a line). Understanding the encoding of information in neural population activity is important, both for grasping the fundamental computations underlying brain function and for interpreting signals that may be useful for the control of prosthetic devices [Sanger, 2003]. Encoding information as patterns of activity within populations of neurons may also have added benefits, e.g. boosting resilience to injury, improving the precision of action, and increasing the ability to learn [Sanger, 2003]. Moreover, neuronal variability actually represents an advantage: the variation in the population response is a direct measure of the reliability of the observation. The information is used when it combines information from various sources [Deneve et al., 2001; Ma et al., 2006; Pouget et al., 2003].

**22** Personal communication with Christian Keysers, University of Groningen.

Understanding the population patterns of activity may help us comprehend how the brain's 'neural code' is read. In the case of brain-machine interfaces, such information will be important for controlling external electrical interfaces and prosthetic devices.

Finally, the noisiness of the brain's internal processing may actually cause it to be relatively robust in dealing with noise in the outside world.[23] Systems mimicking cortical computations could inherit the brain's robustness in dealing with uncertainty when trying to guess the user's intentions. This may also be relevant when the actions of the person controlling or working with the interface are unreliable, e.g. due to movement disorders [Grossman and Sanger, 2007]. MMI could mimic this behaviour and use ubiquitous sensors, all tuned to different aspects of the environment, to provide the information required for interacting with humans and assign levels of confidence to the information provided.

Take the example of a system working as a perfect butler (see subsection 3.6.2). How would it know about its master's (i.e. user's) state of mind? It could try to estimate this from the momentary situation alone, but better would be if it could use stored information and obtain information from sensing many additional aspects of the environment simultaneously. This is what a human being would do. How to know whether the master is still in bed? It might probe a motion sensing camera in the bedroom, but the master might lie completely still. It might use an infrared camera, but it might be the cat or dog that's on the bed. It might recognize the shape of a human body, but the master might be completely covered by blankets. Additional information might come from measuring changes in room temperature, $CO_2$ levels, humidity, sound (snoring, shuffling, talking). But also a sensor in the door knob could contribute to the total evidence. Each of these sources might not be very reliable in itself, but their combined information, weighted by an estimate of their momentary reliability, might provide a decent estimate. Obviously, measures from other parts of the house or prior knowledge (e.g. how late has he been up last night?) could also contribute.

23 Personal communication with Remko Renken, University of Groningen.

## 3.2.3 Neuroscientific challenges in the field of brain-machine interfaces

*Chris van der Togt*[24]

Brain-machine interfaces (BMIs; see Figure 6) were originally aimed at restoring communication and control to people with severe motor disorders such as ALS (amyotrophic lateral sclerosis), brainstem stroke, spinal cord injury, muscular dystrophies, and cerebral palsy [Wolpaw and Birbaumer, 2002]. This fascinating new approach offers great promise for the near future, in that it will allow paralysed individuals to control the movements of their prostheses and wheelchairs and make communication with locked-in patients possible. Unlike methods that depend on the brain's natural output pathways of peripheral nerves and muscles, BMIs convert neural activity at the level of neuronal action potentials (invasive) and EEG (non-invasive) into signals that control computer cursors or external devices. The BMI paradigm bypasses the normal biological pathways mediating volitional (i.e. desired) movements and employs upstream neural activity that has a complex relationship to motor or cognitive behaviour. The transformation between this neural activity and the required control parameters (for directing the external device) can be facilitated by sampling the relevant activity in the appropriate brain regions, such as the motor cortex cells involved in limb movement. Conversion of these signals can be further aided by appropriate transformation algorithms to generate the requisite control parameters.

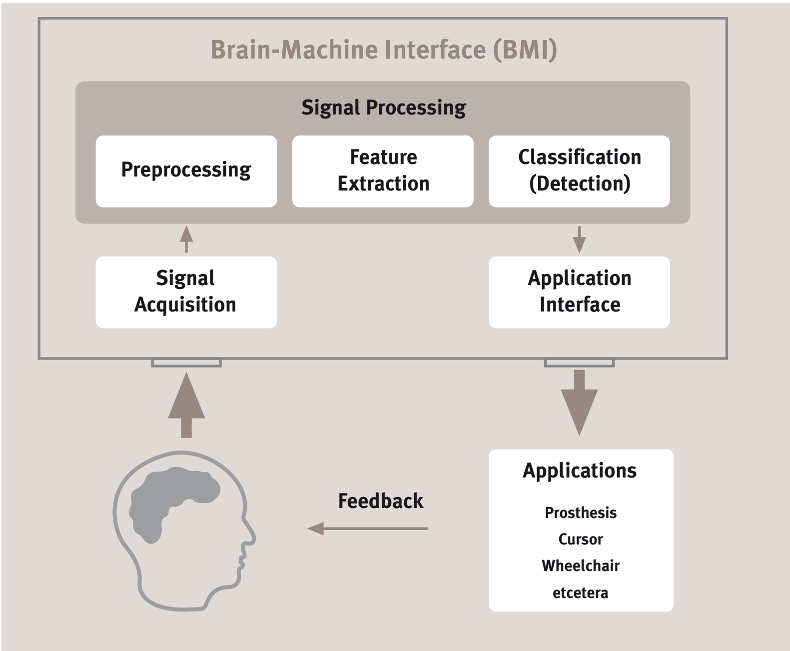



**Figure 6**
*Brain machine interfaces (BMIs) convert neural activity into signals that control computer cursors or external devices.*

**24** Researcher, Netherlands Institute for Neuroscience (NIN).

The feasibility of BMIs depends on a number of factors, for example how well brain activity can be recorded and decoded to translate volitional decisions into specific instructions for mechanical devices or computer interfaces. One important question is whether this decoding of brain activity can be standardised across different users or whether each user is required to train and learn through neurofeedback on an individual basis. In other words, do users have to learn to use their cortex artificially as an output pathway, or can BMIs tap into their intentions directly (see box 2, Locked-in patients cannot learn)? Although spectacular results have been achieved in the laboratory setting, a number of studies indicate the need to overcome fundamental problems limiting their application.

### Variability

Whether human or animal, the BMI user typically assumes a specific posture in a simple stereotyped setting free of distractions, and operates the BMI for brief periods under close supervision. Despite these controlled conditions, one of the hallmarks of the results achieved is their variability. Users do much better operating an external device with their thoughts on some days than on others. Performance can vary widely even within a single session and from trial to trial. This extreme variability is perhaps best illustrated by BMI-based movement control. For example, Figure 7 compares cursor movement times when the cursor is controlled by a joystick to cursor movement times when the cursor is controlled by a set of single neurons in the motor cortex [Hochberg et al., 2006]. BMI control is slower than joystick control and is also far more variable. Such variability appears to be a characteristic feature of all BMI approaches, whether non-invasive (e.g. EEG) or invasive (e.g. electrocorticographic [ECoG] or intracortical).[25]

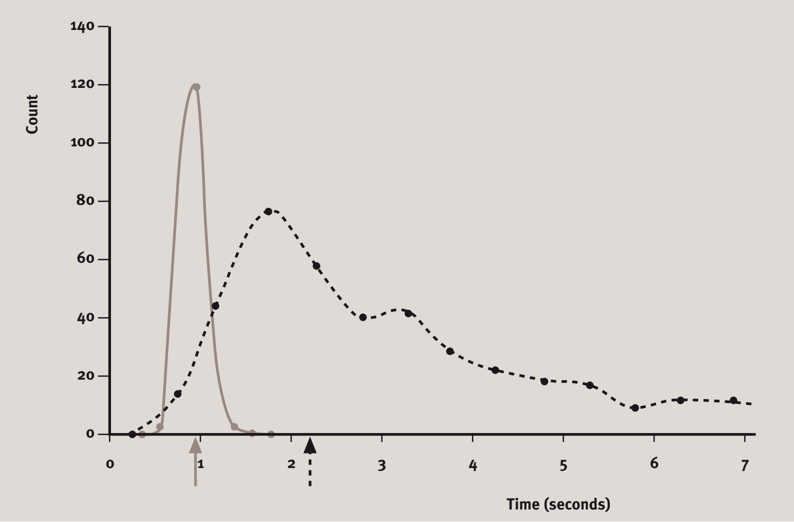
### Invasive BMIs do not necessarily provide better control[26]

The above mentioned research results suggest that current neurophysiological recording methods are insufficient, or at best lack an adequate level of detail. Studies of multidimensional movement control have revealed another surprising feature of BMI performance, however. Although most researchers had assumed that invasive methods using single-neuron activity would provide better control than non-invasive methods using EEG, the results to date do not support this assumption. As Table 1 summarises, the movement control obtained with scalp-recorded sensorimotor rhythms falls in the same range in terms of speed and precision as the control obtained with single neurons. The fact that EEG and single neurons provide similarly defective control suggests that this problem is independent of the recording method.

25 ECoG measures electrical activity across the whole depth of the cortex (grey matter), i.e. between electrodes on the cortical surface and the white matter. This type of activity is a good estimate of local cortical population activity. Intracortical electrodes give an even higher resolution of activity, i.e. record single neurons (single-unit) or multi-unit activity.

26 The expert group was divided over the differences between invasive versus non-invasive brain machine interfaces. According to Chris van der Togt (author of this section), invasive BMIs do not necessarily provide better control of external devices. Other members of the expert group — for example Johan Hoorn (subsection 3.2.4) — do think invasive BMIs are more effective when it comes to measuring brain activity or controlling a prosthesis or computer. They advise measure as locally as possible when it comes to sampling electromagnetic signals. In short, this issue is still part of an ongoing scientific debate, and the reader will notice the differences of opinion in the various sections. What the members of the expert group do agree on, however, is that non-invasive BMIs are preferable to invasive ones, especially for healthy user groups.

**Figure 7**
*Distributions of times needed to move the cursor to the target in a centre-out task for a person using neurons in the motor cortex (dashed line) and for three people using a joystick (continuous line). To appreciate these performance differences, imagine a user who has to hit a moving target by mentally throwing a ball. The user might be very capable at accurately estimating the time of motion onset, the time needed for the ball to reach the target and the point in space where they will meet. However, if his response onset varies widely, as is the case with motor cortex control, the chance that the ball will actually reach the target may be quite slim [Hochberg et al., 2006].*




The reasons why this may be so are not clear: *"The degree of independent control of cells may be inherently constrained by ensemble interactions. Moreover, activity of each cell in the population has some stochastic component which may degrade learning optimal control of any particular cell."* [Carmena et al., 2005].

## The difficulty of measuring intentions directly

The studies cited above did not actually measure the user's intention. What they did measure is the modulation by the user of cortical activity at a certain location after neurofeedback training. A small area of the cortex has artificially become an output channel for volitional control. The difficulty of measuring intentions directly becomes clear when we realise that a large degree of brain activity, euphemistically classified as spontaneous brain activity or noise, may not be related to conscious mental activity at all. The global workspace hypothesis [Dehaene and Changeux, 1997] states that working memory is mediated by ongoing flexible and changing interactions between remote cortical areas, suggesting that only at certain times the activity within some cortical area is relevant for output.

**Table 1**
*The ranges are based on each study's best user. Movement precisions are measured as target size as percentage of workspace and calculated from the dimensions of the targets, the cursors, and the workspaces [Wolpaw and McFarland, 2004].*

| Method | Reference | Movement time (s) | Movement precision (%) | Hit rate (%) |
|---|---|---|---|---|
| Intracortial implant | Serruya et al. [2002]<br>Taylor et al. [2002]<br>Carmena et al. [2003] | 1.5 – 2.2 | 1.3 – 7.7 | 86 – 89 |
| Scalp EEG | Wolpaw and McFarland [2004] | 1.9 | 4.9 | 92 |

Neurophysiologists have traditionally ignored ‘spontaneous’ activity, focusing instead on the average activity of a neuron — induced by repeatedly presented stimulus — as the meaningful representation of that neuron’s response. Similarly, a user must repeatedly make a single stereotypical movement in his mind to obtain cortical response profiles, from which parameters can be deduced to control a robotic arm, for example.

This suggests that it will not be possible to measure intentions from one area of the cortex alone, and that activity at one location of the cortex will at times be irrelevant to estimating control parameters. Without a fundamental change in how we conceive BMI and pursue its development, variability will remain a prominent feature, and the surprising similarity between the capacities of invasive and non-invasive methods is also likely to persist.

**Box 2: Locked-in patients cannot learn**

Locked-in patients are people who do not have any muscular control but whose brain activity shows that they are conscious and mentally active. Although the problems encountered here may not be relevant for healthy subjects, use of BMI methods for locked-in patients illustrates their severe limitations. Healthy monkeys learn to execute more or less complex upper limb movements with activity patterns from motor brain regions alone — without the related peripheral motor activity. This is usually after extensive training using normal arm motion. Clinical applications in human diseases such as amyotrophic lateral sclerosis (ALS), paralysis from stroke or spinal cord lesions show only limited success. Attempts to train patients in BMI communication after they have entered the completely locked-in state (CLIS: no muscular control, no eye movement, no external sphincter control), with no remaining eye movement, have failed. Of the seven human patients with ALS who started training after they had entered CLIS, none acquired sufficient brain control to communicate [Wilhelm et al., 2006]. Loss of the contingency between a voluntary response and its feedback or subsequent reward in completely paralysed individuals is thought to prevent them from learning. This is even the case when afferent input and cognitive processing (attention, memory, verbal imagery) remain intact [Birbaumer, 2006a, b].

*Chris van der Togt* [27]

## A different concept of the human brain is required

One of the distinguishing features of humans is their adaptability to a constantly changing environment. The human cortex is the organ responsible for this capability, and its behaviour should therefore be interpreted in this context. The brain is not a machine or an assembly of automata; it is a society

27 Researcher, Netherlands Institute for Neuroscience (NIN)

of living entities (neurons) that have no notion of the outside world.[28] Their objective is to sustain themselves in a competitive environment. Competition and selection are at the level of synaptic contacts, which determine the rules of interaction and, ultimately, the behaviour of these simple individual neurons. Imagine a big city: the people living there can only survive by doing a certain job and contributing to the whole, by adapting to their environment and specialising in one way or another. The shopkeeper sells goods he thinks other people require; if he sells the wrong products he will eventually go out of business. The classic Darwinian mechanism of variation, competition and selection also applies for neurons. In this case, their activity represents behaviourally relevant features or gestures that lead to reward or punishment for the whole individual to which they belong. Reward and punishment ultimately drives the competition between neurons.

We might argue that a city has a central executive unit that determines its output. However, central administrative units in fact play only a minor role in cities. Compare Istanbul to Amsterdam and note what makes these cities different: history, economic relationships with other cities, the flux and flow of their inhabitants, traditions and cultural differences. Central executive units are more like homeostatic regulators of internal activity. In fact, most of the city's traffic and affairs could be interpreted as unconscious activity. Only during major events like an important football match does a city activate to a state with a single aim, to win that match; this is comparable to conscious activity. It is of fundamental importance to distinguish this type of conscious activity from ongoing 'spontaneous' unconscious activity if we hope to understand the brain and continue to optimise brain-machine interfaces.

### 3.2.4 Engineering challenges in the field of brain-machine interfaces

*Johan F. Hoorn*[29], *Kier Heeck*[30]

From a man-machine interaction perspective, it would be nice to have a direct exchange of information between the human brain and electronic devices without needing touch, visual or sound interfaces. Unfortunately, there appear to be more hurdles than solutions in this respect (see for example subsection 3.2.3), and many potential applications are still far out of reach. Few companies to date have invested the necessary time and money in effective product development, according to the CEO of Cyberkinetics [Ortiz, 2007]. BMI still faces numerous challenges before it is ready for widespread use, although rapid progress is being made in the area of sensor technology (i.e. measuring brain activity). Wireless technology, bio-compatible materials, and safe

**28** See 'The Society of Mind' by Marvin Minsky for similar ideas.

**29** Managing Director of the VU Center for Advanced Media Research in Amsterdam (CAMeRA), VU University Amsterdam.

**30** Technical staff, Condensed Matter Physics, VU University Amsterdam.

insertion methods are quickly becoming engineering problems rather than scientific ones. This subsection will look at the technological features that brain-machine interfaces require. To facilitate the general day-to-day use of BMI, we are in search of interfaces that are portable, non-invasive, cordless and automated — or at least easy-to-use.

Ideally, a person connected to a computer is not fixed to a particular location; in other words, a BMI should be portable. That rules out fMRI as an interface, where the person is contained by the equipment[31]. For even greater mobility, new hardware for brain-machine interfacing should be wireless. BMIs should preferably be non-invasive as well — not many people will like the idea of a device that is literally plugged into their brain tissue just to operate a mobile phone, for example. In addition, BMIs must be more automated. At the moment, the systems are complex to use and their reading of brain activity difficult to interpret. They require experts to perform certain tasks, for example entering the parameters needed for signal processing and adjusting processing to accommodate changing neural systems. In addition, as explained in the previous subsection, BMIs do not actually measure the user's intention directly. It is the user who must learn to use his thoughts to create the brain signals serving as input for the BMI. Such a training programme can take weeks or even months.

Broadly speaking, there are only two possible candidates that may meet most of these requirements in the future. They are electric/electromagnetic interfaces and interfaces that make use of light.

### The use of electric/electromagnetic radiation

There are different ways to measure or influence neural activity non-invasively by means of electric or electromagnetic radiation, for example magnetoencephalography (MEG; see Appendix 1). Some engineers have tried to make these techniques portable. For example, Bob Kraus of the Los Alamos National Laboratory has developed a device that could be considered a portable MEG [Danneskiold, 1998]. Brain magnetic fields are measured by sensors called Superconducting Quantum Interference Devices (SQUIDs), which are cooled in liquid helium. A spatial resolution of .25 mm and a temporal resolution of one millionth of a second are possible. The system consists of an MEG helmet made of lead in which SQUIDs are placed that exclude the earth magnetic field and other interferences reasonably well. Inconveniently, users must be in a room lined with long aluminium sheets to reduce external magnetic interference. In addition, SQUIDs mounted on top of the helmet measure external magnetism so as to correct the signal picked up by the SQUIDs inside the helmet.[32] MEG performs rapid measurements and estimates of the source of the signals in the brain is quite reliable.

31 fMRI is also too bulky and expensive, and its measurement of blood oxygenation too slow to track many of the characteristics of mental processes.

32 There is a patent on measurement in ultralow magnetic fields [Clarke et al., 2006].

All other non-invasive methods using electromagnetic radiation to capture brain magnetic signals are stationary (for example fMRI), and if they are mobile, they need to be protected from external interference, like the shielded room for the portable MEG.

In the end, electroencephalography (EEG) is the method of choice for many BMI applications. EEG measures the electrical activity produced by the brain as recorded by electrodes placed on the scalp. It is fast, cheap and portable. Guger Technologies produced a BMI (i.e. g.MOBIlab) that records EEG relayed by Bluetooth or USB to a laptop for signal analysis.[33] The signals can be used for messaging as well as playing computer games. The Wadworth's Laboratory of Nervous System Disorders has developed the BCI2000 research system, also using an EEG cap.[34] With EEG, the movement artefacts can now be handled by clever signal processing. The only inconvenience is that the electrodes need a conduction paste that sticks to the hair. The search for a reliable dry-electrode technology would certainly represent a breakthrough for the use of EEG in consumer products, games and semi-permanent BMI setups for patients. EEG is used extensively for neurofeedback, and its commercial applications will allow cheaper equipment to enter the market. The only problem is that EEG still produces a very diffuse and smeared-out signal, i.e. it has a low useful information content. A BMI system based on EEG needs time to collect the signals from multiple areas of the brain, separate the signals sent by relevant sets of neurons, and translate them into action.

A general problem with all these technologies is that it is still difficult to localise the source of the signal and hard to identify the cognitive correlate of a signal. Invasive methods are still the best option, although uncomfortable for the user.[35] Researchers are working on portability, but the need to protect the devices from external interference prohibits broad application. The g.MOBIlab of Guger Technologies records EEG on the scalp and is a most convenient method of application for general man-machine interactions.

### The use of light

Another means of measuring brain activity is to use light. Imaging with diffuse light by means of near-infrared spectroscopy (NIRS) and diffuse optical tomography (DOT) is based on the absorption spectra of water and blood, i.e. haemoglobin [Kienle and Patterson, 1997]. It is possible to observe a person's blood flow in 3D while they are performing a cognitive task. This is a relatively slow process, however, limiting the application options for brain-machine interaction. Nevertheless, NIRS is easy to make portable and comfortable to wear.[36]

**33** See www.gtec.at.

**34** See www.wadsworth.org.

**35** See footnote 25.

**36** In the BrainGain project (see box 1), a Dutch commercial spin-off of UMC St Radboud is working on using NIRS as BMIs. See www.artinis.com.

**Figure 8**
*The changes in electrical activity in the brain's visual centre are transmitted wirelessly to the computer to restore Mawg's balance. Photo courtesy of Rob Burke, www.flickr.com.*

## Combination of measures

The ideal neuro-imaging technique for BMIs should be able to measure brain activity in a single individual (i.e. single trial) at a high temporal and spatial resolution, be non-invasive and non-obtrusive. It is clear from the above that this ideal technique does not yet exist. One current trend within neurocognitive research is to combine techniques that have their strengths in different realms. For instance, electrophysiological measures with a high temporal but only modest spatial resolution are combined with fMRI, which has a high spatial but only modest temporal resolution. The combined information should provide the best of both worlds. A combination of measures might also offer more options. For example, the research group MindGames at the former MIT Media Lab in Dublin developed a prototype wireless, non-invasive headset called Cerebus[37]. Cerebus makes use of various measures. It records EEG for a high temporal resolution while using DOT to acquire high spatial resolution. The device has not been brought to market, however.

37 See medialabeurope.org/mindgames. Cerebus can be used to play the Mind Balance game. A creature called Mawg balances on a tightrope over a futuristic city. Cerebus measures 'visually evoked potentials' (VEPs), electromagnetic pulses at the back of the skull where the visual centre resides (i.e. the occipital lobes). If Mawg slips off the tightrope on one side, you can restore its balance by looking at the other side. The changes in electrical activity in the brain's visual centre are transmitted wirelessly to the computer to restore Mawg's balance.

## 3.3 Initial thoughts on applying neuroscientific findings in the field of MMI

*Ira van Keulen, Jan van Erp*[38]

At the first two meetings of the expert group, the members discussed and tried to match recent important neuroscientific and cognitive scientific findings with ideas for improved interfaces from MMI research and practice. The following table expresses their initial thoughts on how best to apply neuroscientific knowledge in order to improve MMI. The table should indicate the breadth of possibilities while at the same time identifying future MMI-related research questions for the neurosciences. These initial thoughts show that most of the projected applications are related to the neurophysiological measuring (but also influencing) of different cognitive functions. At the same time, these are precisely the applications that lie farthest ahead in the future (see subsection 3.2.4).

Some of these initial ideas — indicated in Table 2 — have been elaborated in the final section (3.6) of this chapter. That section also describes various scenarios for neuro-designed interfaces; most of these can still be called science fiction and a few may even remain so. Nevertheless, they may inspire future collaborative research between neuroscientists and MMI researchers and developers.

The table is divided into different domains: perception and interpretation, learning, motivation and reward, attention and alertness, and miscellaneous. It is important to note here that the table is based on the specific expertise of the members of the expert group (see the Project Organisation section at the end of the book). A different mix of expertise would have resulted in a different range of ideas.

**Table 2 (on the next pages)**
*Possible applications of neuroscientific findings in the field of MMI.*

**38** Chief Scientist of the department of Human Interfaces, TNO Human Factors.

| FINDINGS FROM THE NEUROSCIENCES | QUESTIONS FROM MMI R&D PERSPECTIVE | AIM OF POSSIBLE APPLICATIONS |
|---|---|---|
| | *Perception and interpretation* | |
| Interpreting perception, i.e. brain-imaging techniques (fMRI) allow us to see how people interpret a certain stimulus. We can see how interpretations develop over time and whether an interpretation ceases to exist *(see example XIII)*.<br><br>Predicting interpretation, i.e. brain-imaging (fMRI) allows us to see and predict what a person has observed when presented with an ambiguous stimulus. | At what level of detail can an interpretation be measured (e.g. can fMRI show us whether someone interprets the word bill as 'an invoice' or 'a duck's beak'?)<br><br>To what extent is it possible to predict interpretations at the level of semantic meaning (e.g. not just red or green)?<br><br>How reliable are the neural signals underlying interpretations and do they always represent what we want to know? | Influencing the sense of fiction-reality so that users perceive fiction as reality or have a better understanding of what is real.<br><br>Establishing whether a user has interpreted something incorrectly or has observed something, e.g. a visual warning.<br><br>'Teaching' a system how the human brain processes and interprets ambiguous signals in order to make the system function more effectively.<br><br>Application areas: assessment of eyewitness reports, classification of visual material, advertising, national security agents. |
| Imagining (mental representation) and observing (perception) are closely linked. When we observe something, we actually use our imaginative and interpretive capabilities much more than we used to believe, i.e. we complete or fill in a lot of what we think we actually 'see' mentally. | Can we detect whether a user has a wrong mental model of a machine? Can we measure the extent to which a person perceives something as fiction or reality? Is it possible to shift the criterion value of fiction-reality?<br><br>What do people actually 'see' and is it possible to *force* them to see something instead of mentally completing it or filling it in? | We can easily change pictures without attracting attention, provided that we retain certain key points.<br><br>Improving interfaces on the basis of feedback on what people do see.<br><br>Application areas: low cost simulations, gaming environments. |
| The concept of neural binding, i.e. understanding how people use various inputs to arrive at one coherent, complex interpretation. | Is it possible to formulate rules or conditions under which neural binding does or does not happen?<br><br>Which modalities bind better than others (smell, taste, vision, hearing, etc.)?<br><br>How does the brain weigh various sensorial inputs? | Designing multimodal interfaces in such a way that the relevant or perhaps no binding happens.<br>Increasing the face validity and immersive experience of a virtual environment.<br><br>Inducing the feeling of wet hands by the sound of rubbing one's hands or other cross-modalities. |

| | | |
|---|---|---|
| | | Application areas: virtual reality, (serious) gaming, telepresence. |
| Specific representations of certain things or persons (chair, table, house, fish, Bill Clinton, Jennifer Aniston) exist on the neuron level in the brain. | Can these specific neurons make a mistake, i.e. do they also fire when someone looks like Bill Clinton? | Comparing photographs, film and reality: is this the same offender?<br><br>Application areas: safety (disguises?), classification of images, interface design. |
| Face recognition is strongly localised in the brain in the Fusiform Face Area (FFA). | What do we know about the neural mechanisms behind interpersonal communication, i.e. recognising emotions, faces, etcetera? | Making interfaces more humane by having the system recognise and anticipate the emotions of the user.<br><br>Developing machines that look and act more humanlike.<br><br>Neurally measuring the need for social contact, e.g. to help the elderly reduce their potential social isolation. |
| | How can we measure and manipulate perception at neural level (i.e. beautiful, pleasant, delicious)?<br><br>To what extent can emotions be differentiated neurally? | Application areas: consumer products and advertising, emotional adaptive gaming (i.e. adaptive systems based on measuring emotions such as stress perception, etc.) |
| Third hand experiment: the respondent acquires a feeling of ownership of the artificial arm by manipulation, i.e. by looking at the artificial left arm while his own left arm is being stroked invisibly (*see subsection 3.6.4*). | How can we measure and manipulate the feeling of physical ownership? | Developing avatars about which the user has a feeling of actual physical ownership, i.e. improvement of virtual reality (*see subsection 3.6.3*). |
| | *Learning* | |
| Autonomous learning, i.e. the brain is much more plastic than we thought. Without external guidance, the brain autonomously determines the best way to adapt to its environment, resulting in representations of optimal behaviour. (*see subsection 3.6.1*). | Could we use this autonomous and powerful mechanism to benefit explicit learning?<br><br>Does the same mechanism apply to cognitive learning and/or acquiring skills? | Developing autonomous learning robotic systems.<br><br>Application areas: training and education. |
| Automatic processes take place in the basal input-output system. If modulation or control is needed, the prefrontal system becomes active. | To what extent can we measure neurally whether a user relies too much on automated actions, i.e. is 'cognitively falling asleep'? | Indicating when someone is using a system in an incorrect automated manner. |

| | | |
|---|---|---|
| Involved brain activity and structures decline if a skill is automated.<br><br>Lifelong learning is important to maintain certain cognitive capacities (e.g. to prevent neurodegeneration in the elderly). | How can a process arrive at a basal level as soon as possible (so as to efficiently use our limited 'cognitive sources' for other urgent tasks)?<br><br>What is intuition in neuroscientific terms? Can we apply this knowledge in MMI-related R&D?<br><br>Is it possible for elderly people to counteract neurodegeneration by means of neurostimulation of certain brain areas (i.e. passive behaviour)? If it works, does it work for young people too?<br><br>Supporting flexibility by focussing on a strategy or rather supporting several strategies broadly. | Designing a system in such a way that any decline in cognitive functions, e.g. attention or memory, will draw the user's attention. For example, a new system for elderly people that aims to 'complete' shortcomings in cognitive functions, e.g. through exercises. |
| Mirror neurons may play a role in the close link between perception and production of motor actions. Such neurons are active not only while performing these actions but also while perceiving them. | Is the mirror neuron system related to speech perception and production well localised?<br><br>Is it possible to selectively stimulate mirror neurons to improve pronunciation (*see subsection 3.6.6*)? | Developing interfaces (neurostimulation or neurofeedback) to improve non-native speech sounds in non-native language learning. |
| Speech comprehension by listeners is based on their understanding of the speaker's articular movements (i.e. motor theory of speech perception). Mirror neurons may play an important role in establishing this link between the perception and production of speech (*see subsection 3.6.6*). | | |
| | *Motivation and reward* | |
| Explicit representation of reward in the brain. | What is the link between reward and addiction? When does someone become addicted? | Evaluating interfaces and systems against the mechanisms of reward in the brain.<br><br>In case of 'persuasive technology': how can the mechanism of reward be utilised? |

| | | |
|---|---|---|
| | | Application areas: gaming, learning, behavioural changes. |
| | What is known about the neural mechanisms behind the psychological concept of 'flow'? | Challenging and engaging users sufficiently to get them to acquire the technology without any help function or help screen.<br><br>Application areas: serious gaming, 'pleasurable frustration'. |
| | What is known about the neural mechanism behind motivation and/or challenge? Can motivation be measured neurologically? | Developing interfaces that keep users engaged without feeling they are losing control.<br><br>Developing persuasive technology that motivates and provokes certain behavioural changes, i.e. lifestyle coaching. |
| | *Attention and alertness* | |
| The brain generally learns incidentally or implicitly. The brain rarely learns explicitly and only in the event of explicit attention.<br><br>EEG can measure alpha brain waves, found predominantly during periods of waking relaxation with eyes closed. Alpha waves are thought to represent the activity of the visual cortex in an idle state. | To what extent is it possible to measure the attention or alertness of one or more users with stable neuro-imaging techniques? | Measuring selective attention at a certain moment, e.g. in traffic or distance learning.<br><br>Within a user group: if a user's attention wanes, someone or something else will take over automatically.<br><br>Designing a system in such a way that it stimulates selective attention.<br><br>Designing a system based on mechanisms of implicit learning. |
| Effective communication largely depends on those brain mechanisms that divide our attention and determine what we focus on. People are only able to pay attention to a limited number of features and actions at a given moment (i.e. the attention bottleneck). | What is the most effective strategy (e.g. speeding up or delaying images) for gaze capturing?<br><br>What is the influence of other modalities (sound, smell) on gaze capturing?<br><br>Is it possible to determine when a certain gaze is or is not intended? This is a fundamental problem in the world of interfaces. | Developing future ICT systems that make use of gaze guidance in order to help users exploit the opportunities of their limited attention capacities effectively. |

| | | |
|---|---|---|
| *Miscellaneous* | | |
| Magnetic stimulation of the organ of balance (while retaining the visual input) can give a person an out-of-body feeling (*see subsections 3.6.3 and 3.6.4*). | | Replacing expensive motion-based (flight) simulators.<br><br>Application areas: patients with a balance disorder, spatial disorientation in pilots, gaming, entertainment. |
| | What do we know about the neural mechanism behind creativity? | Optimising the design process by stimulating creativity and serendipity. |
| EEG can measure a 'readiness potential' (RP) in persons preparing to perform simple motor tasks 350-400 msec before a conscious realisation of the intention can be measured. The cerebral initiation of a simple, spontaneous and voluntary task is therefore subconscious. It is unclear whether this applies for intentions at a higher level as well. | Is it possible to detect the user's intention before he himself becomes aware of it? | Developing technology that knows what the user wants without his conscious input (*see subsection 3.6.5*). |
| Error-related negativity (ERN) is a negative peak in EEG activity within 100 ms after an action has been performed indicating that the user realises he has made a mistake. | Is it possible to tell from a user's brain activity when he notices that he has made a mistake and immediately wants to correct his action (*see subsection 3.6.5*)? | Developing smart environments and considerate systems. |

## 3.4 Ethical and social aspects of neuro-centred interface design

*Gert-Jan Lokhorst*[39]

This section describes various aspects of the neuro-centred design of MMI that give rise to ethical, legal and social concerns. The overview is brief but nevertheless aims to identify the main issues.

### Increasing reliance on machines

Optimising MMI will increase our reliance on machines. Future BMIs will exacerbate this problem because we will come to depend on machines for even the most basic, typically human tasks, such as perceptual, cognitive or motor activity. Although this is welcome in some cases — for example locked-in patients — it also diminishes human autonomy and raises responsibility-related issues. To give a real-life example: a surgeon who carries out laparo-

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scopic surgery or some other type of minimally invasive surgery must rely on the visual interface in front of him to obtain information about the inside of the stomach. This is the surgeon's only window into the patient. Suppose that the interface informs him that there is a tumour in the vicinity of the target. What should the surgeon do? Remove it or take no action? The alarm may be a false positive. Both courses of action may have severe consequences, but it is not clear who is to blame if the wrong decision is taken: the surgeon, the interface, the designers of the system, or those who tested or installed it? Ethicists describe this as the problem of epistemic enslavement, and it clearly comes up in almost every case of man-machine interaction.

Humans have long been aware that our equipment may make us less autonomous — and more vulnerable when that equipment fails. In 'The Gallic War' [book VI, 14] Julius Caesar (100–44 BC) explained that the ancient Celtic Druids forbade their teachings to be put down in writing to prevent their pupils from relying on the written word and neglecting to train their memories, *"for it is usually found that when people have the help of texts, they are less diligent in learning by heart and let their memories rust"*.

### Wideware

The design of MMI goes beyond the engineering. For example, in an air traffic control room, the employees are linked closely to their equipment. Neither can function adequately without the other. The human factor merits close attention in the design of such control rooms. For example, how should the staff be trained? What checks and balances should be built into the equipment, considering the limitations of human information processing capacity? The hardware, software and human components are so closely integrated that designers and philosophers nowadays use the term 'wideware' to refer to this complex ensemble. In the past, ethicists concentrated on the human factor and engineers on the machinery; in the future, a more balanced and interdisciplinary approach will be needed. Neuro-designed interfaces are in fact a step in this direction. This new generation of interfaces aims to adapt as much as possible to the user's limited but unique cognitive capacities. Take, for example, the AugCog program by the American Defense Advanced Research Projects Agency (DARPA). This program develops technologies *"to mitigate sensory and cognitive overload and restore operational effectiveness by extending the information management capacity of the war fighter."*[40]

### The extended mind hypothesis

The extended mind hypothesis proposes that the mind is not confined to the body but extends out into the environment. For example, a notebook might serve as the memory of a brain-damaged person with no internal memory;

40 www.darpa.mil/dso/thrusts/trainhu/warfighter/index.htm.

in such a case, the notebook should be seen as part of that person's mind (namely, his memory). This idea is related to the previous point because it is the whole socio-technical system ('person-plus-notebook') — the wideware that includes part of the environment — that is the material substrate of the extended mind [Levy, 2007]. In future, neuro-designed interfaces will make the interaction between technology and the human mind as close as possible. The line between tool and user will become very flimsy. The tools will be more like parts of the person's mental apparatus, especially as technologies are increasingly tailored to humans, for example in the case of BMIs that feed back brain activity (i.e. on cognitive workload) to the device.

### Instrumental reason

In 'Computer Power and Human Reason: From Judgment To Calculation' [1976], Joseph Weizenbaum decried the tendency to view reason as no more than an instrument employed to reach specific goals. In his view, human reason was much more than mere problem-solving, and in this sense immensely more powerful than computer reasoning. In the literature on brain-machine interfaces, the brain tends to be seen as an instrument susceptible to improvement and enhancement. One good example is DARPA's Cognitive Technology Threat Warning System, a binocular enhanced by an alerting system that taps the wearer's prefrontal cortex: *"DARPA aspires to integrate EEG electrodes that monitor the wearer's neural signals, cueing soldiers to recognise targets faster than the unaided brain could on its own. The idea is that EEG can spot 'neural signatures' for target detection before the conscious mind becomes aware of a potential threat or target."* [41] We may wonder whether viewing the brain as an instrument will lead to a sense of alienation, comparable to the one noted by Weizenbaum. In other words, will this not lead to the idea that our brain is merely the instrument through which the soul expresses itself, rather than our very essence, the very core of our personality?

### Incidental findings

This is a well-known problem in the literature on neuro-ethics. In the course of experiments carried out for non-medical purposes, medical abnormalities may come to light, for example brain tumours detected in brain scans carried out for psychological purposes and involving apparently healthy subjects. What should one do in such cases? Refer the patients to medical specialists? This has at least one drawback: it may cause undue anxiety. It should also be borne in mind that the experiments, for example those involving brain scanning, are usually performed by non-medical personnel. On the other hand, should the findings be kept secret? This may have other unwelcome consequences, for example a death that could have been prevented. There is no consensus on this point, and practices vary from country to country. In

41 See www.wired.com/gadgets/miscellaneous/news/2007/05/binoculars.

Sweden, problematic findings are hidden from the subjects; in the USA, the subjects are referred to specialists to avoid allegations of malpractice. The same problem will inevitably come up in some of the contexts involving BMI brain activity monitoring, as described elsewhere in this chapter.

### Treatment and enhancement

Is there a natural dividing line between treatment and enhancement? Evidently not: the bioethical literature is full of cases that can be classified only with great difficulty. Treatment gives rise to ethical issues. For example, there have been massive protests against cochlear implants organised by deaf people who refuse to see deafness as an illness [Blume, 1997]. Enhancement is even more problematic. Should 'cosmetic neurosurgery' [42] for cognitive enhancement be forbidden in the same way that doping is forbidden in sports? Should commercial advertising for cosmetic neurosurgery be prohibited? What about peer pressure and social pressure, comparable to the pressure felt by adolescent girls to have breast implants? Do we really want to change our very selves by neurotechnological or pharmaceutical means? And what if the government decides to apply neurotechnology, for example deep brain stimulation (DBS), to certain individuals with abnormal opinions or behaviours? For example, moral delinquents (cf. the discussion about chemical castration)?

### Privacy

In some of the applications described in this chapter, especially those involving ambient intelligence[43], the device stores quite some information about the user's activities. This could lead to privacy issues, especially if the device is part of a network. Government, industry or other organisations could, in theory, keep a close eye on the user's every movement — and with the introduction of BMIs or neuromarketing (see example III), perhaps even on some of his or her thoughts, intentions, emotions and inner motives. Some fear that reading someone's thoughts or mind constitutes the ultimate breach of privacy. This issue, sometimes referred to as the right to 'cognitive liberty', certainly merits attention. In the United States, a non-governmental organisation — the Center for Cognitive Liberty and Ethics (CCLE) — has even been founded with the aim of *"develop[ing] public policies that will preserve and enhance freedom of thought into the 21st century"*.[44]

### Potential abuse

This issue follows on logically from the previous one. The following quote speaks for itself: *"Robots should be designed to protect human life and should be incapable of endangering it. So reports out of Korea of newly developed guard robots capable of firing autonomously on human targets are raising concerns about their potential uses... Ethicists have always questioned*

**42** This term is used, somewhat facetiously, to refer to neurosurgical interventions aimed at enhancement with no medical indication, for example memory improvement or raising a client's IQ.

**43** As the concept of Ambient Intelligence develops, privacy merits its continuous attention from both industry and society. The Dutch government is following this discussion closely in order to modify legislation if needed. AmI privacy issues are addressed in a report coordinated by ECP.nl, published in May 2008.

**44** See www.cognitiveliberty.org.

*the use of technology in weapons development, but the new robots are causing additional disquiet because of their self-directing capabilities... It is the responsibility of all technology professionals to ensure that those in our organization and within our influence are both responsible and ethical in the way they develop and apply technology."* [Argy, 2007].

Another illustration that is perhaps more relevant in the present context: when Dutch neurosurgeons announced that deep brain implants in the thalamus can cause remarkable changes of personality, they were immediately called by Chinese military prison officials, who saw this technology as a promising new method for dealing with stubborn prisoners.[45]

## 3.5 Discussion

*Ira van Keulen, Maurits Kreijveld[46], Jan van Erp[47]*

This chapter looks at many different ways to exploit neuroscientific knowledge and technology in order to improve man-machine interaction (and vice versa). MMI can clearly benefit from the neurosciences, and not only when it comes to brain-machine interfaces (BMIs) controlling external devices, but also in other ways, for example employing neuro-mimicry (i.e. using the brain as the source of inspiration) or evaluating interfaces through neuro-imaging (i.e. checking whether the interface activates the relevant brain areas). Table 2 summarises all the various ways, touched on in this chapter, that the neurosciences can support MMI research and development (and vice versa) in future.[48]

In short, this chapter supports the idea of developing a new scientific field *beyond* BMI: the neuro-centred design of interfaces. It would be a field in which different neuroscientists — neurophysiologists, neurobiologists, cognitive neuroscientists and neuropsychologists — work with people from academia and industry in the field of MMI. Neuro-centred interface design is all the more important if we look at trends in the field of MMI (e.g. ambient intelligence and user-centred design) and in society in general (i.e. the increasing complexity of the information society). The neurosciences can and should key into these trends because they can offer the relevant knowledge and neuro-imaging technology, if not now then certainly in the future.

In this final section, we describe the opportunities and threats associated with cooperation between the neurosciences and MMI. We also consider the need for focus and driving applications in the new field of neuro-centred interface design.

45 Based on a confidential personal communication.

46 Senior Policy Advisor of ICT and Innovation, Ministry of Economic Affairs.

47 Chief Scientist of the department of Human Interfaces, TNO Human Factors.

48 Please note that machine-brain interaction, i.e. influencing brain activity by means of neurostimulation, was not discussed in this chapter.

| How can the neurosciences support MMI R&D and vice versa? | | MMI R&D | |
|---|---|---|---|
| | | **Interfaces** | **Systems** |
| **NEURO-SCIENCES** | **Growing knowledge of the brain and cognition (off-line)** | – Improving traditional interfaces based on our growing knowledge of different cognitive functions.<br>– Improving virtual reality by manipulating the neural mechanisms behind physical ownership ('real virtuality').<br>– Using virtual environments to learn about the structure of perception and the workings of the brain. | – Improving man-machine interaction by using the brain as a source of inspiration for systems (neuromimicry).<br>– Improving systems by bypassing unique characteristics of the brain (e.g. the impulse control mechanism of the prefrontal cortex). |
| | **Using neuro-imaging technology (on-line)** | – Directing and controlling systems through invasive or non-invasive measuring of brain activity ('brain-machine interfaces').<br>– Optimising man-machine interaction by providing feedback on specific criteria during interaction, e.g. user intention, cognitive workload, task engagement, decision-making, indignation, anger, fear, hapiness. | – Improving systems by exploiting unique characteristics of the brain (e.g. pattern recognition).<br>– Optimising man-machine interaction by evaluating the effectiveness of the stimulus (i.e. does the interface activate the relevant brain areas?).<br>– Learning to control simple aspects of one's own brain signals through feedback on specific neural activity ('neurofeedback'). |

**Table 3**
*Chapter 3 in a nutshell: neuro-centred design of MMI.*

### 3.5.1 Differences between the neurosciences and MMI

The neurosciences and the field of MMI do not make natural bedfellows. The initial meetings of the expert group certainly proved that. There were some startling differences between the members. For example, neuroscientists generally gravitate more towards fundamental research (lab), while MMI scientists — even at universities — are much more focused on applied research (real life). We can explain neuroscientists' preference for the lab by noting that they are very circumspect about their knowledge of the brain. They tend to focus on the larger questions, i.e. understanding consciousness or neural binding. And indeed, there are still many unanswered questions. As yet, there is no grand theory of the brain, the way genomics has DNA and chemistry has the periodic table. However, in their quest for the Holy Grail (i.e. the model that explains the workings of the brain), neuroscientists at times seem to forget that even

**Example VI**

**Inspired by the sophisticated biology of the rat, British scientists have developed a small mobile robot which can assess its surroundings with artificial whiskers. The device dubbed 'Whiskerbot' can be used to investigate enclosed spaces such as piping systems, or to search for victims of earthquakes.**

There are many mobile robot applications in existence that can check out ducting systems or underground structures, but they lack tools sensitive enough to assess their environment in detail.

# Whiskerbot: a robot with rat whiskers

The facial whiskers of rats – and of many other animals – help them to sense the surface textures and shapes in their surroundings. As the animals interact with their environment, the mechanical deformations of the whiskers are translated into sensory information. The brain of the animal interprets these signals and generates the appropriate actions.

The Whiskerbot team, made up of robotic engineers and computational neuroscientists, has designed an array of characteristically curved whiskers moulded from glass fibre. These tactile sensors are seven times thicker than the largest whiskers of a rat, and four times longer. The sensory structures at the root of the whiskers, inside the robot, are made of micro strain gauges. These tiny devices measure deformation as their electrical resistance alters upon deformation. Advanced digital signal processors combined with specific hardware and software translate the signal real-time onto a model of a neuronal circuit, which in the end generates the appropriate response of the robot to its surroundings.

The robot whiskers, like those of the rat, can actively sweep back and forth to monitor the environment. The robot imitates the muscles of the rat with a metal alloy called BioMetal in the shape of a wire. By switching an electrical current on or off, this wire heats up or cools down, and relaxes or contracts. The wires allow the Whiskerbot to move its whiskers in a manner analogous to the rat.

The British engineers are not the first to develop a mobile robot with whiskers. Since 1984 various research groups have constructed such devices, based on an abstract interpretation of whiskers. The British team's system, however, is based on the biological analogy of the brain, and represents an initial attempt

Original publication: Pearson et al. (2007). *Adaptive Behavior*, 15, 223

at constructing brain-based systems that coordinate more complex behaviours. The team plans to expand their model by adding other neural models of the rat brain, including the hippocampus for memory and map building.

Unlike conventional sensors such as infrared, ultrasonics, radar or vision, whiskers can operate effectively in confined, noisy and dark or otherwise visually occluded spaces. A Whiskerbot may therefore be useful not only for investigating collapsed buildings or ducting systems, but also for security or military operations. Internal signal processing also makes the system robust and flexible enough to adapt to damage to the whiskers. This makes it potentially suitable for submarine, extra-terrestrial or intracorporal medical investigation.

minor neuroscientific findings can be of huge relevance in applied sciences such as MMI. It is not necessary to understand the whole brain and its mechanisms in order to apply neuroscientific knowledge. In other words, the neurosciences should be more aware of the innovation paradox, i.e. the fact that sound scientific research is scarcely ever applied in practical terms.

One interesting example of the modesty of at least some neuroscientists was illustrated in a discussion within the expert group about validation. The neuroscientists argued that validating cognitive theories constitutes a major part of their work. One neurophysiologist phrased it this way: *"Neurobiologists in particular add very little to the behavioural research conducted by psychologists. Neuroscientists are only looking to explain behaviour at the level of the brain"*. He did not argue that the biological explanation of behaviour was not useful; on the contrary, he considered it to be crucial for designing pharmaceutical interventions. But in other cases relevant to interface design, for example determining a user's workload or attention span, he thought that behavioural tests were more than sufficient. Interestingly, other members of the expert group — MMI and cognitive researchers — disagreed. According to them, neurophysiological or neurocognitive measures can be very useful since they are a more direct way of determining a user's cognitive activity (e.g. as feedback information for a computer to anticipate ) or even cognitive ability (e.g. to establish a cognitive profile for educational purposes).

Another difference between the two research fields is that MMI covers many different domains of application, including security, entertainment, health care and retail. The neurosciences, on the other hand, are usually geared towards the medical domain and clinical applications, at least in terms of applied research. This is understandable, as there is a lot of important work to do here. Many patients are suffering from chronic neurological and psychiatric disorders (in the Netherlands nearly six million people suffer migraines, anxiety, depression, addiction, dementia, and other similar disorders.[49]) and this number is increasing steadily as society ages. Nevertheless, there is a lot for the neurosciences to gain by considering applications in other fields, for example ambient intelligence, virtual reality or gaming (see Figure 9). When it comes to BMIs, however, there is always the question of whether a BMI is the most efficient and effective way for a healthy user to operate a computer or other electronic devices. After all, evolution has made the motoric actions of our hands and other limbs our brain's most effective output so far.

One way that the two fields could begin to cooperate more closely is to start collaborating on interface design for the elderly. This would involve taking the characteristics of the neurodegenerated brain — the subject of much clinical

**49** European Journal of Neurology, June 2005.

research - into account when developing more accessible interfaces or even specific assistive technology for the elderly. In the case of BMI, another option would be to keep it simple: develop a BMI based on a neural substrate that correlates one-to-one with certain specific behaviour while looking for simple applications or applications within a controlled environment. A similar example is the BCI2000 system developed by the Wadsworth Center's Laboratory of Nervous System Disorders, which is used to help people with speech problems. This BMI uses EEG to measure the P300 brainwave, which spikes as the user experiences an unexpected or significant sensory stimulus. The user is shown a random list of words or images and his P300 is measured when he 'recognises' a particular word or image.

### 3.5.2 Opportunities for cooperation between the neurosciences and MMI

Even though brain research has produced promising applications, man-machine interaction based on this rapidly growing body of knowledge is still in its infancy. So far, the demand appears to outstrip the supply: MMI raises more questions than can be answered by the neurosciences. The table in section 3.3 — noting the expert group's initial ideas for possible applications based on symbiosis between the two fields — points out some of these interesting but hard to answer questions. To name a few: can we detect whether a user has the wrong mental model of a machine? Can we measure the extent to which a person perceives something as fiction or reality? How does the brain weigh various sensorial inputs? To what extent can we measure at neurophysiological level whether a user is relying too much on automated actions? What do we know about the neural mechanisms behind the psychological concept of 'flow'? The fundamental neuroscientific questions that must be answered are almost limitless. And every new scientific breakthrough raises new questions. What is needed to drive the research agenda for the neuro-centred design of MMI is a clear goal.

The real gain (i.e. innovative progress) generally lies in areas where multiple disciplines collaborate by focusing on an application, in this case most probably in the medical or military domain. The application should become the focus or the driver that speeds up progress in the neurosciences in general and in the field of neuro-designed interfaces in particular. The big question is who or what will be the drivers. Will it be large companies seeking innovation and added value in their own markets? Or will it be the start-up firms hoping to exploit new opportunities arising from advances in our fundamental knowledge of the brain? Or will society as a whole be the driver, for example in relation to major issues such as the ageing of the population? Companies, regardless of their size, can play a very important role in turning technology into

**Figure 9**
*TNO Human Factors and Human Media Interaction at the TU Twente study the possibilities of BMIs for healthy users, e.g. gamers. Photo courtesy of department of Human Interfaces, TNO Human Factors.*

products and societal benefits. A dynamic system that brings universities and fundamental research together with commercial applications and demand-driven innovations will provide fertile ground for further economic growth.

When technologies are multidisciplinary, as is the case with neuro-designed interfaces, driving applications are a vital means of focusing the research agenda and ensuring that society benefits in the short term from advances in knowledge. These drivers come from the interaction between technological push and societal pull. Society's demands must be converted into products and a corresponding technology roadmap. On the other hand, the short-term benefits derived from the cooperation between MMI and the neurosciences will find their way into exciting new products that bring new value to customers. Even simple advancements may lead to significantly enhanced or completely new products. That is the challenge facing industry. The first step, however, is to recognise the full potential of the new opportunities arising from neuro-centered design of interfaces. The second step is to get the various disciplines cooperating more closely, whether in academia or the private sector. We hope that this study will contribute to these first two steps.

At the same time, there are also opportunities for the neurosciences to profit from MMI research and development. In the first place, MMI can support the neurosciences through cooperation on applied research on neural and cognitive processes, specifically related to human interaction with technology or environment. MMI can thus provide fundamental neuroscientific research with an anchor in the real world and extend the ecological validity of neuroscientific findings. In the second place, MMI can offer interesting research tools for the cognitive neurosciences. Virtual Reality is already used by neuroscientists in research paradigms, e.g. using a driving simulator in fMRI research to study spatial cognition, but many more applications of VR in combination with studying certain cognitive functions are possible. For instance, virtual environments are a powerful and flexible tool that can be used to learn something fundamental about the structure of (self) perception and the workings of the brain (see subsection 3.6.4).

## 3.6 Visions on neuro-centred design

What would a foresight study be without presenting inspirational views of the future, even though they may still qualify as science fiction? This section gives researchers, industry and policy-makers a glimpse of what the future of the interdisciplinary field of neuro-centred interface design may hold. Each subsection — or view of the future — identifies a generally desirable trend in MMI development, for example the perfect butler (for measuring the intentions of the user) or 'real virtuality' (for intensifying the experience of virtual reality).

The subsections each offer a brief scenario (what will the future application look like when it is integrated into daily life?), a description of the purpose and relevance of the application, a specification of existing and required neuroscientific and cognitive knowledge, and, finally, research and development questions for the future.

### 3.6.1 Autonomous learning robotic systems

*Gezinus Wolters*[50]

Imagine the year 2025. A spacecraft departs on a voyage to the planet Venus. Its mission is to explore the possibility of setting up mining operations for minerals that are reaching depletion on earth. On board is a group of ten robots equipped with an array of sensors and capable of moving around and manipulating objects. Most importantly, each one possesses an artificial brain with which it can perceive and classify objects, set and flexibly adapt its own goals, make intelligent decisions and control its actions. The robots can do all these things because their artificial brains are capable of learning from experience. They have been trained to cope with situations similar to what can be expected on Venus. Not everything can be foreseen, however, and they are therefore endowed with the capacity to learn and to

50 Associate Professor of Cognitive Psychology, Leiden University.

adapt flexibly to unanticipated situations. After accomplishing their mission, they decide to return to earth, bringing with them all they have learned and experienced safely stored in their memories.

The foregoing scenario may seem futuristic, but in fact it may be feasible to build smart robots such as those described within only a decade or two. Unlike ambient intelligence, which seeks to create a smart environment that senses and responds to the needs of a human user, smart robots would be devices capable of performing complex tasks in a human-like manner. Smart robots are systems capable of learning from interactions with their environment, and they are able to use what they have learned to perform complex tasks flexibly and to generate and select solutions.

Two recent developments have given the field of artificial intelligence new impetus to start thinking about constructing smart robots. The first is the realisation that biological systems learn to understand and represent the world by interacting with that world (i.e. 'situated cognition'). The second is that the cognitive neurosciences have enhanced our understanding of the structure and functioning of the brain. Combining these ideas opens a window to creating a novel class of intelligent robotic systems, capable of learning complex skills and of performing these skills autonomously (i.e. without remote control) in novel and unanticipated situations.

The starting point for developing such robotic systems is our growing knowledge of the structure and functioning of the human brain. Humans are equipped with a brain that receives input from its environment and generates output to control behaviour. Most importantly, this brain has the potential to learn. It is capable of storing input and creating associations between input and output in its myriad neural connections. The capacity to learn has already been used in models for perceiving, classifying, and recognising visual patterns, and in models that learn adaptively to control movements. What is lacking so far are adequate memory and control systems. The memory systems should be capable of storing previous experiences (tasks, contexts, actions, and action results), and allow the gradual extraction of underlying general structures and relations. These memory systems would have to mimic our explicit (episodic and semantic) and implicit memory systems. Control systems are required for planning, prioritising tasks and setting goals. These control systems will have to mimic the human working memory and its ubiquitous 'central executive' [Baddeley, 2003] or 'supervisory attentional system' [Norman and Shallice, 1986]. Knowledge about how these control systems are implemented in the brain is still very much incomplete, but important insights have been gained lately in computational cognitive neuroscience [Maia and

Cleeremans, 2005; Leech et al., in press; Miller and Cohen, 2001; Rogers and McClelland, 2004; Wolters and Raffone, in press]. The general idea is that modules in the prefrontal cortex are able to maintain and flexibly combine present input and information retrieved from memory to simulate states of the world. This allows planning, problem-solving and decision-making. The resulting neural states exert top-down control by selectively modulating input and output processes.

What is very unclear is the extent to which smart robots can or should be endowed with emotions. Obviously, emotion is an important variable in human behaviour. It greatly affects learning and memory and continuously influences our goals and decisions. In human behaviour, the main function of emotion is probably to ensure the ideal balance between risk-seeking and risk-avoiding behaviour. Introducing 'emotional' processes may be a necessary feature for developing really smart robots, but we need to know much more about where emotion may be needed (e.g. in motivating behaviour and in promoting learning and memory), and where smart robots can do without it (e.g. in accepting orders to perform potentially harmful actions).

The cognitive neurosciences are beginning to understand the modular structure of the brain. With this knowledge comes insight into how these neural modules classify and store patterns of input, how they associate input patterns with motor responses, and how they exert control over input and output processes in the service of performing particular tasks or reaching goals. Implementing this knowledge in computational systems is a major challenge, one that is already being met (e.g. The PACO project[51] [Lacroix, 2007]) and that may well lead to the development of smart robots (see Figure 10). Unlike present-day robots that either perform well-defined tasks in pre-specified conditions or serve as remote controlled platforms for surveying instruments, smart robots would autonomously learn to carry out tasks in unspecified conditions, flexibly adapting to unanticipated events and circumstances.

Smart robots could be used to perform any task requiring exploration and manipulation in situations and conditions that are hostile or dangerous for humans (e.g. deep sea and space exploration and construction; mine detection and dismantling; construction and repair in radioactive, toxic or disease-infected areas). Another possibility is to develop smart automatic pilots by adding the capacity to learn from experience to current systems. As a final point, there is the need for an ethical debate on whether the autonomy of smart robot systems should be allowed to exceed the limits of human control.

51 See www.paco-plus.org.

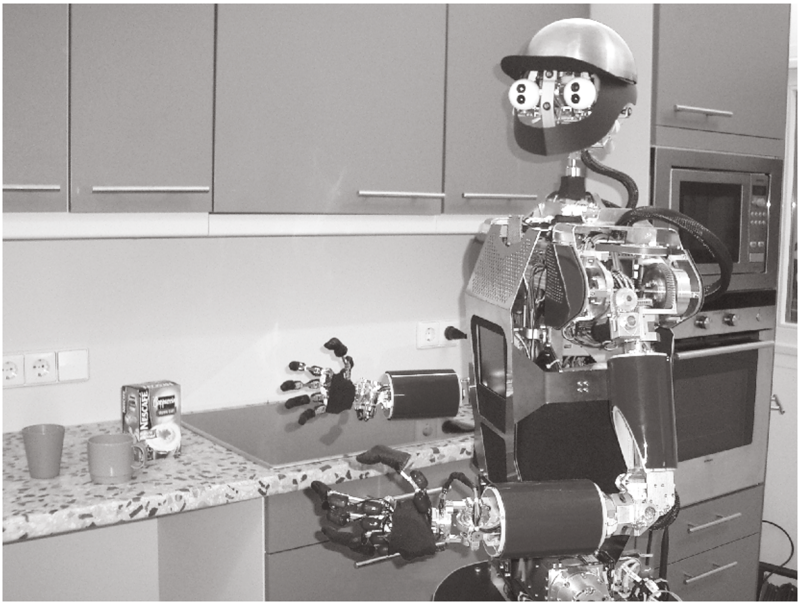

**Figure 10**
*The research programme Paco Plus is "building robot systems that will display advanced cognitive capabilities. They will learn to operate in the real world and to interact and communicate with humans. To do this they must model and reflectively reason about their perceptions and actions in order to learn, act and react appropriately." Photo of Armar-IIIa in the kitchen, courtesy of Universität Karlsruhe, Rüdiger Dillmann.*

Research and development questions for the future

- More knowledge of the structure of the human brain, especially the workings of the control structures in the prefrontal cortex. This will require extensive fundamental cognitive neuroscientific research.
- Development of (better and more complete) computational network models for learning, perception, memory, action and control processes. This will require a multi-disciplinary effort to translate neural structures and mechanisms into artificial network models.
- Implementation of embodied robots equipped with artificial learning brains. Large-scale efforts and investments are required in each of these areas, but that does not necessarily imply large-scale, coherent programmes. Multiple programmes on small or intermediate scales may offer a more productive route towards exploring the development of domain-specific smart robots.

### 3.6.2 The perfect butler: smart environments and considerate notification systems

*Huib de Ridder*[52]

Imagine you come home after a long hard day and your central home control system recognises the mood you're in. Based on this information, the system immediately starts to create your preferred relaxed atmosphere by setting the various lights at a certain colour and level, turning on your favourite music and setting the thermostat to the appropriate temperature.

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These settings are automatic because they are derived from your profile, created on the basis of previous experiences in similar situations. The home control system then evaluates all incoming messages. Should the system deal with these without letting you know, or should it alert you to the most urgent ones?

One of the characteristic features of truly smart environments is that they are considerate to their users. The term ‘considerate computing’ was first used by the Scientific American journalist Wayt Gibbs [2005] to denote devices that consider user attention when adapting their behaviour. For instance, a considerate car notices that the driver is looking away when his attention is needed and subsequently activates an alarm drawing the driver’s attention back to the car ahead. The term considerate systems should not be confined to attentive user interfaces only, but refer to all systems and products that aim to optimise their behaviour by considering the user and the context. Discussing trends in wearable technology, Cough [2003] noted that this technology will evolve into a *“perfect partner…that proactively works on your behalf. It understands you and your context well enough to make accurate predictions of your needs… It will improve its predictive capacity by observing you.”* Cough’s statement applies to any considerate smart system that wishes to be accepted by the user, but the notion of a perfect partner must hold in particular for the many notification systems owing to the increasing number of information services entering our daily life. For example: traffic updates sent to commuters by voice messages on mobile phones; new mail announced by auditory signals on computers; washing machines emitting irritating beeps to indicate that the laundry is ready; medicine reminders; burglar alarms; weather and news updates notifying users of interesting events, etcetera. Research has shown that the acceptability of a notification in the home depends primarily on the urgency of the message, but what the user is doing at the moment of notification also plays a role [Vastenburg et al., 2007]. The preferred timing of a notification depends on its acceptability: immediate interruptions are acceptable for highly urgent messages, while less urgent ones should be presented at a later, more appropriate point in time, or not at all. A considerate system must be able to meet user demands in order to avoid annoying situations, for example a mobile phone emitting a low-battery warning in the middle of the night [Picard, 1997].

The low-battery warning suggests a nice analogy for considerate systems: the butler. An experienced butler knows precisely when to offer his services to his master. That is, he can correctly interpret the situation and knows what he has to do. But a truly perfect butler does nothing even when the situation seems to require action but in fact is unwished for by his master. It is like automatic

**Example VII**

# Training brain wave activity to enhance cognitive performance

**Brain training to control electrical activity can result in an improvement in working memory and more focused attention, preliminary studies show. Neurofeedback is a technique by which individuals can learn how to influence the electrical activity on the surface of their brain, the cortex. These brain waves come in various frequencies, ranging from 1 to 30 Herz, and represent different mental states, ranging from sleepy to alert wakefulness to aroused. They can be visualised via an electroencephalogram (EEG).**

In a neurofeedback session, a participant gets feedback from a computer about which brain waves are present in the brain region of interest. If the desired frequencies are present, the brain receives a reward: a tone is heard, music gets louder, or points in a computer game are gained. If the desired waves are absent, there is no reward. In this way, most participants can learn to increase a specific component of their EEG within several neurofeedback sessions. Various studies have shown success with this technique in ameliorating diseases characterised by an abnormal electrical activity of the cortex, such as epilepsy and attention deficit hyperactivity disorder (ADHD).

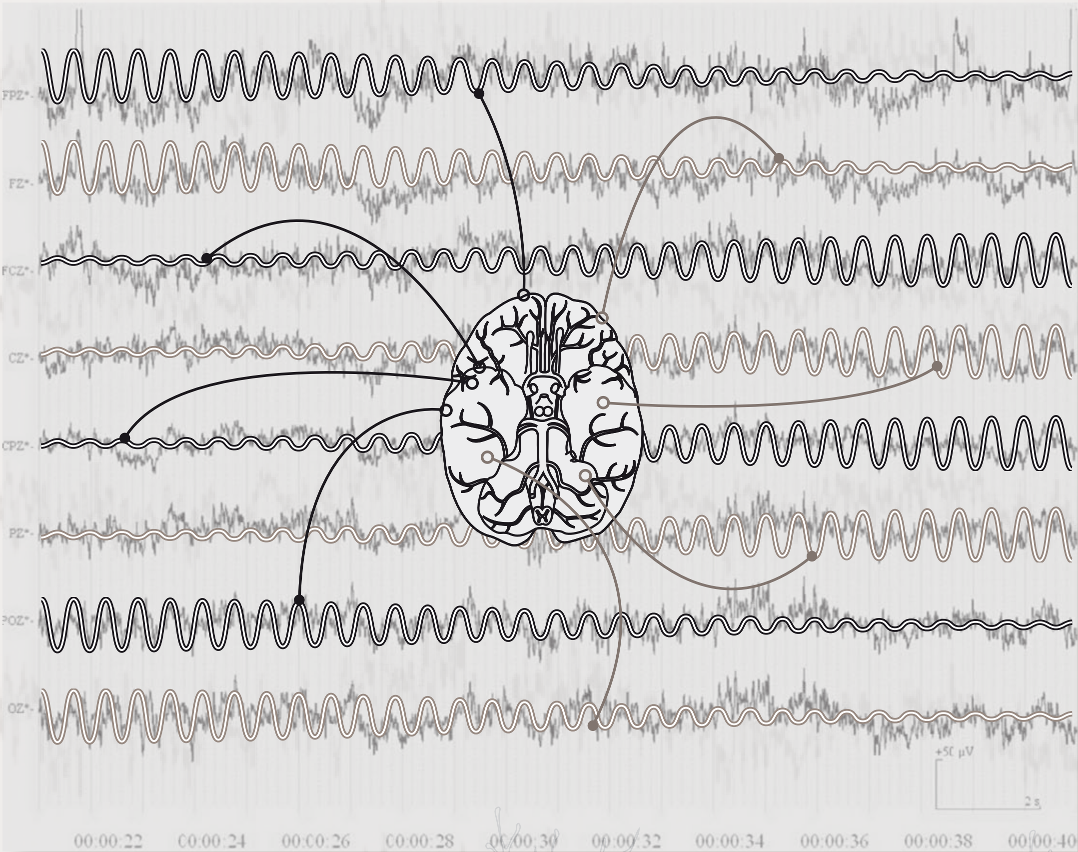
A small study by neuroscientists from the Imperial College London suggests that neurofeedback may improve cognitive performance in healthy people too. The scientists trained ten healthy people with a protocol to increase their sensorimotor rhythm (SMR) activity (12 to 15 Hz), and ten others to improve their theta activity (4 to 7 Hz). Theta activity is associated with working memory performance, and SMR activity with attention. Ten additional people formed the control group and did not train their brain.

All participants completed two cognitive tasks, both before the training sessions began and afterwards. One test measured attention performance, the other semantic working memory performance. After eight training sessions (two per week) the people in the SMR group had learned to increase their SMR activity. Compared to the other groups, the participants in this group were more accurate on aspects of the attention task and the accuracy of their working memory had also improved.

The theta group did not show signs of neurofeedback-induced learning. The researchers suspect that their training protocol, with both visual and auditory feedback, is not adequate for training theta brain waves, as these

Original publication: Vernon et al. (2003). *Int J Psychophysiol.*, 47, 75 mark a relaxed, near-to-sleep state. They suspect that methods with only auditory cues will work better, as participants can keep their eyes closed.

Many brain training companies and therapists offer neurofeedback training for a wide variety of ailments. While the evidence that neurofeedback is an effective treatment for epilepsy and ADHD is mounting, there is only little evidence that it improves cognitive performance.



doors: when someone merely passes by and has no intention of entering the building, the doors should remain closed. This is only possible when the person's intentions can be interpreted correctly. Researchers are putting a great deal of effort into understanding intentions indirectly through observable behaviour. For example, they record motion patterns in order to categorise social interactions [Blythe et al., 1999]. The question now is whether the neurosciences can help to derive users' conscious and unconscious intentions more directly from brain activity, for example by using BMIs. More specifically, the neurosciences could help determine when a user realises he has made a mistake. Research has been carried out on Error Related Negativity (ERN)[53] [Bruijn, 2007]. Smart products can use that kind of information to respond almost immediately to the new situation, an aspect that is becoming increasingly important in the field of MMI. It is related to the topic of intuition or 'thin-slicing', as Malcolm Gladwell refers to it in his book 'Blink' [2005]. Thin-slicing involves rapid but often correct decision-making when initially sizing up humans and situations. Or, in the words of Gladwell: *"...the ability of our unconscious to find patterns in situations and behaviour based on very narrow slices of experience..."*

Research and development questions for the future

- Is it possible to interpret user intentions more directly and rapidly from neural activity? Can we also derive the underlying mental model from neural activity?
- Is it possible to tell from a user's brain activity when he realises he has made a mistake and wants to correct it immediately?
- What can brain activity tell us about almost instantaneous interpretations of new situations?
- What data can be derived from neural activity that can be used as input parameters for smart sensors in considerate systems?

### 3.6.3 'Real virtuality': the neuroscientific contribution to improving virtual reality

*Evelijne Hart de Ruijter-Bekker*[54]

Imagine you are planning your summer holiday in the year 2025. Rather than just reading a pile of tourist information booklets or surfing the internet as many of us do today, you can actually take a preview trip to a set of desired destinations. Say you choose island hopping in Greece. After logging on to the website from your living room, the virtual and real world quickly merge into one. 3D images are displayed everywhere around you. You are immerged in a lifelike experience of Greece, standing on the deck of

53 ERN is a negative peak in EEG activity within 100 ms of performing an action indicating that the user realises he has made a mistake.

54 Senior Scientist at the User Experience Group, Philips Research.

a massive sailing boat, approaching Corfu. You are enjoying the spectacular view and hear the sound of the waves splashing on the boat. The gentle rocking motions of the boat relax you. You smell the salty water and feel the sun on your skin. Since you are not used to this kind of weather, you start feeling somewhat hot and uncomfortable. But then, suddenly, cool drops of water sprinkle your face and a pleasant breeze is blowing through your hair. Looking to the right, you see a group of dolphins chasing the boat. This unique encounter fills you with joy. This calls for a celebration. You turn around and see a waitress walking towards you. She is offering you a glass of champagne. You reach out and pick up the glass. You concentrate on the tingling feeling on your tongue. You are in paradise and you are tempted to book a flight right away. But before you do, you will first check out an alternative adventurous rock climbing trip to the Himalayas.

This scenario may seem a little far-fetched if you look at the virtual reality (VR) products available on the market today. Then again, many researchers around the world are working to improve the status of VR. VR has been defined in numerous ways. In general, it refers to a technology that allows the user to interact with a computer-simulated environment, consisting of a vivid representation of either the real or a fantasy world. One crucial aspect of VR is immersion: the feeling of being part of the simulated environment ('being there'). Ideally, the user forgets he is interacting with a computer. Most VR environments are generated through visual stimulation only. However, some applications induce immersion by adding sound, touch, smell and taste, but also by giving users the impression that they are speaking, walking, jumping, swimming, and even by mimicking facial expressions.

Although we think of virtual reality as a new concept, its history goes back to the fifties. Morton Heilig, who is also referred to as the 'father of virtual reality', wrote about an Experience Theatre in 1955, technology that he claimed enhanced immersion and that included a semi-spherical screen, directional sounds, smells, wind, temperature variations and body tilting (see Figure 11). Ivan Sutherland was in 1968 the first to build a head-mounted display system (HMD) for visual simulation of 3D environments. This system was very heavy, however, and uncomfortable to use. In 1988, NASA provided the first virtual setting responsive to inputs from the user's position, voice and gestures. Their 'data-glove' allowed for actual interaction with the virtual world, for example grasping virtual objects.

Today, non-invasive sensing and simulation equipment has become increasingly affordable and wearable, making it accessible to users at home (see Figure 12). The introduction of 3D displays has enabled visual simulation of

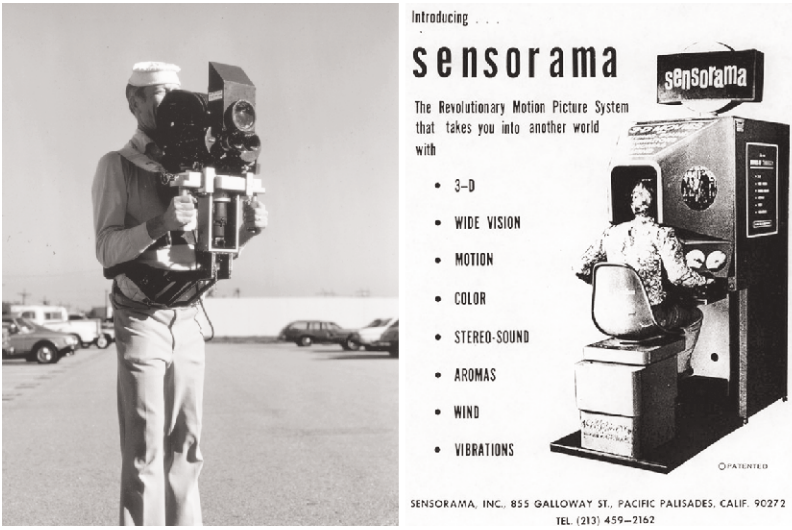



**Figure 11**
*Morton Heilig (left) and Heilig's Sensorama (right), patented as the Experience Theatre in 1962.*

**Figure 12**
*An example of a head-mounted display (HMD): a system worn like goggles that gives the illusion of a floating monitor in front of the user's face to display information and images while viewing the real scene. HMDs can thus be used for virtual reality applications. Photo courtesy of Mirjana Vrbaski.*

3D environments without the need to wear head gear or shutter glasses; the use of multiple cameras in the home has enabled the direct translation of 3D body movements into the virtual world; and the development of wireless EEG headbands (Imec) has enabled interaction with virtual worlds based on intentions and thoughts (or at least mental states) rather than on concrete actions. Regarding stimulation equipment, the focus has shifted from the visual domain (e.g. Philips Ambilight) to the inclusion of auditory and haptic senses (e.g. Philips AmbX; Reachin Technologies & Frictional Games HaptX). Nippon Telegraph and Telephone (NTT) have even created 'the remote-controlled human' by stimulating the vestibular system. Users are thrown off balance by weak electrical stimulation at the mastoids. If the stimulation is strong enough, the user alters his course of movement.

### Applications of virtual reality

Today these new virtual reality technologies are used mainly in the gaming industry. The nature of computer games has undergone a complete transformation over the past few years. Whereas gamers used to play computer games by themselves, they now operate on global game platforms where multiple players interact. The content of a game is to a large extent determined by the players themselves. Also, many game worlds are persistent, which means that the game continues regardless of whether the user is participating or not (for example, Second Life and World of Warcraft). Players are represented by virtual avatars. The appearance, behaviour and, recently, even the emotions expressed by these avatars may or may not correspond to the characteristics of the player it represents [Bessiere et al., 2007].

VR has also been widely used in situations where the reality does not exist (as yet), cannot be accessed, or is too dangerous or too expensive to enter. Examples are training and education (e.g. pilots, surgeons, fire-fighters, parents-to-be), non-pharmacological treatment of psychiatric disorders (e.g. agoraphobia, autism), visualisation (e.g. architects, interior designers, archaeologists), and research (e.g. drug design, astronomy, behavioural neuroscience). As for research in the field of behavioural neuroscience, Tarr and Warren [2002] studied crowd behaviour, in particular 'the social bystander effect' [55], using VR. This would otherwise have been deemed impossible for ethical and practical reasons.

### Contribution of the neurosciences

The most important question here, however, is whether neuroscientific findings or imaging technology can help improve the level of immersion in virtual reality, preferably while avoiding the adverse effects of interacting with a virtual environment, such as 'cyber sickness'[56]. Baumgarter [2006] offers an example of how the neurosciences might contribute to improving VR. He performed one of the few studies on the neurophysiological underpinnings of immersion. He found that stronger feelings of immersion during a virtual roller-coaster ride were paired with lower levels of activation in the brain's prefrontal control regions (in children as opposed to adolescents). Baumgarter's findings might help us select users who are more sensitive than others to immersion; it might become possible to manipulate the user's sense of immersion by influencing neural activity in the prefrontal cortex.

Another contribution that the neurosciences can make to real virtuality is the use of BMI to control avatars. The interpretation of the user's conscious and/or unconscious data (e.g. selective attention, emotions, engagement) and their translation to the avatar could give users a closer sense of identification

55 The effect whereby people are less likely to help someone who is being attacked when there are others present.

56 A kind of motion sickness caused by viewing moving scenes while remaining physically stationary.

with their avatars (and thereby enhance immersion?). Physical identifying with one's avatar may enhance the sense of actually 'being there'. This notion may not even be that futuristic. Research has indicated that the brain's representation of the physical body is flexible and can be modified by information provided by the senses (more on this research in the next subsection, 3.6.4). Lenggenhager et al. [2007] has also shown that the spatial unity between the self and the body can be disrupted by presenting conflicting visual-somatosensory input. An out-of-body experience may reflect the ultimate form of real virtuality: users feel as if the virtual body presented on the (computer) screen in front of them is their own.

#### Research and development questions for the future

- What external factors play a role in making the virtual environment as realistic as possible? Stimulation of what senses or combination of senses is crucial for immersion?
- What internal factors play a role in immersion? Are people with certain personality traits or in certain mental states more prone to experiencing immersion than others?
- Is there a way to measure neurophysiologically whether users perceive virtual reality experiences as being real? Could we adjust the level of stimulation by activating their prefrontal regions?
- How should neurophysiological sensor data reflecting the user's emotions be interpreted and converted into a realistic interpretation in the virtual world? What is the added value of 'emotional avatars'?[57] Does a closer identification with an avatar (e.g. by translating the user's emotions to the avatar) alter the nature of social interactions in virtual worlds?
- How should neurophysiological sensor data reflecting the user's movement in the real world be interpreted and converted into a realistic representation in the virtual world? What time lag is acceptable between the user's movement and its representation?

### 3.6.4 Malleable body images: mediated environments as a tool for investigating brain plasticity, body consciousness and self-perception

*Wijnand IJsselsteijn*[58], *Antal Haans*[59]

Evidence is mounting that suggests that human brains are able to support highly and rapidly malleable body images. In line with such observations, our sense of bodily self-identification — the ability to distinguish what is contained within versus what is beyond our familiar biological shell — is also a flexible, temporary construct and not a fixed property. A particularly interest-

57 By 'emotional avatar', we mean expressing the user's emotional state through his avatar (i.e. an inhabitant of a virtual world) or rather, through its appearance.

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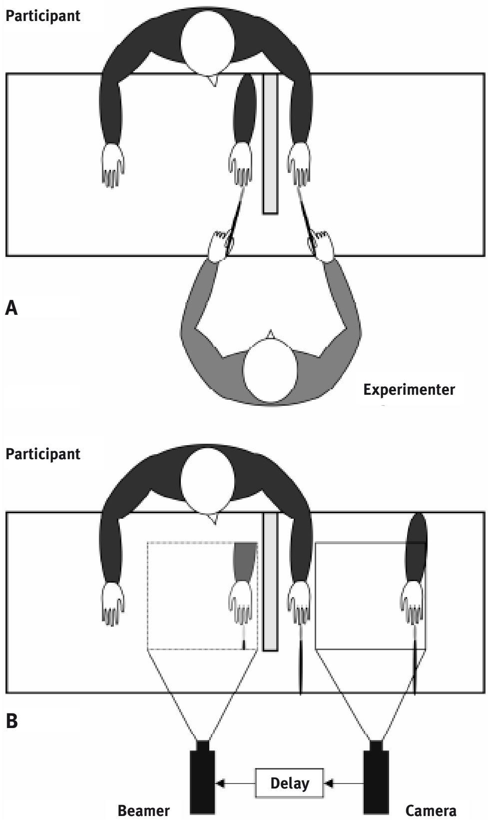
59 PhD candidate, J.F. Schouten School for User-System Interaction Research, Eindhoven University of Technology.

Figure 13
*The experimental set-up of the rubber-hand illusion (A), and virtual rubber hand illusion (B).*




ing and relevant phenomenon in this respect is a recently reported intermodal perceptual illusion known as the ‘rubber-hand illusion’ (RHI). When a person is watching a fake hand being stroked and tapped in precise synchrony with his own unseen hand, the person will, within a few minutes of stimulation, start experiencing the fake hand as an actual part of his own body (see Figure 13).

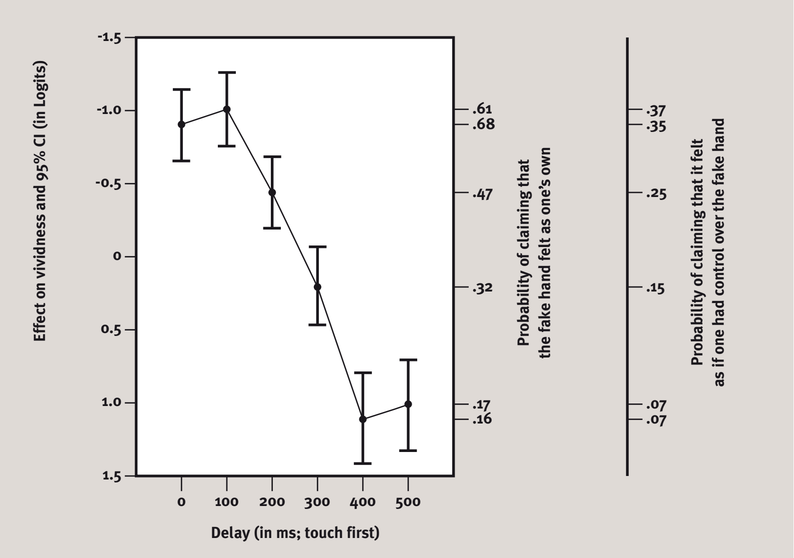
**Box 3: The Pinocchio illusion**

The Pinocchio illusion is a short and informal experiment. It goes like this: two volunteers take a seat in two chairs positioned exactly behind each other, such that the person in the rearmost chair is looking at the back of the head of the person sitting in the front chair. The researcher takes a position to the left side of the people sitting behind each other. Next, the researcher asks the person in the rear chair to close their eyes while the researcher takes their left hand — in particular the index finger, gently folding away the rest of the hand. The researcher then proceeds to touch the nose of the person sitting in the front chair using this index finger, thereby necessarily stretching the arm of the person sitting in the rear chair. At the same time the researcher uses his or her own index finger to touch the person in the rear chair on the nose at exactly the same spot, and with the same pressure and movement. He or she continues with such a synchronous tapping and stroking motion for about a minute or so, asking the person in the rear seat to meanwhile verbalise what they are experiencing. After a few minutes, over two thirds of the volunteers report that they feel as if their nose is significantly elongated, sometimes to a full arm's length. What is especially surprising about this illusion is the speed with which it occurs. Remember that we are talking about our nose here, a part of our body we have been intimately familiar with throughout our life. It would be fair to assume that whatever body representation the brain has of the nose, it is fairly stable and not prone to rapid alterations. However, quite to the contrary, this informal experiment illustrates how malleable or plastic the human brain really is. Underlying this Pinocchio illusion is the realisation that the representation of the body is dynamically inferred from various sensory streams of information (in this case touch and proprioception[60]); a continuous process rather than a static, hard-wired template.

The correlation between visual, tactile and proprioceptive information can be thought of as self-specifying for bodily self-identification, as the brain has learned from a very early age onwards that it can only be the body, and no other object, that registers these specific intersensory correlations [Botvinick, 2004]. In the RHI, people perceive the fake hand as part of their body because their perception of it matches the body-specific sensorimotor contingencies. If this is no longer the case, for example when participants try to move the fake hand, or when there is a small delay between the visual and tactile stimulation, the illusion will diminish or break [Armel and Ramachandran, 2003; Botvinick and Cohen, 1998; Tsakiris and Haggard, 2005]. The strength of the RHI is also considerably diminished when the artificial object is incongruent to the human body, for example when a tabletop [Armel and Ramachandran, 2003], a wooden stick [Tsakiris and Haggard, 2005], or a flat piece of skin-like texture [Haans et al., in press] is used as the artificial object, or when the fake hand is in an anatomically incorrect orientation [Ehrsson et al., 2004; Pavani et al., 2000; Tsakiris and Haggard, 2005]. Relevant in this respect is the finding that neurons in area five of the primate parietal lobe, which are thought to be involved in monitoring arm position and movement, respond to an artificial object as well, but only when it resembles a monkey's arm that is correctly orientated [Graziano et al., 2000]. These findings suggest that the strength of the RHI depends not only on matching body specific sensorimotor contingencies, but also on the correspondence between the artificial object and a cognitive model of what a human body is like [De Vignemont et al., 2006].

**60** Proprioception is the sense of the position and movement of body parts, based on receptors in the muscles and tendons.

**Figure 14**
*Effect on vividness of the 'rubber-hand illusion' of controlled asynchrony of between 100 and 500 ms.*




## Embodiment in mediated environments

Research demonstrated that the RHI can also be elicited under mediated conditions [IJsselsteijn, de Kort and Haans, 2006]. The researchers performed an experiment where they investigated this illusion under three conditions: unmediated condition (replicating the original paradigm of Botvinick and Cohen), virtual reality (VR) condition (where both the fake hand and its stimulation were projected on the table in front of the participant), and mixed reality (MR) condition (where the fake hand was projected, but its stimulation was unmediated).[61] As expected, the unmediated condition produced the strongest illusion. However, the VR and MR conditions also produced the illusion to some extent, thereby providing a basis for researching bodily self-identification under mediated conditions. For example, using a projection of the rubber hand makes it possible to investigate the impact on the RHI of introducing a time delay between the visual and the tactile signals. Although an 'asynchronous' condition is used by most researchers (as a control condition which is thought not to elicit the RHI), the time delay is typically only impressionistically determined — usually between 0.5 and 1 second — and reliable stimulation depends on the skills of the experimenter. Using the mediated RHI (see Figure 13B), Haans, Kaiser and IJsselsteijn [in preparation] were able to demonstrate the impact of a time delay on the strength of the RHI [see also Haans and IJsselsteijn, 2007]. Figure 14 illustrates the results of introducing controlled asynchrony of between 100 and 500 ms. Whereas the RHI under a 100 ms delay between haptic stimulation and the video is still comparable to that evoked by synchronous stimulation, longer delays quickly diminish the vividness of the RHI (i.e. at around a 500 ms delay, it is highly unlikely that the participant will experience the illusion).

**61** Dependent measures included self-reports (open-ended and questionnaire-based) and proprioceptive drift, that is, the offset between the felt position of the hidden hand and its actual position.

This paradigm has also been adopted by other researchers [Sanchez-Vivez and Slater, 2007] who investigated the rubber hand illusion using a virtual environment. They report that stimulating a virtual arm — a 3D stereoscopic projection of an arm seemingly coming out of a participant's body — in synchrony with the participant's real arm results in similar feelings of body ownership. Other recent investigations have shown that stimulating a video projection of a full body in synchrony with one's physical body can result in an artificially induced out-of-body experience [Ehrsson, 2007; Lenggenhager et al., 2007].

### Mediated environments as a tool for investigating brain plasticity and body self-perception

Mediated environments (including mirror images, video projections and computer-generated images) allow for a host of controlled manipulations of factors that potentially influence our sense of body ownership and, consequently, our sense of self. They uniquely enable transformations of body perception, changing perceptual regularities and feedback. When we are offered a fully immersive virtual environment that contains a real-time responsive and realistic rendering of our body, mapped onto our bodily movements in minute detail, we expect a significant level of identification with that virtual body, and consequently, a sense of presence in the virtual space. Moreover, depending on the fidelity of haptic feedback, a sense of body ownership is likely to occur.

Ownership of a virtual body would not only enhance the feeling of immersion and presence in a VR environment (see subsection 3.6.3), but it would also allow us to investigate potential determinants of body ownership and self perception. To paraphrase Frank Biocca, media environments are like cyclotrons of the mind; they are a powerful and versatile tool we can use to learn something fundamental about the structure of perception and the workings of the brain. By experimentally decoupling and transforming the intimate ties between body morphology, proprioception and self-perception, we can break a seemingly coherent and stable experience down into its constituent parts. This, in turn, enhances our fundamental understanding of the phenomenal experience of self, and sheds light on the brain mechanisms involved in self-representation.

### Research and development questions for the future

At a basic perception level, initial experiments could focus on the *required fidelity of the virtual body*, that is, the extent to which a full and accurate representation of the participant's body is required in order to experience ownership. Similarly, the required level of body tracking and match with proprioception, both in terms of temporal properties[62] as well as spatial detail[63], is another issue that needs to be determined empirically. In addition, it would be

**62** How fast does the virtual body need to respond to our body movements in order to be convincing? Our RHI data suggest less than 200 ms, but these data may be valid only for passive stimulation, as no movement of the real hand is allowed in the current RHI paradigm.

**63** How many points on the body need to be tracked? This is a field where know-how based on motion capture in animated (computer-generated) movies may be relevant.

interesting to determine the effects of dramatic alterations in body perception, for example remapping of action-perception couplings between existing body parts, adding non-existent body elements (e.g. a tail) under the control of a specific body part (e.g. the buttocks)[64], changes in responsiveness of body parts (e.g. slow motion movements), and so on.

Socially meaningful transformations could include simple body shape alterations, such as body weight or height, or more complicated changes, including changes in perceived race, gender, age, etcetera. Provided the sensorimotor mappings are convincing enough for participants to identify with their new virtual bodies, interesting social science research may investigate and even influence implicit attitudes concerning *perception and biases in social judgments*. The impact of the social perceptions of others on our sense of self is also potentially significant, and can be studied systematically under mediated conditions. For example, an important driver of our sense of self is the social acknowledgement we receive from our environment, varying from simple nods or glances to greetings and full-blown social interactions.

Research on perceived body morphology, bodily self-identification and self-consciousness would traditionally depend on investigating anomalies of body perception, such as those found in clinical populations suffering from a variety of body agnosias, neglect syndromes or body dysmorphias. Such patient populations are hard to investigate in large enough numbers, however, and participants often suffer from brain damage that impairs multiple functions at once, and not merely the ones under study. Working with healthy participants that have an *experimentally induced transformed perception of self* based on a well-controlled mediated or virtual body offers a promising way forward for research in bodily self-perception, both for understanding healthy as well as pathological functioning. Understanding anomalous processes of self-perception, such as those occurring in body dysmorphias and eating disorders, may eventually lead to improved therapeutic interventions, where both diagnosis and treatment may benefit from the use of virtual bodies with which one can truly identify.

Finally, the study of mediated embodiment is clear relevant to the *development and optimisation of mediated environments* themselves. Understanding the conditions under which body identification and ownership may or may not occur has implications for the design of virtual environments, tele-operation and mixed reality systems. In most current virtual environments, much of the time we are like the Invisible Man or Woman, with only a simple virtual hand to interact with virtual objects, and no body to speak of, let alone appropriate shadows or reflections as one moves about in the virtual world. The presence

64 This would be the virtual equivalent of the Third Hand, a piece of cyborg performance art by Australian artist Stelarc. He has incorporated a third, robotic arm, connected to the lower part of his right arm, and controlled by muscles in his abdomen and upper thigh. See: www.stelarc.va.com.au/third/third.html.

of a believable virtual body will likely improve our interaction performance in mediated environments, especially for the kinds of naturalistic tasks that typically benefit from increased levels of user embodiment.

### 3.6.5 Split-second decisions and actions

*Jan van Erp*[65]

> Imagine Jack who has his final exam qualifying him as an air traffic controller scheduled for next week. He is getting pretty nervous because he is still not performing up to the level needed to pass the exam. He knows he has problems taking the right decisions in the right amount of time. He generally chooses the best solution, but it takes him way too long to come to the right conclusion. Sometimes air traffic controllers have only a fraction of a second to resolve a potential conflict between two approaching aircraft. Today, his instructor will introduce him to a new technology that may help him speed up his decision-making process. Before going through the normal exercises, he will undergo a transcranial magnetic stimulation (TMS) session (see Figure 15). His instructor explained that the TMS apparatus is something like a big magnet that will be placed on specific areas of his head. The magnets will activate certain areas in his brain that are involved in learning, especially learning perception–action loops. This may help him learn faster and more efficiently during the exercises and take split-second decisions that he in fact takes so many times a day in normal life, for example hitting the brakes when the traffic light turns red. The TMS session turns out to be not exactly as he expected. He was seated in a comfortable chair while the TMS specialist placed some markings on his head to position the magnets correctly. The session lasted for about twenty minutes. He felt nothing and only a slight buzz of the magnets told him that something was happening. Strangely enough, he did notice that his performance improved over the following days, especially in applying standard 'if-then' rules. As soon as he saw the radar screen and heard the 3D warning sounds, he pushed the right buttons. Almost as in a reflex, like the time when he saw a child suddenly dart out into the road and he braked and swerved in a split-second without thinking.

In everyday life we are constantly performing actions without thinking. Although we are not aware of it, many of these actions are based on the perception-decision-action loop. Interestingly, we either take these steps by reflex, or we are so well trained in them that we may not even be aware that we have taken a decision. Examples include maintaining our balance on a bicycle and braking or swerving when the car in front of us suddenly hits the

65 Chief Scientist of the department of Human Interfaces, TNO Human Factors.

**Figure 15**
*Transcranial Magnetic Stimulation (TMS) uses magnetic pulses generated by a double coil of wire to induce electrical currents in the cerebral cortex just beneath the skull. Photo courtesy of Clinical Neurophysiology, UMC St Radboud Nijmegen, Erik van 't Hullenaar.*

brakes. The latter may involve taking a split-second decision to turn either left or right. This implies that the brain can employ very fast neuronal circuits that are able to interpret the information supplied by the senses, apply a decision rule and initiate an action. Gaining access to this mechanism may improve split-second decision-making skills indispensable not only to air traffic controllers but also to soldiers (friend or foe?) or referees (deliberate dive or penalty?), and in many of our own everyday activities.

There are two important reasons why this mechanism is interesting for MMI. First, as stated above, it is very fast. And secondly, it does not depend on slow, serial, and often heavily loaded cognitive processing. The advantage of an MMI that can access this powerful mechanism is evident in collision avoidance systems in automobiles. TMS equipment is commercially available; TMS is for instance already being used as a 'knock-out' technology (i.e. virtual lesioning) to study causality in fMRI studies and repetitive TMS is being used as a therapy for severe depressed patients. TMS could potentially have a major impact across a wide range of potential applications, but the details of the workings behind TMS are still being being explored.[66]

The mechanisms involved are linked closely to skilled behaviour (i.e. closed-loop performance such as car driving). It seems reasonable to expect that skilled behaviour uses some of the same brain mechanisms, and so a knowledge of these mechanisms may have several spin-offs. One interesting application might be the ability to stop or slow down the degradation of skilled behaviour, for instance caused by ageing or illness. This may enable the elderly to continue to drive safely and to maintain their quality of life. Going a step further, artificial sensors could be included coupled to the relevant

**66** A risk of both TMS and rTMS is that the technology can produce seizures.

brain mechanisms, for example to help the elderly maintain their balance and keep them from falling. Another application is the more effective and efficient training of skilled behaviour, something that could have social and economic implications. For instance, we would need less time and fewer lessons to learn how to drive a car, ski or cut a diamond. Finally, being able to control or improve split-second decisions and actions implies faster rehabilitation after an accident or illness.

Research and development questions for the future

- What brain areas are involved in the fast perception-decision-action mechanism? How is this mechanism activated?
- How can we affect the forming and consolidation of perception-decision-action loops?
- How can we enlarge the plasticity of the brain during learning processes? What processes can be implemented by this mechanism (e.g. if-then rules)?
- Are there other neural mechanisms in the brain that we can use to improve split-second decision-making, for example Error Related Negativity (ERN)?
- Can we tell what the brain's decision is before the action (e.g. braking) is planned and executed? In what cases do we want to 'bypass' the cognitive or action system?
- What would a method or device that operates on the basis of the perception-decision-action mechanism be like (e.g. TMS, psycho pharmaceuticals)?

### 3.6.6 The gift of tongues: a neurocognitive approach to articulatory-motor learning

*Niels Schiller*[67]

Imagine Nina and Paul, an American couple in the Netherlands. Nina is an academic and came to the Netherlands because of a temporary job opportunity. Paul followed her since he is a computer programmer and can easily find work pretty much anywhere. Both had to learn Dutch when they moved. Now that Nina's job has come to an end, they face moving again, probably to Germany. Paul is not happy about that because he has trouble learning new languages. However, there may be a way to help Paul learn German using a brain-computer interface and neurofeedback. Paul may be able to activate articulatory-motor learning by stimulating the motor neurons responsible for controlling the pronunciation of speech. This may help Paul to acquire the necessary pronunciation of German without much effort. Of course, articulatory-motor learning does not equal learning a new language, but it is an important step towards fully mastering another language.

67 Professor of Psycholinguistics and Neurolinguistics, Leiden Institute for Brain and Cognition (LIBC), Leiden University.

## Producing spoken language

Verbal (i.e. spoken) communication is based on the interplay between speech production and speech comprehension. Speech production or speaking is one of the most complex forms of skilled cognitive behaviour [Levelt, 1989]. For instance, to be able to name an object, speakers have to recognise and conceptualise the object, retrieve a semantic concept from long-term memory, and look up a corresponding word from their mental lexicon [Levelt et al., 1999]. Once a word form has been identified, speakers have to encode the word form phonologically, including segmental retrieval (i.e. which segments or phonemes[68] does the word have?) and metrical retrieval (i.e. where is the main lexical stress of the word located?). The final part of the word production process concerns articulation, i.e. the coordinated motor actions of jaws, lips and tongue to modify the stream of air generated by the respiratory system (e.g. the lungs). Listeners are able to decode the variations in sound pressure conveyed by air molecules through their auditory perceptual system and interpret the perceived speech signal semantically.

It takes children a number of years to use language with any skill. Syntactic development can take at least ten years, while phonetic and phonological acquisition is usually faster. Children learn language in phases, starting with babbling and then producing isolated words before the first simple syntactic structures emerge. Their pronunciation improves, their syntax becomes more elaborate, and their lexicon grows very rapidly, i.e. they quickly learn new words. It has been claimed that language acquisition is tied to a 'sensitive period' which ends approximately around puberty. This is also the time in life when the plasticity of the brain starts to decline. Although it is still possible to learn languages after the onset of puberty, and even at much higher ages, it is no longer possible to fully master a new language without assistance, and structured learning instructions become necessary.

## Speaking more than one language

The issue of language production becomes even more complex when people acquire a second language. Bilingualism and multilingualism are age-old phenomena — people have always had to switch between their local dialect and the standard language, for instance — but in the multicultural and multilingual society of the European Union, it is becoming increasingly important to speak other languages.

Speaking a non-native language includes, among other skills, the correct pronunciation of words. Pronunciation is the result of fine-grained articulatory movements of the tongue, the lips, and the jaws. Often, sounds are pronounced very similarly (but not identically) in two languages, for instance the

**68** A phoneme is the smallest structural unit that distinguishes meaning, e.g. the [t] sound in the word tip, stand, water and cat. These instances of [t] are considered to fall under the same sound category, despite the fact that in each word they are pronounced differently. See www.wikipedia.org.

**Example VIII**

**A new device combines the processing power of the human brain with computer vision. It helps people to search through large numbers of images or video footage much faster than humans or computers can on their own.**

# Human brain power speeds up computer performance

The Cortically Coupled Computer vision system, or C3 Vision, was developed by scientists at Colombia University in the United States. DARPA, the Defence Advanced Research Projects Agency in the US, funded the research.

The C3 Vision system makes use of electrical activity in the brain. The system consists of many electrodes in a swimming cap-like hat that record the activity as an electroencephalogram (EEG). Unlike a computer, the human brain excels at spotting novel, unusual or rare elements. If a person sees an image that grabs his attention, it appears 300 milliseconds later on the EEG as a spike. This is known as the P300 peak, which occurs well before the event has entered the participant's consciousness so that he can press a button to indicate that he saw something out of the ordinary.

While the user looks at the images streaming by, the system registers which images elicit the P300 peak. After this sifting process, the user can thoroughly examine the selected pictures. Computer vision algorithms can be added to the system to pre-select the pictures, in this way reducing the number of images and speeding up the scanning process. A computer vision system can, for example, identify all pictures taken during the day, or all pictures that depict water.

The developers tested the system among five volunteers. The participants were confronted with 2500 images of outdoor scenes, and they had to identify pictures with people in them. This is a hard task for a computer. Each picture was shown for just 50 milliseconds. In one run the volunteers had to press a button when they spotted a person, and in another run they used the C3 Vision system. Their response speed and accuracy was faster with the C3 Vision system, with a detection accuracy of about 92 percent. The system also produced false responses, when the participant was distracted by something other than the target picture.

Original publications: Parra et al. (2008). *IEEE Signal Processing Magazine*, 25, 107; Gerson et al. (2006). *IEEE Transactions on Neural Systems and Rehab. Engin.*, 14, 174

In a second experiment, six participants trained for the task had to identify helicopter platforms on overhead satellite images, by hand and after a prescreening session with the C3 Vision system. In particular when target pictures were sparse (about 1 percent of all pictures), all twenty targets were identified within thirty minutes after prescreening, whereas examination by hand took three hours and identified only thirteen targets.

As image and video databases grow exponentially, we all face the problem of how to search these enormous and often diverse databases efficiently. The C3 Vision system can be useful for federal agents, for example, who have to search through hours of surveillance video footage of a crime scene, or for doctors who scan medical images.

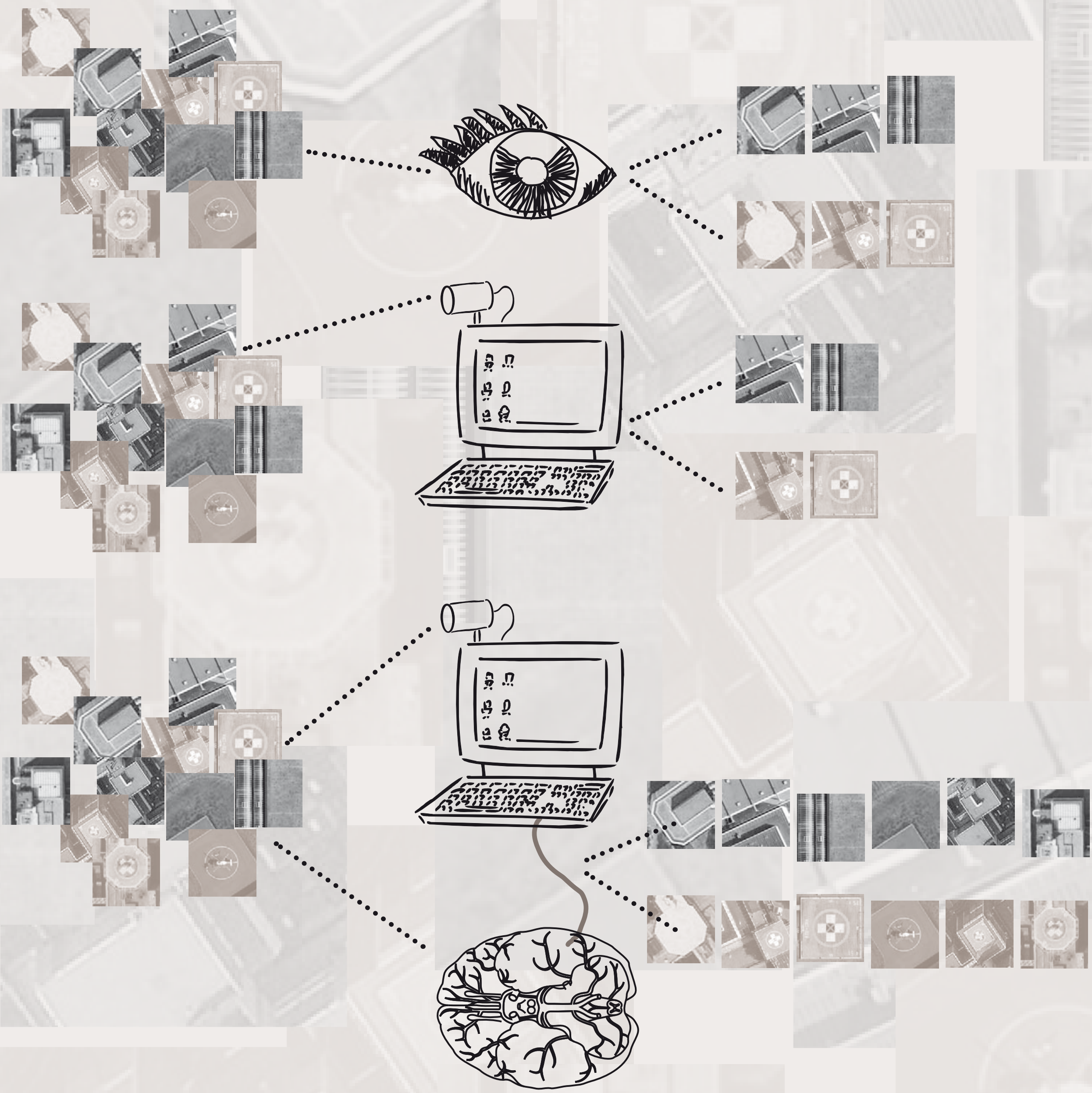
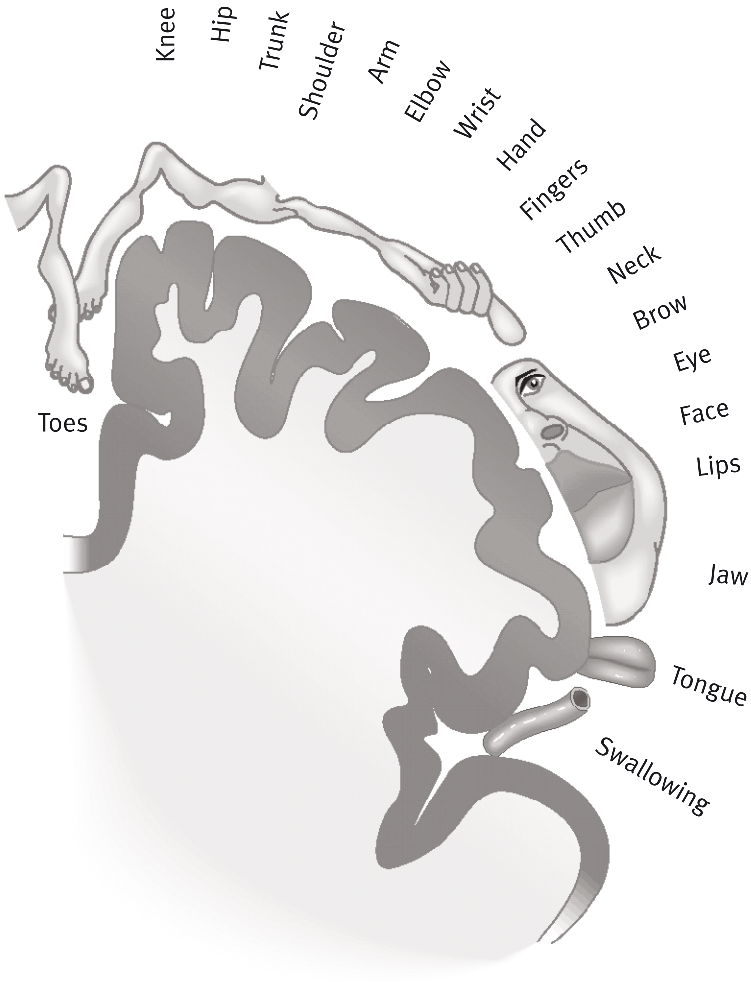


**Figure 16**
*Brain homunculus: this model shows the motor cortex in the right cerebral hemisphere. It illustrates the projections of various body regions on the motor cortex which are not proportional to the size of the body parts, but rather to the complexity of the movements that they can perform. As one can see, a large proportion of the motor cortex is devoted to the lips, jaw and tongue needed for speech. Source: www.spinacare.wordpress.com.*




German [b] and the Dutch [b], the latter of which is pre-voiced. The acoustic difference between the German [b] and the Dutch [b] is quite subtle; native German second-language learners of Dutch therefore have a tendency to pronounce the Dutch [b] like the German [b]. There are also instances of sounds in a non-native language that do not exist in the native language. The English 'th', such as in the definite article 'the', does not exist in either Dutch or German, for example, and Dutch or German speakers have to learn to pronounce that sound from scratch. German speakers tend to pronounce the English 'th' like an [s] or [z], i.e. a voiced [s], because these fricatives in the native German phoneme inventory bear the most similarity to the English voiceless and voiced 'th' sound.

As mentioned above, the correct pronunciation of non-native sounds is the result of appropriate articulation. The appropriate articulation of new, non-native sounds includes a form of motor learning, comparable to acquiring the skilled movements needed to play a new sport (e.g. the precise method of hitting a ball with a racket). Humans can learn new motor patterns by imitating others. The role of verbal imitation has already been emphasised for learning new words and syntactic structures; when it comes to motor-learning, speakers have to listen to correct pronunciations of non-native sounds produced by native speakers and then imitate those pronunciations by performing the same articulatory-motor actions. Very subtle modifications in motor behaviour can lead to rather large acoustic changes. It is therefore important to coordinate the movements of the articulators very precisely. As a matter of fact, articulators, such as the tongue and the lips, have rather large areas of representation on the human somato-sensory and motor cortices, which provide the neurocognitive basis for making the articulators' precise movements possible.

### A neurocognitive approach to articulatory-motor learning

The intimate relationship between listening (hearing) and speaking (articulation) has been illustrated above by the process of speech-motor learning. In fact, the motor-theory of speech perception states that the listeners' speech comprehension is based on understanding the speaker's articulatory movements [Greenberg, 1996; Liberman et al., 1967; Liberman and Mattingly, 1985]. A close link between perception and production is indeed desirable for imitating articulatory-motor movements, and it may be the case that similar neurocognitive mechanisms govern the perception and production of speech [Ivry and Justus, 2001]. Mirror neurons may play an important role in fulfilling this link. These neurons are not only active while motor actions are being performed (e.g. grasping) but also while the same actions are being perceived. Mirror neurons were first discovered in pre-motor areas in monkeys [Gallese et al., 1996], but it has been suggested more recently that they may also exist in the human cortex, including Broca's area where recognition of gestures is localised [Rizzolatti and Arbib, 1998]. It may even be the case that specific mirror neurons are active both while producing certain speech sounds (i.e. speaking) and while perceiving the same speech sounds (i.e. listening) [Kohler et al., 2002; Sundara et al., 2001; Watkins et al., 2003].

How could we make use of mirror neurons to improve the pronunciation of non-native speech sounds in non-native language learning? It would be interesting to explore the effect of selectively stimulating the mirror neurons responsible for motor-learning the correct pronunciations of non-native speech sounds. One way to do this might involve BMI and neurofeedback. We know from previous research that participants can voluntarily activate and de-activate particular brain regions [Caria et al., 2007; Weiskopf et al., 2004], even to such a fine-grained degree as to manoeuvre a cursor to play a computer game (known as 'brain-pong').[69] It may be possible to use neurofeedback or neurostimulation of some sort (e.g. through TMS) to improve motor-learning for non-native speech sounds. If speakers can voluntarily activate areas in the brain that include the mirror neurons responsible for articulatory-motor learning, then they may be able to facilitate the correct pronunciation of non-native speech. One important requirement is that the mirror neuron system in question must be well localised. Only if that is the case they can be stimulated precisely enough using BMI and neurofeedback. If a particular mirror neuron system is widely distributed in the brain, neurostimulation cannot be as effective.

Of course, articulatory-motor learning via BMI and neurofeedback is just one example of motor learning. Because we know that mirror neurons for manual motor skills exist, it should be possible to learn any complex manual movement sequence, for instance typing. Whether there are also mirror neurons for other types of motor actions, such as leg movements, remains to be seen. However, all motor actions are planned and controlled by the human motor cortex, structurally a relatively well-defined strip of the cortex. It is therefore very likely that the learning process described here for articulatory-motor learning can be extended to other areas of motor learning.

### Why is good pronunciation important?

The efficiency of verbal communication can be hampered if the production or comprehension process is impaired. For instance, speech errors (slips of the tongue) usually require the speaker to correct them, thus hampering the fluency of speech. Speakers can try to prevent speech errors through their internal verbal monitoring system, which detects and corrects errors even before articulation [Levelt, 1983; Christoffels et al., 2007; Ganushchak and Schiller, 2006; in press-a; in press-b; Schiller, 2006]. The communication process can also be disrupted by misperceptions (slips of the ear). One source of misperception is the unclear pronunciation of speech sounds. It is clear that pronouncing non-native speech sounds correctly may contribute significantly to those same sounds being comprehended by listeners. Correct pronunciation may also prevent non-native language users, such as immigrants, from being stigmatised due to their marked language use.

### Research and development questions for the future

- What brain areas support articulatory-motor learning?
- Is there a mirror neuron system involved in articulatory-motor learning?
- Is it possible to stimulate this system selectively? What technology (e.g. TMS) can be used for this purpose?

**69** This was achieved by providing on-line feedback so that the participants learned physiological self-regulation of the BOLD (Blood Oxygen Level Dependent) signal.

- Can articulatory-motor neurons be affected by neurofeedback or neurostimulation?
- Can the principle of motor learning by neurofeedback and neurostimulation be extended to other forms of motor learning?

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# 4

# Personalised learning

## 4.1 Introduction

*Ira van Keulen* [1]

Education is second to health care as the area of application named by neuroscientists and cognitive scientists as likely to derive particular benefits from our growing knowledge of the brain. Not surprisingly, there are already quite a few international research schools and academic programmes (see box 1) focusing exclusively on brain research for educational purposes. Most of them got started under the new designation, 'educational neuroscience'.

1 Projectmanager, STT.

**Box 1: International and national initiatives in educational neuroscience**

The main programmes in educational neuroscience are at Harvard, Cambridge and Dartmouth College, but there are also some important initiatives in Japan, Denmark and Germany. An international platform was even founded in 2004: the International Mind, Brain and Education Society (IMBES), which recently launched its own journal at Blackwell Publishing. The Organisation for Economic Co-operation and Development (OECD) has also made great efforts to explore the field, resulting in the recent report 'Understanding the Brain: the Birth of a Learning Science'. This report also reviews educational neuroscience initiatives all over the world: in Cambridge, Harvard, Denmark, Germany and Japan. Another initiative worth mentioning here is the large-scale Science of Learning Centres programme run by the US National Science Foundation (NSF). This programme supports multidisciplinary research *"that anchor new lines of thinking and inquiry towards a deeper understanding of learning."* So far a couple of centres have been set up and amply financed [National Science Foundation, 2004].
The Dutch academic world is not lagging behind. The Brain and Learning Committee of the Netherlands Organisation for Scientific Research (NWO) organised a seminar week in 2004 entitled 'Learning to Know the Brain'. About fifty Dutch neuroscientists, cognitive scientists and educational scientists as well as educational practitioners gathered together to talk about the importance of brain and cognitive research for education. A report on this week focused on different themes, such as life long-learning, motivation and individual differences. A number of research projects on neuro-evidence-based educational interventions have begun in the Netherlands, including one called Talentenkracht (i.e. TalentPower), a programme in which a wide array of scientific disciplines focus on the talent and qualities of children aged three to five. NWO's Programme Council for Educational Research is also investigating the relevance of neurocognitive science for educational research purposes [Van Gog et al., 2007].

*Ira van Keulen*[2]

The goal of all these different initiatives is more or less unequivocal: to develop a science of learning in which a range of disciplines — educational scientists, neuroscientists, cognitive scientists and educators themselves — work towards 'evidence-based learning' (i.e. informing the curriculum and the various phases and levels of education by neuroscientific and other scientific insights).
It is precisely this concept of evidence-based learning that interests the Dutch Ministry of Education — and in particular the research and science policy division — in the neuroscientifically informed approach to learning. One of the Ministry's key arguments encouraging the idea of evidence-based learning

2 Projectmanager, STT.

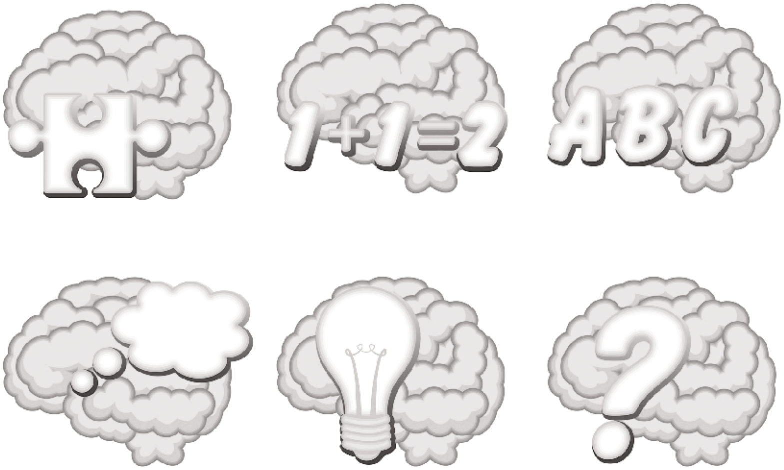



**Figure 1**
*Neuroscientists and cognitive scientists can make a valuable contribution to education by investigating what type of training at which intensity and for what length of time is most effective and for whom, based on differences in the way the brain is organised. By Joto24, www.dreamstime.com.*

was mentioned by the former minister — Maria van der Hoeven — herself in 2006[3]: *"Education is the biggest expense item in the national budget. Modern brain research offers opportunities to gain new, proven insights in the best way to learn. I am convinced that our educational system can benefit enormously from it. Future changes in methods and curricula should be based less on opinion and more on the results of hard scientific evidence."*

What valuable contributions can the neurosciences and cognitive sciences make to educational science and practice? To answer this question, we need to know that the human brain is shaped by interaction with the environment, a process known as neural plasticity and the basic principle of learning. From this perspective, learning is something we do at all times and everywhere, and not only in an educational or professional context. It is indeed one of the most important neuroscientific findings of the past decade that the brain is much more plastic than we used to think.[4] For example, monozygotic twins — who have the same genes — already have differences in their brain structures at the moment of birth. The brain also develops from the moment of conception until late in life, and not only until the age of twenty, which was the traditional view before the nineties. Neurons still grow, connect and differentiate after the age of twenty (although fewer of them do, and they do so more slowly), and new neurons are even generated (i.e. neurogenesis). There are infact parts in the brain — the prefrontal cortex — that only develop after the age of fifteen [Jolles, 2007]; see also section 4.6.

Knowing this, neuroscientists and cognitive scientists can make a valuable contribution to education by investigating what type of training at which intensity and for what length of time is most effective and for whom, based on differences in the way the brain is organised. Indeed, one of the most important

3 See www.nwo.nl/nwohome.nsf/pages/NWOA_6Q4K9Z.

4 Psychiatrist Norman Doidge has called neuroplasticity *"one of the most extraordinary discoveries of the twentieth century."*

goals of educational neuroscience — as explained by American neuroscientist Michael Gazzaniga when he talked about children's reading abilities — is to determine which teaching methods promote the formation of the most efficient neural connections [Gura, 2005]. These individual differences in brain structure are due to both genetic and environmental influences.[5] Whereas genotype defines the upper and lower boundaries of academic achievement, the environment will define the achievement level between those biologically defined boundaries.

It will take time and a concerted effort between the neurosciences, cognitive science and educational science and practice to improve the educational system on the basis of scientific evidence. It is not easy to transpose neuroscientific knowledge to the classroom, for a variety of reasons. In the first place, we have differing levels of knowledge about the brain, at molecular, neural and system level, the latter having the closest link to human behaviour. The step from molecular or genetic research to explaining behaviour is bigger than from neurocognitive research (compare sections 4.3 and 4.4). This means that it is easier to transpose the functional approach taken in cognitive research to the classroom than neurobiological findings on genes, proteins, synapses or individual neurons. General rules extracted from neurobiological processes are usually not directly applicable.

Secondly, most of our neurobiological knowledge about learning has been derived from lab experiments on animals, usually rats. There is, for example, little or no research on the development of the human brain at cellular level; the only human study was carried out on the brains of dead persons in different age groups [Huttenlocher and Dabholkar, 1997]. Nevertheless, neurobiological research involving animals provides clues about human learning, as long as we are careful not to over-extend those findings to educational practice.

Thirdly, most of the neurocognitive research on cognitive processes and development, is based on functional magnetic resonance imaging (fMRI; see Appendix 1) studies with adults, and not with children. In the Netherlands, this is because children up to eight years of age can only be placed in an MRI scanner for medical purposes. Indeed, medical ethical committees often hesitate to allow MRI research on children older than eight; they consider the procedure too emotionally invasive. But children and adults use their brains in different ways; young people activate more brain areas, and their activations are more diffuse than in older people [Casey et al., 2005]. Considering these differences, we must also be careful about transposing the neurocognitive findings of research involving adults to classrooms filled with the brains of young children.

5 Genetic and epigenetic factors play an important role at the start of brain development, whereas the proper development of the brain's network is guided by behaviour under the influence of environmental factors.

Finally, we have only a limited understanding of the details of human brain development. Only one study has quantified the development of synapse densities in three areas of human post-mortem cerebral cortex from prenatal age to old age [Huttenlocher and Dabholkar, 1997]. The possible consequences of this study for education have led to fierce debate [Bruer, 2006]. To enable the transposition of neuroscientific findings to the educational system, we must conduct more quantitative and other histological[6] studies of human brain development. In addition, it is very important that we establish how the microscopic structure of human brain is linked to cognitive abilities [e.g. Shaw et al., 2006]. While structural and functional MRI have led to important new insights into the development of cortical white and grey matter in humans[7], these studies are usually also limited to children aged eight and older.

In summary, we must be cautious about transposing cognitive and neuroscientific knowledge to education, and continue our research, especially on young humans. Or, as the OECD report states: *"There are few instances where neuroscientific findings, however rich intellectually and promising for the future, can be used categorically to justify specific recommendations for policy or practice."*

There are, non the less, instances where the neurosciences and cognitive science can generate interesting educational information in four different ways (see also the four illustrated examples in this chapter). In the first place, they can confirm existing theories from other sources. For example, the idea that children work with a spatial mental number line has long been broadly accepted in the educational sciences. This line is a universal mental representation of numbers in which smaller numbers are represented on the left and larger numbers are represented on the right. But it was not until the early nineties that fMRI studies provided neuroscientific evidence of this mental number line and located it in the parietal area [DeHaene et al., 1993]. Evidence for the same theory from different scientific disciplines is valuable, even more so when the biological mechanisms behind a theory become apparent, as that can help to identify new or more efficient interventions. For example, if claims are made that a particular training method improves the mental number line, neurocognitive research can demonstrate the involvement of the underlying brain mechanisms.

Secondly, neuroscientific findings may imply an interesting extension of traditional learning theories that play an important role in theories of instruction underlying educational practices. Traditionally, learning theories define learning as a process that causes persistent changes in performance (or behav-

6 Histology is the study of brain and other tissue, sectioned as a thin slice using a light microscope.

7 The cell bodies of neurons and the glial cells supporting the neurons constitute the grey matter of the brain. White matter is composed of the axons connecting the different areas of grey matter to each other carrying the nerve impulses between neurons.

ioural potentials) as a result of the interaction of the individual with the world [Driscoll, 2005; Anderson, 1999]. These theories propose that there are various types of learning, depending to a certain extent on differences in the learning task and content. Another issue is the importance of individual differences in learning. There are various theories about what causes these differences, resulting in the idea of different cognitive styles to explain the different ways individuals organise and process information. Neuroscience will enrich such theories, for example fMRI studies revealing functional-anatomic correlates of different verbal and perceptual strategies in memory [Kirchhoff, 2006; see example XII].

Thirdly, neuroscientific research will create new theories and practices. The expert group discussed the neuroscientific finding of mirror neurons a number of times. One suggestion was that *"You can learn things just by looking at something. Thinking about a five-finger piano exercise has the same effect — in terms of neural changes — as practising the exercise. Imagining a particular activity activates the same neural systems as those actually engaged in that particular activity."* (Van Turennout, FC Donders Centre for Cognitive Neuroimaging). In one particular Dutch school, teachers have already tested this idea and achieved learning improvements with pupils by merely demonstrating arithmetic problems on the blackboard without offering any explanation (Gankema, KPC advisory group). Learning by looking is not a totally new idea of course, but it is interesting to see just how far this method can be stretched (see also example IX).

Finally, neuroscientific and cognitive research can test current practices and methods. It has already done so for medical interventions, for example by comparing the effects in the human brain of cognitive behavioural therapy versus antidepressants [Goldapple et al., 2004]. In an educational context, it would be interesting to compare the effects on children's brains of two different approaches to learning: the current Dutch practice of having students look up information (such as rules and exceptions in mathematics or physics) versus the traditional method of learning such information by heart.

### 4.1.1 How to read this chapter

The STT expert group on Learning — which produced this chapter — was a transdisciplinary group with members from various neuroscientific and cognitive scientific disciplines, educational practice and policy. In that sense, the group was an example of a design experiment in which *"educators and researchers establish a common ground to create a shared problem representation and develop a mutually beneficial research program."* [Ansari and Coch, 2006]. The group's assignment was to propose an inspirational view of a future in which neuroscience and cognitive science would meet educational practice. The group was free to think far ahead (fifteen to twenty years) — one of the qualities that set this particular think tank apart from other similar initiatives — and decide what a desirable future would be for both science and practice. The group began by comparing notes: what do we know and what will we know twenty years from now (science) and what do we want to know and what pressing questions or problems do we face (practice)? The following issues were identified as important by both scientists and practitioners:

- *Early detection of children's learning potential and abilities*. Mapping abilities (not only literacy and numeracy) and the relationship between these abilities; developing individual learning routes in order for children to preserve their abilities; the need for better and more reliable tests of intelligence and learning potential; insight into the supposedly new skills of the e-generation.
- *Compensation for abilities*. Discovering how to compensate for less developed abilities through different training methods; prioritizing what to learn when and, in the case of weak ability, focusing on the stronger ones.
- *Learning strategies*. Developing tools to improve information processing in different contexts (what to learn how); applying imaging techniques such as fMRI to optimise different learning methods; identifying the optimal periods and intensities for offering specific learning methods; understanding differences in strategies at individual and group (gender) level.
- *Motivational aspects*. Understanding the motivational processes behind learning in relation to age and intervention methods; understanding the relationship between motivation and involvement, boredom or self-esteem/uncertainty; knowing what to expect from self-guided learning and dependence on the teacher, insight in the motivational factors behind gaming.
- *Learning environment*. Developing a personalised learning environment based on individual developmental profiles; understanding the influence of emotions, sleep, etcetera on the learning process; developing computer models that deliver personalised learning material.
- *Meta-cognitive skills*. Introducing cognition as a subject in school (e.g. teaching children how to learn based on research on memory); developing meta-cognitive learning methods.
- *New skills of the ICT generation*. Understanding the motivational aspects behind gaming (the challenge or the experience) and whether these incentives can be used in the educational system; understanding the influence of the use of information and communication technology (gaming, surfing, etc.) on children's brain development.

One key factor in all these issues is that the neurosciences and cognitive science expect to provide added value when it comes to individual differences in learning abilities, learning strategies and motivational aspects. Both the practitioners and the scientists[8] identified 'personalised learning' as an important guiding principle for the future and as a crucial direction for research in the educational neurosciences (see section 4.2).

The following statement by one of the experts illustrates the idea of personalised learning nicely: *"What I see for the future is early identification not so much of learning disorders but of an ideal period in which to offer specific learning material and methods at a particular intensity. We should make optimal use of the period in which children learn best, comparatively speaking. I'm referring here to custom-made differentiated learning, based on individual development profiles and an individual learning environment that provides for and supports all this."* (Swaab, Leiden University). The concept of personalised learning should not be misunderstood, however. 'Personalised' does not mean individualistic. On the contrary, it means customised learning, geared to the needs and interests of the individual and taking place in what is primarily a social environment.

As the STT expert group agreed on personalised learning as a future direction for research in the collaborating fields of the neurosciences, cognitive sciences and educational science and practice, this chapter focuses on the different dimensions of personalised learning. Section 4.2 begins by explaining the need for personalised learning from different perspectives: science and practice. It also lists some key elements of personalised learning, as proposed by the expert group. Section 4.3 introduces cognitive learning systems as a first step towards personalised learning. Considerable cognitive research has already been carried out on such systems, but they have not yet been introduced in educational settings. A cognitive system is an adaptive system that monitors various parameters of a student's learning process, resulting in an individual cognitive profile. The system then presents the learning material in a way that matches the profile. Existing knowledge about the memory derived from cognitive psychology (e.g. concerning meta-cognitive skills such as mnemonics or spacing[9]) can be introduced in the system to help the individual pupil optimise his or her learning process. Such a system will be significantly improved — for example by introducing neurocognitive parameters — when we know more on the neural substrates of learning, and so the chapter also addresses current insights and, in particular, future research questions pertinent for the development of personalised learning in basic neuroscience (section 4.4), cognitive neuroscience and neuropsychology (section 4.5 and 4.6). Section 4.5 and 4.6 focus on the various contributions that neuropsychology can make to personalised learning: brain development, neurocognitive functions and motivational aspects of learning. Both sections end with a practitioner's

**8** The expert group consisted of fifteen members: scientists in the field of neuropsychology, cognitive neuroscience, basic neuroscience, educational psychology, pedagogy, practitioners from primary and secondary education and the members of educational advisory boards and organisations.

**9** The effect of offering instructional material in time stages.

view and related questions for science on the subject.

Finally, the chapter ends with some reflections on the conditions for successfully introducing personalised learning in current educational practice, a review of social and ethical aspects of personalised learning, and a short discussion of the most important and thus far unanswered research questions for the future of personalised learning (see section 4.7).

### 4.1.2 Basic assumptions

During the course of its six meetings, the expert group discussed various ideas, issues and questions. Although opinions were unanimous on some issues, it was not feasible to write a chapter completely based on group consensus. Every member has therefore written a contribution based on his or her own expertise and own viewpoints about personalised learning, although these are coloured by the group discussions. These disciplinary differences have given the various chapter sections differing levels of analysis. While the basic neuroscientist looks at the cellular principles behind learning at the micro level, the practitioner talks about differences in educational ideologies on a macro level. Besides differing levels of analysis, the differences in the group's backgrounds also means differences in the authors' writing style. We hope readers are able to bridge the stylistic differences without too much trouble.

It is furthermore important to note that the chapter is a 'work in progress'. It focuses on neural and cognitive mechanisms behind learning, a subject about which we still have much to learn, especially when it comes to applying existing findings in educational practice. The precise implications of neuroscientific research for teaching is in many respects not yet clear.

On the other hand, by focusing on these neural mechanisms, this chapter offers a significantly new perspective on learning compared with traditional theories of the psychology of learning and instruction. Personalised learning is in that way a logical consequence of the neuroscientific concept that everyone 'constructs' his or her own brain because of the huge differences in environmental niches. Readers should note that for the expert group, personalised learning represents a beginning, a research direction for a future in which the neurosciences and cognitive sciences will work together with educational science and practice. It is certainly not yet an answer.

Before the chapter commences, readers should be aware of the authors' underlying assumptions:

– People learn everywhere and at all times, not only during the time they spend in an educational or professional context. The human brain adapts itself continuously to what is happening in its environment, i.e. our experiences. However, this chapter concentrates on the learning brains of children aged zero to eighteen and focuses in particular on the brain in the educational context.
– The expert group concentrated on the normal learning brain and not on learning disabilities or problems. It is important to note, however, that there is quite a lot of neuroscientific research being done on, for example, dyslexia or dyscalculia, and that these studies also produce insightful information on the workings of a healthy brain.
– The expert group decided to focus on the learner (or student) up to eighteen, and not so much on the teacher, although there is a lot to say about teaching, including from a neuroscientific and cognitive science perspective. Subsection 4.6.1 alone looks briefly at the essential role of the teacher as an 'external motivator'.
– The different members of the transdisciplinary STT expert group differed in their terminology. To help readers understand the concept of personalised learning properly, Box 2 briefly describes some of the expert groups' basic assumptions about the notion of learning.

**Box 2: Basic assumptions about learning**

Firstly, learning results from an activity undertaken by the individual. The traditional idea of educational practice as the 'transfer of knowledge', with adults (and especially the teacher) taking the lead, is a highly inappropriate description of what actually goes on while a child is learning in everyday life or at school. Learning, both inside or outside school, is a process in which the child actively participates and interacts with the demands and challenges of the environment. It implies construction, seeking and finding/not finding, exploring, testing ideas and solutions, seeing what happens, having ideas about success and failure, and trying again.
Secondly, learning results in mastery of a wide variety of cognitive, social and motor skills. This is another reason why the term 'knowledge' is inadequate to describe the results of the learning process. Learning changes and extends an individual's behavioural repertoire in the broadest sense of the word. One topic of recent research into how the brain learns is how learning affects and changes the brain. It is important to note that the idea of learning as a process of active interaction with the environment, resulting in skills of various kinds, does not imply that we should not care about the content of learning. On the contrary, our culture and its future depend on what we (and especially our children) learn. Education and the school system are of the utmost importance in this process. We should consider carefully what children learn, both at school and in the wider environment.

Thirdly, learning implies interaction with the environment. The quality of the context determines the content and the structure of the learning process to a great extent. The presence of a rich, challenging environment that holds a child's attention, gives it the opportunity to ask questions, to investigate and to experiment, cannot be overestimated. The art of teaching involves creating such an environment.
Another important aspect of the context is its social character. To a large extent, environment means: the presence of other people. Learning is greatly enhanced when those people (both other children and adults) are responsive: they stimulate, approve or disapprove, correct, help, punish, praise and blame.

*Jan Rispens*[10]

## 4.2 Personalised learning

*Ira van Keulen, Jan Rispens*[11]

Personalised learning is not a new idea. To illustrate: the term produces some 175,000 Google hits. Some of these refer to a distinct public educational model in California that has been recognised as such by the California State Senate (Resolution 36); here, personalised learning means small-scale learning environments that make it possible to tailor learning to the individual needs of each student.[12] Many other hits concern a project carried out by the OECD's Center for Educational Research and Innovation (CERI) as part of the 'Schooling for Tomorrow' programme. This project explored the idea of personalised learning in-depth and resulted in the publication 'Personalising Education' [OECD, 2006]. As in California and like the OECD, the STT expert group on Learning assumes that personalised learning encompasses a broad view of learning based on the *"awareness that 'one-size-fits-all' approaches to school knowledge and organisation are ill-adapted both to individuals' needs and to the knowledge society at large."* [OECD, 2006]. While the OECD publication pays ample attention to the political and organisational aspects of personalizing education[13], this chapter focuses predominantly on the potential neuroscientific and cognitive basis of personalised learning. The present section looks at the reasons to support personalised learning from both the neuroscientific and cognitive perspectives and from the perspective of current educational practice. Subsection 4.2.1 also addresses the key elements of personalised learning as proposed by the STT expert group. The section ends with a short history of failed attempts to adapt educational instruction to individual differences between students. The lessons learned from these various unsuccessful educational methods help us understand the idea of personalised learning better.

10 Emeritus Professor of Pedagogy, Utrecht University.

11 Emeritus Professor of Pedagogy, Utrecht University.

12 *"The key elements include parent involvement, responsibility, and participation in their children's education; small class sizes; learning programme collaboration between teacher, parent, student, and school; ongoing credentialed teacher training; learning style assessment; flexible learning in multiple environments both within and beyond the classroom; home learning environment support; flexible curricular choices; multiple assessment tools and measurements; technology learning access; and varied pace learning."* See www.theaplus.org of personalizedlearningfoundation.org.

13 The publication also has one section 'Brain Research and Learning over the Life-cycle.'

### 4.2.1 Relevance of personalised learning from the neuroscientific and cognitive perspective

Current educational systems do not make use of many cognitive psychological findings concerning attention and memory. Cognitive sciences can already offer such instruments as adaptive cognitive systems to personalise education (see section 4.3). Basic neuroscience and cognitive neuroscience have less to offer at the moment, but there are many promising areas of research that will benefit the development of personalised learning. They include research on optimising the way in which a human brain learns, including the types of information a brain requires to learn effectively, and research the ideal periods to learn and on what changes occur in the brain to facilitate and promote learning. Personalised learning is an appropriate direction for future educational neuroscientific research and development, as neuroscientists estimate that the answers to the above questions will differ considerably from one person to the next.

Indeed, so far brain research has shown us that there are very large individual differences between developing brains (see, for example, section 4.4). Although the sequence in which certain parts of the brain develop is the same across the board, the length of time that the various parts of children's brains take to develop differs enormously. Some children are frontrunners in such abilities as talking, calculating, motor skills or social skills, but at the end of the developmental period, most of the variation between children has disappeared [Jolles, 2006]. The neurosciences are slowly revealing these hitherto hidden characteristics in individual brains [OECD, 2007].

Besides these natural differences in brain development – especially in early childhood – neurocognitive research has also taught us that emotions are closely connected to cognition. Emotions affect the brain, and are for that reason associated with learning and the outcome of the learning process. This means, for example, that people learn best when they are intrigued and challenged (see section 4.6). Adapting learning material to the individual needs of the students motivates them, reinforces the learning process and lowers their frustration levels. Personalised learning, with its focus on the close relationship between the learning process and the individual's specific needs and interests, contributes to positive feelings about learning. Personalised learning may also prevent students from acquiring incorrect learning strategies, which generally leads to complicated compensation strategies that are very difficult to unlearn.

Before we go deeper into the neuroscientific and cognitive scientific results and research questions relevant for personalised learning, we should explain the key aim of personalised learning, as used in this chapter. According to the

**Example IX**

**Just by practising a five-finger piano exercise mentally for five days, research participants were able to improve their performance markedly. The areas of the brain involved in finger movement enlarged over the period of practice, as it did in participants who practised physically.**

The brain is not a static organ: it is moulded by experiences, environmental influences and physiological changes in the body. It adapts continuously throughout the life span, and its plasticity is the mechanism underlying learning and development. Brain researchers assume that there are two stages in plasticity. First, the brain changes upon acquiring new skills by rapidly reinforcing existing neural pathways. Secondly, new pathways are formed.

# Growing neurons by playing the piano

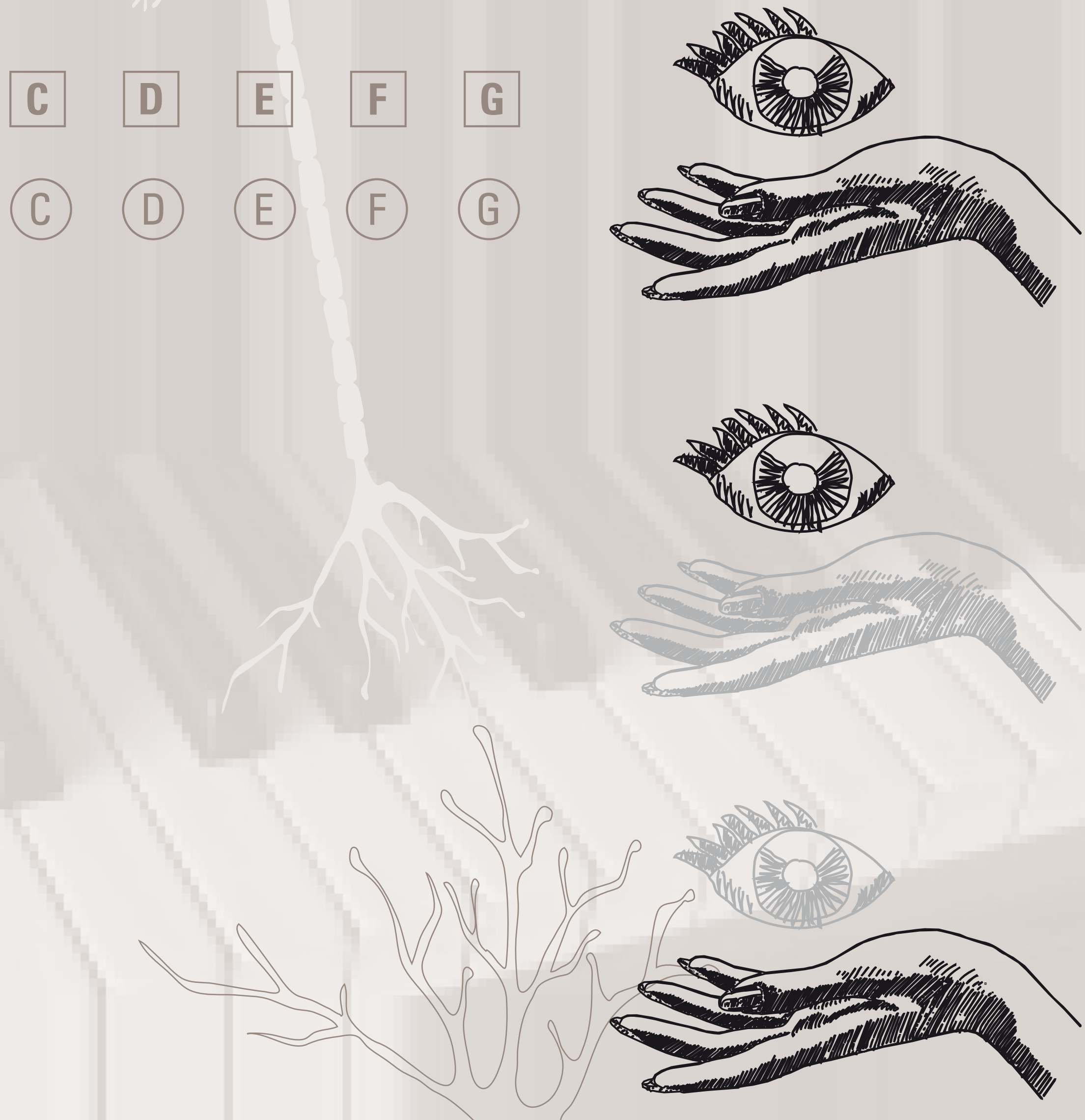
American neuroscientists discovered that individuals can influence the first step not only by practising physically, by also through mental practising. They assigned fifteen people without piano-playing skills to one of three groups: a physical practice group, a mental practice group, and a control group. The people in the first group had to practise a simple one-handed, five-finger exercise on a keyboard: playing the notes C-D-E-F-G-F-E-D at sixty beats per minute. They practised for two hours every day for five days. The second group had to devote the same amount of time to *imagining* that they were performing the exercise while sitting in front of the piano, without moving their fingers at all. The control group played the piano however they liked with one hand for two hours daily.

After five days, both practice groups made fewer sequence errors in the exercise when compared to the first day and the control group. The interval between key presses was also much less variable. However, the number of sequence errors was higher in the mental practice group than in the physical practice group. The performance of the mental practice group on day five equalled that of the physical practice group on day three.

Nevertheless, the representation of finger muscles in the cerebral cortex (as measured by transcranial magnetic stimulation (TMS)), had increased in size by the same amount in both practice groups. This suggests that mental practice leads to the same plastic changes as those occurring with repeated physical practice. The mental exercise made the brain more susceptible to physical training effects. After a single two-hour physical training session on day five, the performance of the mental practice group improved to the same level of that of the group that had been practising physically for five days.

Original publication: Pascual-Leone et al. (1995). *J Neurophysiol.* 74, 1037

Professional athletes and several famous musicians have been using mental practice to improve their skills for decades. Mental simulation of movements seems to promote changes in neural circuits that are involved in motor skills learning. Such simulation results in a marked improvement in performance and places the brains of people who use it at an advantage for learning further skills. Mental practice may also be useful for maintaining motor skills in temporarily immobilised patients, and in rehabilitation programmes.



expert group, that is the early identification and optimal development of the natural abilities of individual children. ‘Personalising Education’ [OECD, 2006] defines personalized learning as follows: *“An approach in educational policy and practice whereby every student matters, and a route to equalising opportunities through fostering learning skills and motivation.”*

According to the STT expert group, the key elements of personalised learning are:

– Adapting and attuning education to *sensitive periods in the development of children’s brains* (see subsection 4.4.3 and 4.5). A sensitive period is a restricted period of time in which specific brain areas or brain functions develop, i.e. a ‘period of plasticity’. There is still considerable debate as to whether such periods actually exist, however. The generally accepted opinion is that the developing individual cannot learn everything in every developmental phase. We cannot learn a particular skill if we have not mastered the basic skill. However, opinions are divided – including within the expert group – as to how critical these sensitive periods are and to what extent they are related to specific learning abilities or activities.
  – *“Insights into the maturation of brain structures indicate that there are specific sensitive periods in brain development. Knowing this, we also know that we can optimise individual development.”* (Jolles, University of Maastricht)
  – *“This knowledge will help us develop optimal individual development routes by identifying the abilities of the individual child and compensating for weaknesses.”* (De Lange, University of Utrecht)
– Regularly *monitoring and assessing individual abilities* in order to give children the ideal degree of stimulation (see section 4.5). Children can then undergo specific learning programmes tailored to their talents and shortcomings.
  – *“We would like to discover the parameters of each individual child in order to work more adaptively.”* (Swaab, Leiden University)
– Because an important aspect of the expert group’s notion of personalised learning is the introduction of adaptive cognitive learning systems (see section 4.3), another key element for children to learn at the level most suited to them.
  – *“The cognitive learning system consists of a database with items — i.e. a lexicon with words — and registers what the child is doing and at which level. The programme can estimate if the current level is too easy or too hard. Depending on the motivation and learning strategy of the child, the system knows when to aim higher or lower.”* (Murre, University of Amsterdam)

– *Preserving and making better use of the abilities* of children (see section 4.6). Especially important is the natural curiosity of children between three and five years, something that seems to disappear when they enter the educational system [Van Benthem, et al., 2006].
  – *"We should not only focus on the abilities of children per se, but also on how to preserve and boost their exceptional talents, for example curiosity, which is the key to learning. As Einstein said: I am not a genius, I am only annoyingly curious."* (De Lange, University of Utrecht)

At the moment, public opinion in the Netherlands is leaning towards the more traditional teaching method, based on the idea of knowledge transfer and setting minimum standards for all students in primary education.[14] Personalised learning may offer an alternative to this penchant for nostalgia.

### 4.2.2 Relevance of personalised learning from the perspective of educational practice

*Henk Derks*[15]

*"I visited a school last week and I walked into a classroom and saw thirty children learning to tell time. The mood in the class was good, the teacher was friendly and focused on the children, and all the pupils had a wooden clock in front of them on their desks. The teacher was explaining hours and half hours to them. I took a seat with a small group of pupils in the back. I whispered: Can you already tell time? Yes, they replied. As I looked around, it became clear that there were quite a few children who already knew how to tell time... The teacher started to ask questions. One child was called to the front and was asked to move the hand on the big clock, which stood at 1 o'clock, forward 30 minutes. The pupil moved the hand forward an hour. The teacher said: Just a minute. Look at this, class... What time is it now? The child replied: twelve thirty. Do it again, said the teacher. Who knows what time it is?"*

This example indicates how inefficiently our educational system deals with children's ages and how clever the teacher was to hold the children's attention after all. It is very difficult to tailor teaching to the individual pupil in the traditional classroom instruction system. As a teacher, you want to give every child the instruction it needs, and efficiency issues generally do not come into play. We see this method every day in many different schools and many different subjects. Children do learn, but the investment is out of proportion to the intended effect. It takes an enormous amount of time and energy to involve children in the lesson, manage classroom behaviour, and interest children in something that poses little challenge to most of them.

14 See www.beteronderwijs.nl.

15 General Director of the educational organization Skozok.

**Figure 2**
*It is very difficult to tailor teaching to the individual pupil in the traditional classroom instruction system. By Millan, www.dreamstime.com.*

Despite all the attempts at educational innovation, classroom instruction — with the teacher applying methods thought up by others — is still the most common instruction method and has not undergone any fundamental changes. The past 25 years of educational innovation have produced very few tangible results. Development and implementation, science and practice, education and school — these are all still miles apart from each other. For example, images, technology and self-management drive the development of today's children, things which scarcely play any role at all in today's schools.

With respect to the latter, Arnold Cornelis says the following in his book 'De logica van het gevoel' [Cornelis, 2000]: *"The question is what requirements a culture must logically meet in order to get people to manage their own learning processes so that human capacity can evolve. That question is the new knowledge impetus that is controlling the drive to learn today and likely for the next century."* According to Cornelis, the modern era requires us to update the 'drive to learn'. What factors or cultural aspects are behind this drive? People — both pupils and teachers — have a natural tendency to focus on development, growth and improvement. The current system of education is so rigid, however, that individual ability goes unrecognised and untapped and so wilts away.

Personalised learning — in which a pupil's individual cognitive skills are monitored regularly and the instructional material is adapted to his or her personal cognitive development — may be the concept that forces the education system to tailor itself to children's abilities. Personalised learning represents the ideal balance between educational demand (i.e. the child's abilities and potential) and educational supply, the important thing being to offer children continuous challenges.

The concept is based on an adaptive learning system, as referred to briefly in the previous section. It is an ICT system that monitors a pupil's individual learning process and offers him or her appropriate instructional material (in relation to basic skills and knowledge). Such a system focuses on the individual and his or her development potential. Children no longer rely as heavily on adults for their cognitive performance. Those elements of cognitive, social, emotional, motor and creative development that cannot be encompassed by the cognitive learning system are provided by teachers or experts, who are also in a position to guide, support and coach the children properly through the systems. Personalised learning can make it possible to create space for other aspects of a child's development in addition to its cognitive performance. One crucial added advantage of personalised learning is that the performance in traditional school subjects is better because there is a closer match between pupil and teaching. The time that is freed can be used to help children grow and develop in other ways. The current system of education, which has held on tenaciously to traditional classroom instruction, lacks the knowledge and tools (for example the right hardware and software and the physical space) for such efficiency improvements.

Finally, if we define personalised learning as a form of learning based on the master craftsman-apprentice model, but largely supported by ICT and with the knowledge and traits of the master being matched to the skills and abilities of the apprentice, then personalised learning could enable us to improve our current educational system fundamentally.

It will not be easy to design a system of personalised learning that functions well in educational practice. That is made clear in the following section, which describes earlier attempts to adapt teaching to individual differences.

**Box 3: The benefits of personalised learning from the perspective of educational practice**

- Personalised learning is all about the drive to learn and how to maintain it in pupils. The drive to learn stands for curiosity: a child's desire to explore the world around him. The drive to learn is the intrinsic motivation to learn.
- Personalised learning is tailored to the pupil's abilities and his individual drive to learn. For example, in gaming children will make endless attempts to improve their score. That drive to learn is not recognized or made use of by schools.
- Differentiation is optimised by applying the notion of personalised learning with respect to pacing, learning strategy, didactics and content. By tailoring teaching to the individual pupil, children will not feel as frustrated and have a much more positive basic attitude to learning.
- ICT can be used in personalised learning, for example adaptive cognitive systems (depending on the learning objectives). Doing so embeds cognitive development (i.e. tailored to the pupil) firmly into a continuous process (i.e. one that does not depend on a person, place or time).
- The teacher is only marginally involved in the cognitive aspect of learning; that role is assumed largely by the cognitive learning system. That way, the teacher can spend more time on pedagogical aspects or on the child's creative, social and motor skills. The system also relies less heavily on the teacher's individual skills for teaching cognitive knowledge.
- Personalised learning systems pay close attention to the educational process (for example meta-cognitive skills), because today more than ever, children are being required to continue developing. Children learn how to discover their own talent and, in particular, how they do learn and how they could learn.
- The learning efficiency improves because the cognitive learning system can offer continuous quality and is tailored as closely as possible to the learner's learning characteristics. It is also possible to achieve greater output efficiency, with a wider range of subjects being offered using the same resources and in the same amount of time.
- Individual pupils will be shown to have more and different abilities, placing them in a different light during assessment. Personalised learning not only pays closer attention to cognitive performance, but it also has more scope and appreciation for creative abilities.

*Henk Derks*[16]

16 General Director of the educational organization Skozok.

### 4.2.3 Personalised learning from a historical perspective

*Jan Rispens*[17]

Personalised learning may indeed help solve the most intriguing problem in education, namely how to adapt instruction to individual differences. This problem stems largely from the fact that the classroom is the cornerstone of a school: a group of pupils and their teacher constitute the small universe where learning takes place. Classroom instruction is necessary not only for economic reasons — only very few parents can afford a tutor for their children — but primarily because the social and cooperative aspects of learning are essential in a modern society.

However, children differ considerably on aspects relevant for teaching, such as aptitude, speed of learning, willingness to learn, interests. A teacher therefore faces the task of adapting the instruction to these differences if he or she wants the children's full cooperation. Ability grouping has been the traditional solution to this problem. After some kind of selection, pupils of more or less the same ability are taught together, the similarity in ability reducing differences between them. In the Netherlands, ability grouping is standard only in secondary education. Also known as streaming or tracking, it has never been popular in primary education. There, the mixed ability group is standard, with only one way of reducing differences that become too large for the teacher to handle: pupils who lag too far behind are forced to repeat a year.

Mixed ability grouping causes practical problems when it is combined with the notion of the same content for all in nearly the same amount of time. Many children are having trouble keeping up with standard instruction, while the

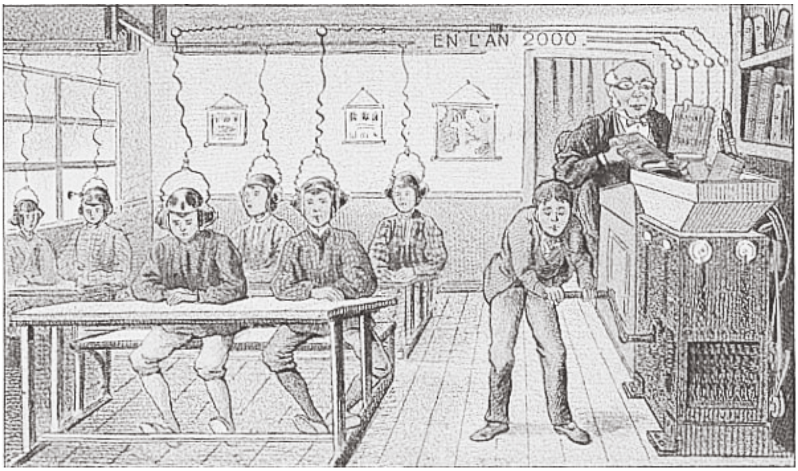



**Figure 3**
*"At school in 2000" as envisaged by Villemard in 1910, from the collection of the National Library of France (BvF)*

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most gifted do not get enough to satisfy their intellectual appetite. Various organisational adaptations, such as the Dalton system or the Jena plan system, mitigate the age group philosophy to a certain extent. These systems are used in a limited number of schools, but the problem of adapting instruction to individual differences remains unsolved. There is still no theory explaining how to gear instruction to individual needs that has been tested empirically, although the concepts of adaptive teaching, Aptitude Treatment Interaction (ATI) and cognitive styles have all tackled the problem of individual differences in the classroom. Unfortunately, none of these has been very successful so far. However, the results of ATI and cognitive style research may help us design various learning environments, while adaptive teaching may help overcome some of the organisational problems inherent to adapting instruction to individual differences.

### Adaptive teaching

The idea that teaching should accommodate individual needs and that schools should provide customised instruction has gained wide acceptance owing to cultural and social trends that stress individual autonomy. The concept of adaptive teaching, first introduced in the nineties, is one response to this challenge. The concept itself is not very clear, unfortunately, but in everyday practice it involves establishing a core curriculum for all the children (covering a minimum of what should be learned at school) and allowing the more competent children to pursue their interests and do extra work. Schools apply the concept of adaptive teaching by organising their pupils into flexible groups.

A recent evaluation of the results of adaptive teaching concludes that the current educational system does not support adaptive teaching sufficiently to make it effective. As a result, 75% of lessons do not involve adaptive teaching. Some progress has been made, but a great many problems remain [Reezigt et al., 2002]. In other words, organisational solutions that alter the content or the speed of learning do not provide a satisfactory solution to the problem of how to adapt instruction to individual differences.

### Aptitude treatment interaction

This conclusion is not new. In a famous article Cronbach [1957] stated that the traditional (and improper) response to differences in aptitude has been to repeat the standard instructional procedure, to proceed more slowly, or (if neither strategy is successful) to skip parts of the curriculum. Cronbach argued that the proper response consists of instruction based on a psychology theory of differential learning that fully recognises the nature of differences and, based on experimental evidence, adapts instruction to these differences. The concept of ATI reflects this notion. The implication is that one treatment may have different outcomes owing to differences in aptitude. It is therefore necessary to search for aptitudes and match them to the appropriate treatment, so that pupils can be given the instruction that suits them best.

Although the concept of ATI is very attractive, researchers have not been successful in their search for interactions between aptitudes and treatments [Jonassen and Grabowski, 1993]. Cronbach concluded that *"…the results on any one ATI hypothesis are still inconclusive."* [Cronbach, 2002]. One of the problems is that it is difficult to demonstrate the validity of potential differences between aptitudes, given the lack of interaction with treatments. Brain research could contribute to the process of validation: if an assumed difference in the relationship between an aptitude and a treatment is not reflected in differences in brain activity, the validity of that relationship must be questioned. The disappointing results have discouraged nearly all researchers from exploring the concept of ATI further.

### Cognitive style

A related idea involves applying the concept of cognitive style for instruction. A cognitive style refers to an individual's system of cognitive control: the way he or she consistently organises and processes information. There is ample evidence that individuals differ with respect to how they process information. A well-know example is the field dependence/independence dimension, which measures the degree to which our perception of information depends on the setting of that information. Another well-known dichotomy is the verbaliser-imager cognitive style. Visualisers learn better with visual methods of instruction, whereas verbalisers prefer a verbal approach. Although researchers were able to demonstrate that verbalisers and visualisers in fact do differ [Mayer and Massa, 2003], they did not find a relationship with instruction, and especially with the need to differentiate instruction according to cognitive style [Massa and Mayer, 2006].

Concepts such as adaptive teaching, ATI, and cognitive style do not provide an immediate answer to the question of how to handle individual differences in instruction. The same will probably be true of personalised learning, which emphasises the necessity of giving students ample opportunity to encounter a rich variety of materials and procedures. It is a programme, a start — not yet the answer.

**EXAMPLE X**

**Odour cues can help to anchor memories in the brain during deep sleep. When participants in deep sleep were exposed to the same fragrance they had smelled while playing the game 'Memory', they were better able to reproduce the placement of the picture cards after awakening.**

# Smelling roses while snoozing enhances learning

A good night's sleep can consolidate a new memory in the brain. But how exactly does sleep contribute to learning? One of the prevailing theories is that fresh memories need to be reactivated during deep sleep.

German neuroscientists manipulated the reactivation of memory during deep sleep with a contextual cue. In their laboratory, eighteen volunteers played the game 'Memory' on a computer screen. They had to remember the location of fifteen pairs of pictures. While they were learning, the researchers repeatedly exposed them to the scent of roses.

After learning, the participants went to sleep with electrodes taped to their scalps to monitor sleep phases. Human sleep comprises two states: rapid eye-movement (REM) sleep with dreams, and non-REM sleep. The latter is further divided in four phases, which can be distinguished by their well-defined pattern of oscillating electrical activity spreading over the outer layer of the brain, the cortex. Deep sleep is characterised by slow oscillations. It is therefore called slow-wave sleep.

If the participants were exposed to the scent of roses during slow-wave sleep, they remembered 97 percent of the card pairs they had learned before they went to bed. Without the odour cue, participants remembered only 86 percent. The smell of roses presented during REM sleep or during wakefulness did not improve memory.

Functional magnetic resonance imaging (fMRI) revealed significant brain activity upon odour re-exposure during deep sleep in the main brain structure for this type of memory, the hippocampus. The same procedure did not have any effect on learning a procedural memory task, i.e. long term memory of skills and procedures, which is not dependent on the hippocampus.

Original publications: Rasch et al (2007). *Science*, 315, 1426; Marchall et al. (2006). *Nature*, 444, 610

In 2006, researchers from the same German laboratory showed that slow-wave sleep benefits the consolidation of hippocampus-dependent memories. By artificially inducing slow-wave sleep with a small electrical current ten minutes before this sleep phase actually set in, they improved the recollection of previously learned word pairs in their participants from two to nearly five words.

While applying an electrical current to the brain is something preferably done in a controlled laboratory setting, exposure to a lovely smell is not. It may help students to further improve the beneficial effect of a good night's sleep on consolidating what they have learned. However, different kinds of memories (for example memorising word pairs, how to play the piano, or recalling an emotional event) seem to consolidate during different stages of sleep, and often comprise a series of events. Sleep researchers will not be finishing their work overnight.

## 4.3 Cognitive learning systems: a first step towards personalised learning

*Jaap Murre*[18]

Education today makes virtually no use of the findings of educational and cognitive psychology. While it is true that our present state of knowledge does not permit us to generalise about the most effective learning methods for particular instructional materials and individual pupils, by offering a pupil material on a computer and registering his response digitally, we can in fact construct an accurate model. Once we have set the parameters, the model will — in time — tell us how a pupil will respond to specific instructional material. We can then answer the following questions for each individual pupil: How much will I learn this week? When will I have forgotten what I have learned? What score am I likely to get on the test next week Friday? How can I learn the material as quickly as possible? We can basically already answer all these questions, provided we develop the right systems for doing so.

Research conducted by Atkinson in the seventies [e.g. 1972] marks the first attempt to optimise learning by applying learning models and computers. Despite these early successes, which clearly demonstrated the advantages of cognitive models, they did not become popular. Perhaps there were not enough computers around in the seventies to continue developing and applying the new methods, or perhaps the influence of Artificial Intelligence (AI) shifted the emphasis away from educational and cognitive processes towards programmed instruction (i.e. rule-based systems). That is now changing, thanks to the growing interest in using cognitive/neurocognitive research findings in education.

How does a cognitive learning system work? The most important factor is that the system knows what the pupil knows. That means that the system must be used as much as possible in the learning process itself, or else it must be 'fed' the relevant information indirectly, for example by being told that the pupil has studied pages 132 to 147 of a particular book. Indirect reporting is naturally less reliable and complete than direct observation. If the system is part of the learning process itself, then it can basically register, second by second, what the pupil is doing, what responses he has given, where he has asked for help, and what he does with the system's feedback. This means the system can build up an accurate picture of the material the pupil has mastered and what he is having trouble learning.

By building up a database on a pupil's progress, the system can construct a

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cognitive profile of the pupil. The underlying parameters can be estimated; they may, for example, indicate how quickly a pupil learns different types of material and how soon he forgets what he has learned.

Learning proceeds in a number of different stages (for example from short-term to long-term memory and from long-term to very long-term memory). How rapidly it moves from one stage to the next may also constitute a parameter. In addition, there may also be parameters related to how a pupil responds to feedback. Will he learn faster if the material is challenging (fewer hints) but with a higher risk of error? Or is it better to give him lots of hints (easier material)? Parameters such as these probably depend in turn on more general parameters, for example self-confidence.

If we assume that the pupil does much of his work with a learning system of this kind, the following becomes possible:

– *We can track the pupil's progress.* Teachers can see precisely how many hours every pupil has spent studying, their results, where things are going wrong and where they are going right.
– *We can predict and manage the pupil's progress.* We can predict, to a fairly high degree of accuracy, the pupil's final attainment level by looking at his learning curves and planned learning sessions. If he is at risk of under-performing, we can intervene.
– *We can predict what the pupil will forget.* The system is good at estimating each pupil's cognitive parameters. How quickly does he forget the meanings of words? How soon does he forget the past tenses of verbs? How quickly does he forget the rules of multiplication and division? The standard for such an estimate can be set by the group average (same gender, age and intelligence), but refined for individual performance. This makes it possible to schedule review lessons around the time that the pupil starts to forget.
– *We can optimise the learning process.* We have known for quite some time that 'cramming' (also known as massed learning) may well lead to good short-term performance, but that pupils do not retain what they have learned. Regularly spaced, shorter study sessions lead to better long-term retention, even if the overall time investment is the same. Optimisation is important here: spacing the learning sessions too far apart may lead to poorer performance because the pupil forgets what he has learned. It now turns out that it is possible to calculate the ideal spacing using an underlying learning model such as that described above (in other words, with individual educational and cognitive parameters). The system can advise on the optimal learning moments, and once the times have been set, it can calculate the best material for the pupil to study at specific points in time.

The learning objective is naturally important in this regard. The clearer it is what material should be mastered when, the more specific the system's advice.

### 4.3.1 General rules for optimised learning

There are many different factors involved in learning that can be controlled with the help of cognitive models. We can naturally also attempt to define general rules for good or optimised learning. For example, we can look at how much help is generally required (a lot of hints or only a few). Amnesia patients are a pertinent example; it has been found that they can remember people's names or other such facts only if they are constantly given enough hints to keep them from making mistakes. It is not yet clear how this works in normal pupils. The difficulty of the material is a related issue. Should you make it so difficult that pupils answer an average of 80% of the questions incorrectly? Or should you make it so easy that pupils make very few mistakes? The retrieval practice effect [e.g. Roediger and Karpicke, 2006] suggests that pupils learn best when they can still recall the material correctly. The implication is that repeat material should be easy enough to produce a low error count, but also not too easy. The question remains: what is the optimal condition [e.g. Pashler et al., 2007]? General rules of thumb are probably only of limited value, however, because pupils tend to display enormous differences in learning and cognitive parameters (and other cognitive aspects). Hence the need for more personalised learning methods.

One important variable in this connection is the effect of spreading the material out over time, usually referred to as spacing in experimental psychology. It has been shown time and again in research that it is better to space the learning sessions rather than 'cram' everything together in a short period of time [Glenberg, 1976; Greene, 1989; Melton, 1970; Rumelhart, 1967]. The sessions should also not be spaced too far apart, so the question is: what is the optimal spacing? This is contingent on the material and the student. Related research involving television commercials reveals a similar contingency pattern: commercials for new brands should not be spaced too far apart, but commercials for strong brands benefit from more extreme spacing [Chessa and Murre, 2007].

### 4.3.2 Elaboration methods

In addition to these predictions and optimisations, psychology also offers a whole range of methods conducive to learning. For example, education makes too little use of elaboration methods, although their effectiveness has been proven again and again [e.g. Higbee, 2001]. Elaboration methods make the material easier to remember by giving it more meaning. Say that we are asked to memorise the name of an imaginary, inflammable chemical element, Prlwitzkovskium. An elaboration method would work like this. We would break up the word into random fragments: prl with kov ski um. We would then come up with an association for each fragment, for example a visual one: pearl, white, cow, ski, yummy. We would then construct a complete image (or sequence) from these fragments, combining the associations to picture something. It could be something absurd or bizarre: a cow wearing white pearls, skiing down a hill and shouting 'yummy'. Even better is when we can come up with an association for a trait of the element, for example inflammability: the cow's skis would leave a trail of flames. After doing this exercise, a pupil would be likely to have memorised the difficult word. Research has shown [Higbee, 2001] that such mnemonic aids are much more effective than simply repeating or learning things by heart. Elaboration can be computer-supported with 'wizards', which analyse an item and help the pupil formulate the elaborations.

### 4.3.3 Future features

It will not be long before we can develop systems such as those described above. Their applicability can be improved considerably over the long term if we can move the interaction away from the computer keyboard. For example: a pupil plays the piano and the system offers her musical compositions and analyses her progress (responses). Or a pupil practices his tennis serve and the computer analyses his progress. Or a language student has a conversation with the computer (with a good speech synthesis and recognition system), and the system optimises the interaction so that the student always achieves the optimal learning effect.

Other future options are online brain measurements, for example electroencephalography (EEG; see Appendix 1) or other tests (see Box 4), used to measure the effectiveness of certain manipulations or exercises directly instead of indirectly via verbal and other responses.

**Box 4: Neuro-imaging in educational settings**

There are quite a few possible uses for brain scanning techniques in educational settings. The ability to 'read' the brain as it functions is already opening up astonishing possibilities. For example, it is possible to use an fMRI scan to predict whether a person is looking at a house, a face, a bottle or a chair [Haxby et al., 2001; Cox and Savoy, 2003; see example XIII]. Brain reading of this kind will undoubtedly become much more refined in future. It is still highly speculative whether it will ever be possible to follow the interim phases of the thought process in detail, for example when someone is solving an arithmetic problem. What we can already do is see whether or not the person's working memory is activated (the working memory is located somewhere in the frontal lobes). If the working memory does not show up on the fMRI as having been activated and the pupil keeps making mistakes while doing mental arithmetic, then he is evidently having trouble remembering the interim results, a problem for which he ought to receive separate attention. Of course, this is all assuming that the pupil is lying in the narrow tube and strong magnetic field of a noisy fMRI scanner.

Another example of an interesting neuro-imaging application concerns the degree of consciousness at which processing takes place. Highly automated processes have a weaker effect on the frontal lobes than thought processes that require conscious attention. Learning generally follows a pattern from highly conscious monitoring and attention to virtually unconscious performance. Learning to drive a car is a good example; learning a new language could be as well. We first take a lot of trouble applying the rules of grammar; later, we do so almost without thinking about it. fMRI scans can be used to track these processes. People who learn complex movements (for example in sports and music) also show evidence of a shift from the external (conscious) loop to the internal (unconscious) loop. These loops are interconnected brain areas in the motor cortex.

EEG can be deployed in a comparable manner. It shows, for example, whether a person is reading a word of which the meaning doesn't fit into a sentence, for example 'He drank a pizza'. The word 'pizza' evokes what is known as the N400[19] phenomenon. The same measure could be used to see how long it takes in milliseconds for a foreign language student to display the N400 phenomenon. We can expect that at first, when his language skills are weak, the student will take longer to recognise a wrong word (e.g. 650 ms) but that this will happen more quickly as his competence increases (up to approximately 400 ms after seeing the word – hence the name). You could, for example, see how long it takes the N400 phenomenon to occur in someone studying French when he is presented with short sentences like 'il mange son vin'. If a test such as this is combined with a cognitive learning system, the system can continue to quiz the student until he reaches the right N400 level. Of course, it must first be established whether the N400 actually says anything useful about someone's mastery of a language, for example his ability to respond quickly enough in conversation. The N400 can then be used as an indirect measure of conversational skill, something that may well be quite difficult to test otherwise.

Finally, also eye movements can provide a lot of information about brain processing. The usual hypothesis is that people focus longer on a word or image that they find harder to process. This makes it possible to identify, fairly directly, the problem spots in the material. Is it the case endings? Certain combinations of vowels? Atypical eye movements during reading (called 'scan patterns') can also indicate a faulty reading strategy.

19 The N400 is an event-related potential (ERP) component typically elicited by unexpected linguistic stimuli. N400 is characterised as a negative deflection, peaking approximately 400 ms after the presentation of the stimulus. In models of speech comprehension, N400 is often associated with the semantic integration of words in sentence context. See www.wikipedia.org.

**We have mentioned quite a few options that can already be applied today, if we had the scanning equipment at our disposal. It is difficult to extrapolate to the decades ahead, but it will be clear that the techniques and applications will only become more refined. What techniques educational practice actually chooses will depend on their ease of use, their cost and their practical advantages for learning. We can already make use of eye movements[20], and if EEG is developed to the point that brain signals are easier to read, it could also be used in educational settings. fMRI will take much longer, unless there is an unexpected technical breakthrough.**

*Jaap Murre*[21]

Pupils learn for different reasons. Besides optimising the learning process, one of the big advantages of personalised learning is that the pupil is free to choose the instructional material himself to a great extent. The underlying model can, after all, assist him in his decision and support him, for example by offering him specific exercises ahead of time to help him understand the material, or by supporting him while he is doing the work and learning the material. In some cases, the system can determine the sequence in which exercises should be done in order to achieve a specific aim, for example teaching students from Indonesia who plan to study in the Netherlands to read technical texts in Dutch, or teaching a student to read Ibsen in Norwegian. In the first instance, it is important to learn a long list of technical terms; in the second, it is not. The system can have 'knowledge of a particular vocabulary' as its aim and select or generate exercises that build up that knowledge in stages.

Pupils can be expected to feel more motivated because they have much more choice, understand the learning process better, receive more relevant feedback and perform better (see Figure 4). All too often, pupils today are forced to learn a number of brief lessons, cannot tell when they have studied enough (usually they have not), receive too little feedback before a test and then get only a mediocre mark. That is demotivating. In personalised learning, the pupil selects the material (within certain limits), is guided through the learning process, continuously sees how much he is learning (and forgetting), and gets good marks on tests. Official tests are superfluous in this approach because the system has continuous access to all the relevant information about the pupil's progress. It can also predict when the pupil's knowledge will dip below a certain limit.[22] For example, it is important for pupils in mainstream education to know how soon they will forget what they have learned.

Personalised learning can produce a wealth of information for research and development. It becomes possible to offer new methods and study their impact in detail. Which children are capable of working with the new methods?

**20** The equipment for measuring eye movements is becoming increasingly smaller, more accurate and less invasive (and therefore more comfortable for everyday use).

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**22** This is also important in business, for example in critical safety procedures: do forklift truck drivers still know all the safety procedures? And what about the pilots working for Ryanair?

**Figure 4**
*Cognitive learning systems can help to answer the following questions for each individual pupil: How much will I learn this week? When will I have forgotten what I have learned? What score am I likely to get on the test next week Friday? How can I learn the material as quickly as possible? Photo courtesy of NMTeach3, www.flickr.com.*

How old do they need to be? What other criteria apply in order to elicit a positive response to this method? By using modules in this manner, we quickly gain an impression of their effectiveness and applicability, and can make a contribution to evidence-based education.

### 4.3.4 Future challenges

Ultimately, we can identify two key challenges. Firstly, we must determine the neuroscientific basis of the cognitive theories and models described above. Secondly, implementation research into cognitive learning systems is crucial, specifically with respect to two questions: can neurocognitive measures help us understand pupil responses better? And: how can we get computer systems to analyse the pupil's own compositions for comprehension?

Regarding the first question, many types of pupil responses are difficult for a computer system to follow. For example, when a pupil reads a text, it is not clear how much he understands. This problem will require more fundamental research. What is the relationship between learning words and rules and being able to comprehend specific texts? Enriched measures, for example incorporating eye movements, pupil size measurements or advanced forms of EEG may be of use. Although we cannot measure comprehension directly with these tools, we can see whether the brain response matches our expectations. By constructing clever exercises, we can estimate the level of comprehension.

The second question concerns material or responses in which meaning plays a major role. Can computers analyse a pupil's own compositions for comprehension? To a certain extent, they already can. Landauer and his colleagues have shown that their method, Latent Semantic Analysis [Landauer and Dumais, 1997], usually awards the same marks to compositions about a psychology text as a psychology teacher. We may expect to see further developments in this area.

Cognitive learning systems for personalised learning are already possible and will continue to develop in future. One enormous advantage is that they collect their own data and are therefore always evidence-based. Does it work or doesn't it? Inefficient components can be quickly removed.

## 4.4 Basicneuroscience on individual differences in brain and cognitive development

*Ger Ramakers*[23]

Basic neuroscience studies the molecular, cellular and developmental aspects of the brain and cognition. It has made tremendous progress owing to molecular biotechnology, which has led to the identification of a large number of genes involved in intellectual disability and candidate genes for many cognitive disorders. The functions of the proteins encoded by these genes provide important insights in the brain mechanisms that underlie cognitive development and many aspects of human personality and psychological functioning. In time, these insights — together with insights into other neurobiological mechanisms — will help us understand brain disorders and mechanisms that underlie normal psychological and cognitive functioning.

Basic neuroscience demonstrates that individual differences in learning ability, Intelligence Quotient (IQ) or specific cognitive abilities are the result of interactions between the genome and experience during development, both of which are unique to the individual. Whereas the genotype defines the upper and lower boundaries of academic achievement, the environment defines the actual level of achievement within these boundaries. As a consequence, it is likely that even with excessive training, not everyone can achieve anything. Studies of behavioural genetics studies have, for example, demonstrated that at least 80% of IQ variability from age eighteen onwards can be explained — at least in Western countries — by genetic factors [Posthuma et al., 2002]. At age four, however, IQ variability can be attributed mainly to environmental factors. The importance of the environment for IQ decreases gradually as a child grows to adulthood. Differences in cognitive abilities have also been found to correlate with different brain development rates. Shaw et al. [2006], for exam-

23 Researcher of Developmental Psychology, University of Amsterdam and researcher at the Netherlands Institute for Neuroscience (NIN).

ple, demonstrated that the thickness of cerebral cortex grey matter develops more slowly in children with a high IQ than in children with an average IQ.

This section begins by reviewing the basic neural mechanisms behind individual differences in brain circuitry development and, consequently, cognitive ability: genes, environment and their interaction. In subsection 4.4.3 the occurrence of sensitive periods in brain development is discussed. The section ends by looking at what basic neuroscience will, in future, contribute to education in general and personalised learning in particular.

### 4.4.1 Genetic mechanisms

Genes define the mechanisms for brain development; those mechanisms in turn specify the circuitry for information processing and learning. We see this relationship most clearly in genetic disorders of human cognition, where many causative genes are involved in brain development [Ramakers, 2002; Fisher, 2006; Galaburda et al., 2006]. Many of these genes affect the number of neurons in the cerebral cortex, neuronal layering, neurite outgrowth and the formation and dynamics of synaptic connectivity.

Other genes affect the structural and functional specialisation of different cortical areas and control the size of the cortical areas involved in processing sensory or motor information at the expense of areas involved in other functions. Manipulating the brain structure in mice by altering these genes results in deficiencies in learning and behaviour. The location of a specific gene's expres-

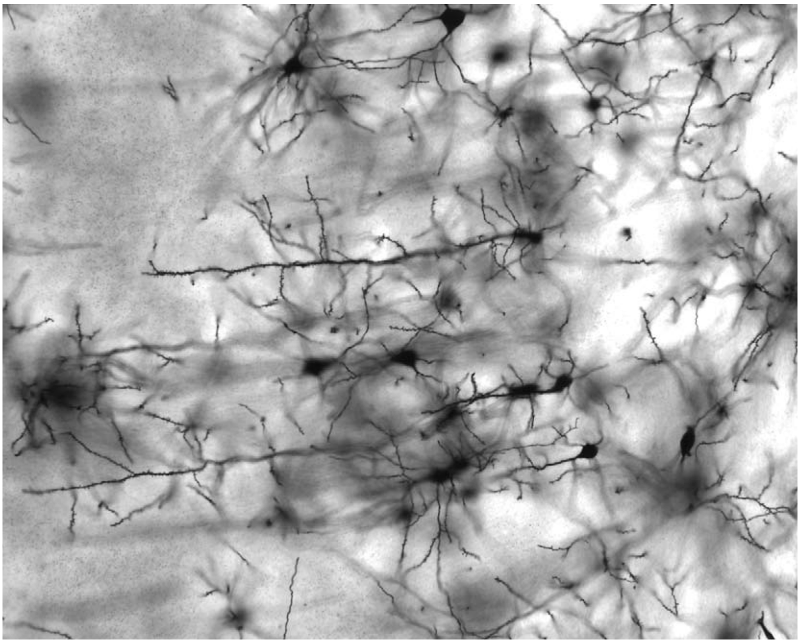
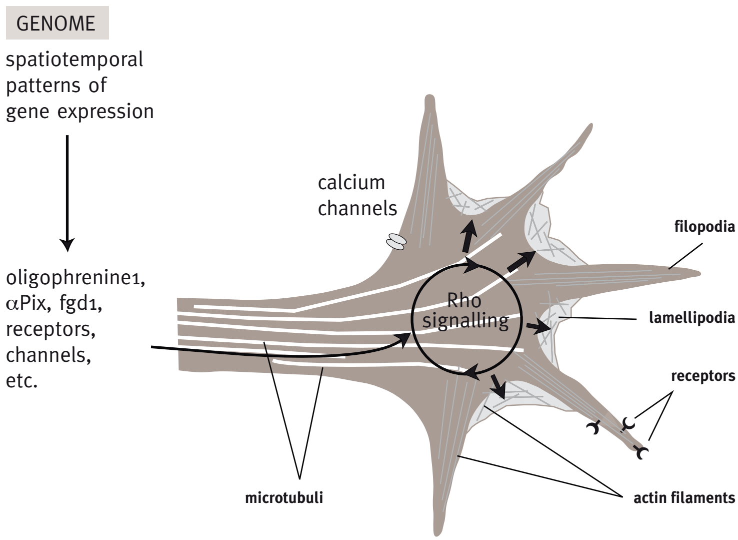
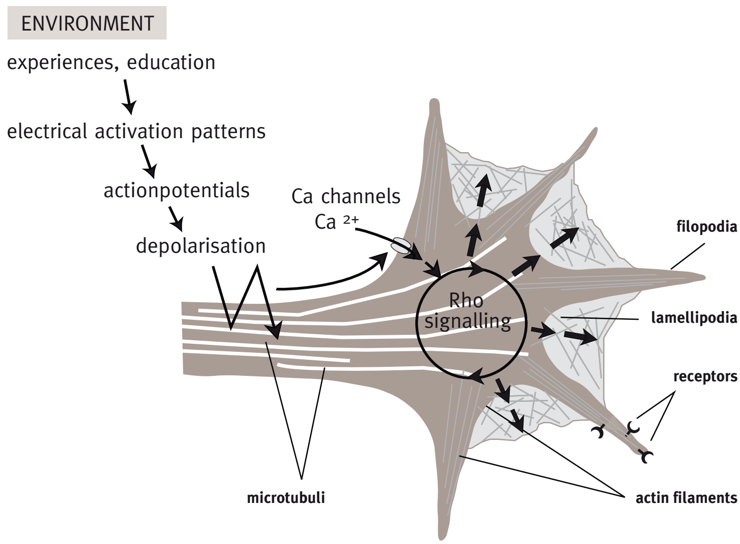


**Figure 5**
*A small piece of cerebral cortex of a mouse, showing only about one percent of all neurons. Most neurons here are pyramidal neurons, with round cell bodies (black 'blobs'), from which one long, relatively straight apical dendrite and several shorter basal dendrites extend. The dendrites show tiny knob-like protrusions, called dendritic spines, which are the receiving parts of excitatory synapses. Cognitive disorders like mental retardation are associated with alterations in the shape and number of spines and dendritic branches. Recent evidence indicates that dynamic changes in spines may be the cellular basis of learning and memory. Human pyramidal neurons are considerably larger than mouse neurons and contain an estimated 10,000 synapses each. Photo courtesy of Ger Ramakers.*

**Figure 6 and 7**
*The outgrowth of axons and dendrites is mediated by neuronal growth cones: an example of a cellular mechanism involved in the development of neuronal circuitry and connectivity.*[24] *While the intracellular mechanisms are specified mainly by gene expression (left), experience, translated into electric activity, can use the same mechanisms to modulate the activity of the growth cone. As more than half of the connectivity in human cerebral cortex is produced after birth, there is ample opportunity for (early) environmental factors to modulate or fine-tune brain circuitry. Scheme courtesy of Ger Ramakers.*

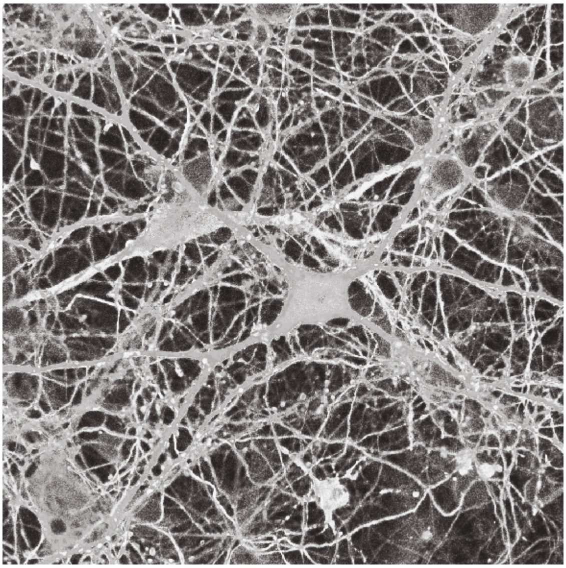



sion determines whether it affects overall brain development and cognition or whether it has a localised effect that may be restricted to specific cognitive abilities. For instance, increasing or lowering the expression of the EMX2 gene (empty spiracles homebox 2 gene) in mice — involved in specifying different cortical areas — affects the size of the somatosensory and motor cortex, with significant consequences for learning and motor performance [Leingärtner et al., 2007]. Similarly, the timing of the expression of specific genes may affect the degree to which a brain area is more or less susceptible to environmental modification. It is important to note that the expression of many genes is also controlled to some extent by neuronal electric activity generated by sensory organs as a result of environmental factors such as education.

24 The growth cone is a specialised structure at the tips of axons and dendrites that guides their extension so as to enable highly precise connectivity over enormous distances. It does so by sensing 'guidance cues', integrating these signals and deciding on which course to take in outgrowth.

**Figure 8**
*The complexity of a neuronal network exemplified here in a network of cortical neurons grown in tissue culture and stained for different neurotransmitters (in red and green). An excitatory (red) and inhibitory (green) neuron are shown with their thick dendrites embedded in a meshwork of thin axons. Synaptic elements (stained blue) mediate the communication between neurons. Photo courtesy of Ger Ramakers. See book cover for coloured print.*

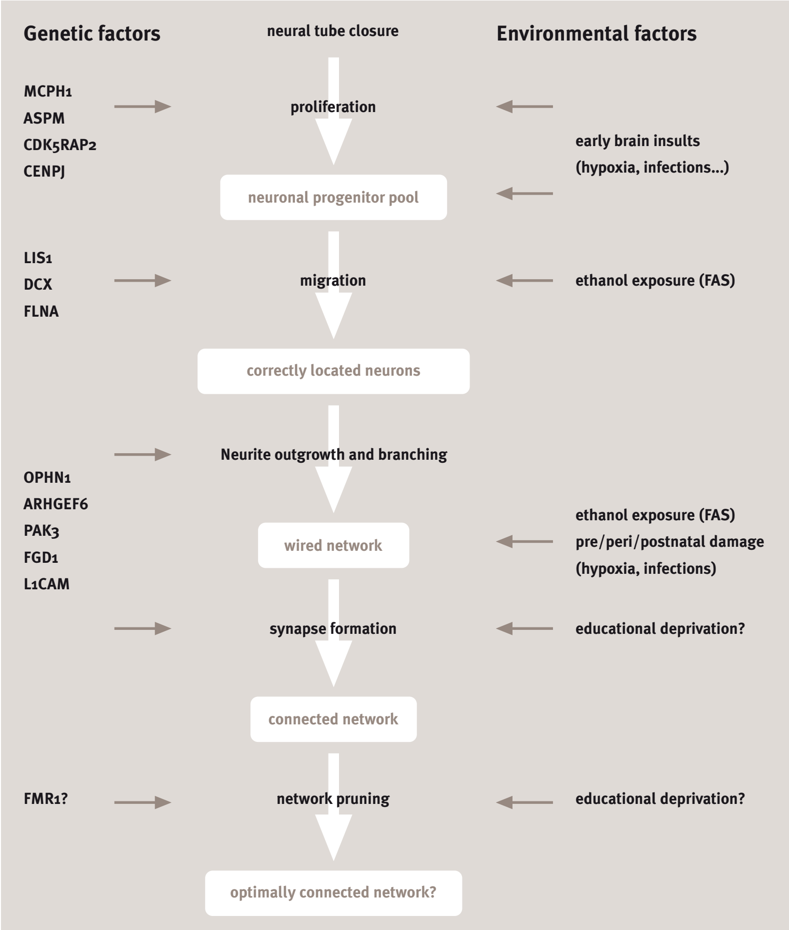


Many aspects of cognition and school performance are causally affected by specific genes. Researchers have identified many genes that cause intellectual disability upon mutation [Ropers and Hamel, 2005], as well as plausible candidate genes for dyslexia [Ramus, 2006] and other cognitive disorders. Milder alterations in these or other genes — known as polymorphisms — are likely to be involved in determining IQ variations in the general population. The functional relevance of polymorphisms in many human genes is currently under serious investigation. At the moment, DNA technology enables simultaneous detection of polymorphisms in many genes. It is entirely feasible that researchers will produce a DNA chip within the next decade that provides an individual profile of polymorphisms in the genes relevant for cognition. It is also likely that we will be using genetic technologies in the near future to assess and treat cognitive disorders, for instance to identify subtypes of these disorders that are susceptible to certain educational or pharmacological interventions but not to others [Chamberlain et al., 2006].

Epigenetic regulation should also be mentioned here.[25] Several of the epigenetic regulators are controlled by electric activation, and are clearly linked to cognition in humans, with mutations in these genes resulting in mental retardation (e.g. MECP2 gene (methyl CpCr binding protein 2) in Rett syndrome [Zhou et al., 2006]). Moreover, chemical compounds that modulate epigenetic DNA modifications can improve learning in normal rodents [Miller and Sweatt, 2007] or restore learning in mouse models of Rubinstein-Taybi syndrome [Hallam and Bourtchouladze, 2006]. Not much is known yet about the role of epigenetics in cognition, but it is possible that many aspects of life experience are stored not only in long-term changes in neuronal connectivity, but also in more or less

25 Epigenetic regulation entails the long-term modification of DNA and/or accessory proteins that could lead to life-long alteration of the expression of specific genes.

**Figure 9**
*A simplified scheme of the different phases of neuronal network development including some genetic and environmental factors that affect cognition in humans (i.e. cause mental retardation) by interfering with specific aspects of neuronal network formation. Scheme courtesy of Ger Ramakers.*

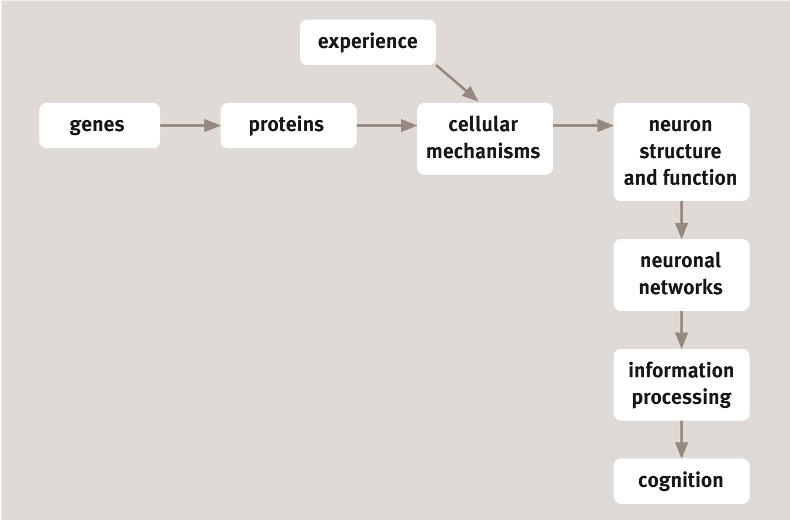



permanent changes in gene expression. One notable example appears to be the effects of early life stress on adult emotional coping and cognition.

### 4.4.2 Environmental influences

Environmental experience uses genetically defined mechanisms to alter the brain circuitry so as to optimise adaptation to environmental demands. More specifically, an environmental factor such as an educational experience is translated by the sensory organs into patterns of electrical activity and hormonal responses that ultimately interface with the cellular mechanisms encoded by the genetic make-up of the individual. Through these combined mechanisms, gene expression, neuronal differentiation and brain circuitry are modified to enable us to learn skills, store information and adapt to dynamic changes in our environment. We see this in studies of early sensory — auditory, visual, tactile — influences on brain connectivity and function. Later on in this section, we look at two other specific environmental influences that have been examined in rodent studies: enriched environments and maternal care.

**Figure 10**
*Convergence of genetic and environmental factors at the cellular level, shaping neuronal network development and thereby human cognition. Note that experience can also use certain cellular mechanisms to affect the short- or long-term expression of genes. Conversely, genetic mechanisms may lead to periods of stronger or lesser sensitivity to certain environmental factors, by tuning up or down relevant cellular mechanisms. Scheme courtesy of Ger Ramakers.*




## Early sensory stimulation

Studies have demonstrated that early sensory stimulation results in structural and functional fine-tuning of the underlying brain circuitry: whereas initially, neurons within certain brain areas show an overall responsiveness to a range of stimulus properties, sensory input will make specific neurons increasingly sensitive to a smaller range of such properties. Early general responsiveness is therefore replaced by increased sensitivity and specificity. For instance, neurons in the primary auditory cortex become increasingly attuned to tones with specific frequencies, essential for rapid and automated sequential sound processing as in speech comprehension [De Villers-Sidani et al., 2007]. Inappropriate auditory fine-tuning may lead to problems in phonological processing, an important cause of developmental dyslexia. Similarly, early visual input from both eyes is important for the specification of the primary visual cortex in kittens and rodents to input from the left and right eye [Hofer et al., 2006]. An absence of appropriate input from both eyes to the visual cortex during the first years of life can have life-long functional consequences. For instance, in children with strabismus[26], timely intervention is essential to prevent cortical blindness to the inputs from the 'deficient' eye. Interestingly, this specialisation of the circuitry to certain stimuli goes hand in hand with decreasing sensitivity to other stimuli. This phenomenon has been observed in the rat auditory cortex and the visual system of kittens. In human infants, the auditory system becomes increasingly sensitive to speech sounds of the language to which the infant is exposed, at the expense of sounds from other languages. The ability to relearn the perception of non-native speech sounds later in life is not lost, but will require considerably more effort than during infancy. It therefore appears that during some periods in life, certain mechanisms are in place that ensure more efficient adaptation of the brain to certain

**26** Strabismus is a condition in which the inputs from the left and right eye to the brain do not match, for example in a child with a 'lazy' eye.

environmental factors, while other mechanisms may exist that decrease the adaptiveness of the brain. Some of these factors have recently been identified in the plasticity of the visual system.

Early sensory input not only promotes fine-tuning of the circuitry to certain stimuli, but also enhances information processing. Postnatal sensory stimulation plays an essential part in optimising the circuitry for 'simple' sensory information processing [De Villers-Sidani et al., 2007]. This circuitry is subsequently used to process more and more complex information — for instance words to sentences — and it adapts while it is doing so. More complex information processing will be handicapped if the circuitry for simple processing is not well established. For example, deficient phonological processing results in dyslexia, which may subsequently limit knowledge acquisition.

### Enriched environments

Laboratory rats and mice are usually kept in an environment that provides very little sensory stimulation. When their environment is enriched to resemble the natural environment of rodents, there is a sharp increase in many of the properties of cerebral cortex connectivity: dendrites grow longer and more branched, and the dendritic spines become denser [Turner and Greenough, 1985]. In addition, the rats perform better on several learning tests. These consistent findings are thought to indicate that brain development and cognition can even be enhanced — rather than merely optimised — by early environmental stimulation. This idea may be true, but the animal studies primarily show the detrimental effects of environmental deprivation, with negative consequences for brain development and cognition.

Important aspects of such 'enrichment' are daily changes that promote exploration and active interaction with the environment.[27] Environmental enrichment can also partly counteract deficiencies in neuronal connectivity and learning ability caused by genetic mutations. For instance, in genetically modified mice that mimic fragile X mental retardation syndrome in humans, environmental enrichment can counteract deficiencies in learning, brain connectivity and synaptic plasticity [Restivo et al., 2005; Meredith et al., 2007].

### Maternal care

The ability to adapt to the challenges provided by our complex society depend not only on our learning ability, but are also influenced by modulatory factors such as motivation, interest, perseverance, frustration tolerance, and emotional and impulse control. These trait markers are controlled both by genetics and the environment. The quality of parenting and of the home environment are important modifiers of these temperamental factors. Recent studies on

**27** Exploratory behaviour is a temperamental trait factor in mice [Matzel et al., 2006], and partly under genetic control. It is likely that differences in exploratory drive contribute to individual differences in cognitive abilities.

early separation stress and maternal care in rats have demonstrated profound life-long effects on brain development and plasticity, the ability to cope with stress and learning abilities [Kaffman and Meaney, 2007]. For instance, rat pups raised for three weeks by a 'good' mother (i.e. a high incidence of licking and grooming) will have a better adaptive stress response and perform better on learning tests in adulthood than pups raised by a 'bad' mother. These long-term effects appear to be mediated by the epigenetic modification — in this case methylation — of the gene that encodes the glucocorticoid receptor.

### 4.4.3 Sensitiveperiods in brain development

One key concept emanating from the studies on early sensory experience is the notion of the sensitive period. The absence of appropriate stimulation during such 'time windows' results in life-long deficiencies in certain functions. Sensitive periods are not absolute, but appear to be 'windows of opportunity' during which certain forms of sensory input are most efficient at adapting the neuronal circuitry structurally and functionally. Some of the mechanisms underlying the closure of the sensitive period have been identified [Hensch, 2004].

Most of our knowledge of the stages of brain development comes from research on rats and mice. When it comes to the development of synaptic densities, there is only one study that quantified this process in human post-mortem cerebral cortex from prenatal ages to adulthood [Huttenlocher and Dabholkar, 1997]. The study is based on only fifteen human brains, however, and shows that synapse densities increase sharply from prenatal week 26 until a peak at about seven months for the visual cortex, three and a half years for the auditory cortex and somewhere around seven years for the pre-

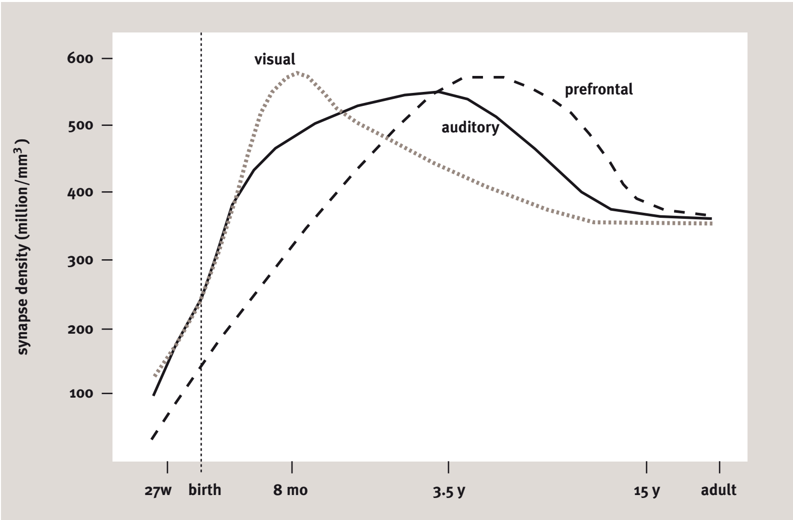



**Figure 11**
*Development of synaptic densities in three different areas of the human cerebral cortex, shows different phases, timing and significant loss of connections before adulthood. Adapted from [Huttenlocher and Dabholkar, 1997].*

frontal cortex (see Figure 11). This peak was followed in all these areas by a 30% loss of synapses, which stabilised towards adulthood. The varied timing of synaptogenesis (i.e. the formation of synapses) in these areas could be reflected in a similar development sequence for visual, auditory and speech, and executive abilities.

Developmental pruning of synaptic connections has also been observed in various brain areas in rodents, and is believed to reflect the optimisation of neuronal circuitry in response to experience. One of the underlying mechanisms may be that synapses compete for a limiting neurotrophic factor (brain-derived neurotrophic factor or BDNF), with active synapses having the edge over inactive synapses [Cabelli et al., 1995]. The expression and secretion of BDNF is activity-dependent. BDNF is an important regulator of structural plasticity, and may therefore be a key molecule in the optimisation of brain circuitry in response to experience. A polymorphism in the human BDNF gene affecting the activity-dependent release of BDNF has been associated with cognitive impairments and psychiatric disorders [Savitz et al., 2006].

### 4.4.4 Conclusion

It is clear from the above that basic neuroscience is making great strides in understanding the molecular and cellular mechanisms behind brain and cognitive development. Within the next twenty years, we may well identify the overall genetic and neurobiological underpinnings of human psychology and the ways in which experience uses these mechanisms to modulate psychological functioning. This knowledge will most probably lead to improved pharmacotherapy for cognitive and psychiatric disorders and improved educational methods and promote rational behavioural therapies.

Current research does not, however, offer any direct applications for educational practice, for the simple reason that most research thus far has been done on rodents. Our knowledge of how neuronal circuitry in the human brain develops is extremely limited. We know more about brain development in rats and mice than in humans. As a result, much of what we assume about human brain development is extrapolated from what we have observed in rodents. Although the underlying genetic and cellular mechanisms are strongly similar and conserved, differences in timing, magnitude and complexity will affect human brain development non-linearly in a way that cannot be easily extrapolated from rodent models.[28]

Animal research is also doing much to help us understand the biological mechanisms whereby individual differences in genome and experience interact to specify human cognitive and learning ability. To allow applying the

**28** The field of comparative psychology studies the extent to which findings about the brain and cognition in animal studies can be translated to humans [e.g. Locurton et al., 2006], although the focus tends to be on cognition and behaviour and not on brain development.

genetic and animal findings to humans and their individual differences in learning, we need more quantitative information on circuitry formation during human brain development. In addition, it is important to establish how human microscopic brain structure is linked to cognitive abilities [e.g. Shaw et al., 2006]. While structural and functional MRI have led to important new insights into the development of cortical grey and white matter in humans, these studies are limited to children ages eight and older.

More micro-level knowledge of individual differences in human brain development will undoubtedly be useful for personalised learning. Basic neuroscience can help answer questions about the flexibility of the brain, the sequences of development, and potentially adverse or positive conditions for growth. At the same time, neuroscientific findings can help validate theories of individual differences developed in the cognitive sciences.

While basic neuroscience may not impact educational practice any time soon, it is certainly set to influence the development of pharmacological agents that promote learning and memory consolidation (see Box 5). Pharmaceutical and biotech companies are already developing potential nootropic[29] drugs (i.e. cognitive enhancers or 'smart drugs') based on novel insights into the neurobiological basis of learning, memory and cognition [Marshall, 2004]. These drugs are primarily intended to battle cognitive problems in neurodegenerative disorders such as Alzheimer's disease or specific forms of mental retardation (e.g. fragile X syndrome), but future effective drugs may well come into more general use as a 'learning or exam pill', as was the case with Viagra or Ritalin.[30] As a consequence, a firm public debate on the ethical, social and health related issues concerning the use of nootropic drugs will definitely have to be held.

**Box 5: Developments in pharmacological agents promoting learning and memory consolidation**

One of the first mechanisms that was targeted for its possible memory-enhancing effect was neurotransmission mediated by acetylcholine, which has been shown to be involved in various memory processes. Agents in this group generally enhance the effects of acetylcholine at its nicotinergic receptor. Piracetam is one of these compounds and probably the first pharmacological nootropic drug. Some other nootropics currently in use are donepezil (an acetylcholine esterase inhibitor with limited efficacy in Alzheimer's disease) and methylphenidate (a concentration-enhancing drug that affects neurotransmitter re-uptake – in particular of dopamine – most commonly used to treat ADHD).

29 Coined word derived from the Greek words 'noos' (mind) and 'tropein' (bend/turn). See www.wikipedia.org.

30 In the United States, healthy children are taking stimulant medication such as Ritalin or Adderol before exams to improve their concentration [Farah, 2002].

Insights into the mechanisms underlying long-term potentiation (LTP), since 1973 believed to be a cellular correlate of learning and memory, have led to the development of Ampakines. These drugs enhance the function of the AMPA receptor (one of the receptors for the major excitatory neurotransmitter glutamate), which shows enhanced synaptic expression upon induction of LTP. The involvement of cyclic AMP signalling and the cyclic AMP-responsive element binding (CREB) protein in synaptic plasticity has led to the development of several potential nootropic drugs. Several of these and other potential nootropic drugs are now being tested in clinical trials. Although the efficacy of the current drugs appears to be limited, economic factors will surely drive further development.

More recent insights have highlighted the involvement of epigenetic regulation in memory processes. Mutations in genes involved in epigenetic regulation often result in intellectual disability.[31] Several compounds that can improve DNA accessibility have been found to promote synaptic plasticity and memory and to reverse memory deficits in genetic mouse models of Rubinstein-Taybi syndrome (RTS). Another avenue for the development of nootropic drugs is provided by the recent insights into the dynamics of synaptic connectivity in the adult mouse brain, as the possible basis of learning and memory. Several scientific reports have shown that pharmacological modulation of the intracellular Rho-GTPase signalling pathways, involved in regulating synapse morphology and dynamics, affect synaptic plasticity and learning performance. As this signalling pathway is also involved in some forms of intellectual disability and Alzheimer's disease, it provides another likely target for nootropic drug development.

As a follow-up to the molecular revolution (i.e. the sequencing of the human genome), molecular, clinical and behaviour genetics are converging in research to identify the positive or negative contribution of polymorphisms in single genes to the IQ variability in the general population. Over one hundred genes have been identified as causally involved in certain forms of intellectual disability, and many plausible candidate genes are known for dyslexia, autism, schizophrenia, etcetera. At least some of these genes will be targeted for nootropic drug development. In view of the magnitude of robotised high-throughput screening for drugs that can interact with targets of interest, it will not be long before potential nootropic pharmaca can be identified. Preclinical and clinical testing will be rate-limiting steps and lead to the elimination of many candidate drugs. However, given the economic potential of nootropic drugs (estimated at 5 billion US dollar annually), their application is just a matter of time.

*Ger Ramakers*[32]

**31** For example CPB (i.e. encoding CREB-binding protein), and the P300 gene in Rubinstein-Taybi syndrome (RTS).

**32** Researcher of Developmental Psychology, University of Amsterdam and researcher at the Netherlands Institute for Neuroscience (NIN).

## 4.5 Brain development, neurocognitive functions and learning

*Ira van Keulen*

This section looks at what developmental neuropsychology tells us about brain development and the relationship between neurocognitive functions — such as attention and memory — and learning behaviour. As it turns out, we still know very little about this relationship, and especially about the link between specific functions and specific aspects of learning such as reading (although we know somewhat more about the neurocognitive functions related to general learning abilities). In order to work towards personalised learning, however, we need such specific knowledge. The use of individual neurocognitive profiles are only useful if we know how certain patterns of strengths and weaknesses are related to learning abilities and how and when we can influence them through personalised learning interventions.

The section also considers the notion, described in earlier sections, of sensitive periods in brain development, which we can interpret as periods in which children are especially sensitive to specific learning experiences owing to the way their brain grows. Neuroscientific research shows that, while we can predict the sequence and length of these periods, the speed of development within the various periods differs considerably from one individual to the next. Such differences underline the need for personalised learning. As we shall see in the second part of this section, the question raised by educational practice — where the notion of sensitive periods has long been important — is: when do these periods of brain development determine cognitive and behavioural development and when are they determined by such development? The answer will help us decide whether to adapt instruction to sensitive periods or stimulate and facilitate brain development through specific, challenging instruction.

### 4.5.1 The neuropsychological perspective

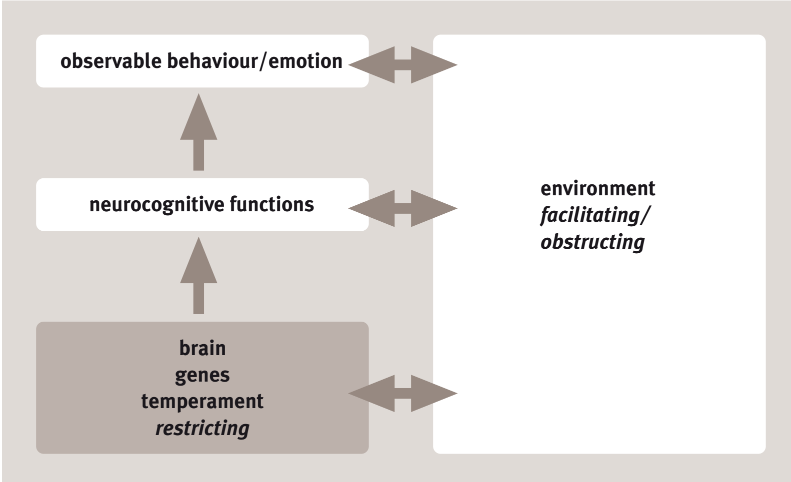
*Hanna Swaab*[33]

Learning processes are not as general as previously assumed. On the contrary, they are moderated by specific abilities and individual neurocognitive[34] strengths and weaknesses, and influenced by the dynamics of age as a development indicator. The neuropsychological view implies that behaviour, like learning, is the result of 'underlying' neurocognitive functions developing from the interaction between genetic factors and environmental influences that begin to play a role at the time of conception (see Figure 12). Studies

33 Professor of Neurodevelopmental Disorders, Department of Clinical Child and Adolescent Studies, Leiden University.

34 The term neurocognition is used when referring to cognitive functions such as attention, memory, etcetera.

Figure 12
*Brain-behaviour interaction and environmental influence. Scheme courtesy of Hanna Swaab.*




conducted by Kim-Cohen et al. [2006] illustrate the effect of gene-brain-environment interaction that eventually leads to specific behaviour (see also section 4.4). The studies — which were based on a sample of over 900 boys — show that a functional polymorphism of the MAOA gene[35] moderates the impact of childhood maltreatment on behavioural outcome. These findings make clear that a certain genetic-biological predisposition can determine the impact of environmental factors or, in other words, the vulnerability of the individual child.

## The growing brain

We can generally predict the sequence and length of time it takes for the brain and neurocognitive functions to develop and for the behaviour resulting from this development to evolve, including the variability allowed for within normal development. Brain and cognitive development is also progressive, implying that one stage of development depends on the quality of the previous stage's development. It is therefore highly important for children to master specific milestones of development, an assertion supported by the notion of sensitive periods (see also section 4.4). These are periods during childhood and adolescence when specific brain areas undergo rapid growth. Such periods are probably genetically programmed, but they are heavily influenced by hormonal changes but also environmental factors such as stimulation. The brain is highly vulnerable[36] during growth, but also predisposed to optimise development in response to optimised stimulation.

Although the sequence of brain development during childhood and adolescence is predictable, individuals differ sharply when it comes to how rapidly various functions develop. This underlines the importance of personalised learning. For example, one interesting study [Barnett et al., 2007] shows the

35 The MAOA gene encodes monoamine oxidase A, an enzyme that degrades amine neurotransmitters, such as dopamine, norepinephrine, and serotonin.

36 During certain 'periods of susceptibility', brain growth can also be threatened by brain trauma, brain infections and brain tumours, but also by intoxication, radiation and medication and by a lack of rest, food and physical and psychological safety.

gender-specific impact of COMT-gene[37] polymorphism on cognitive development in a large, normal population cohort study. Executive functioning and verbal IQ were related to gender as a result of gen-gender interaction, probably modulated by hormone levels. We may therefore conclude that gender and genetic influences result in variance in individual cognitive developmental patterns.

### The impact of neurocognition on development

Research has indicated that specific neurocognitive functions can be identified as 'vulnerability factors' in relation to particular outcome risks indicating specific needs in individual children. Specific neurocognitive dysfunctions appear to be related to specific developmental risks. For example, in a review of prospective studies on neurocognitive precursors, i.e. indicators, of psychosis, Morcus et al. [in press] concluded that problems in motor function, language ability and attention regulation in early childhood are associated with a vulnerability to psychosis.

Most clinicians associate specific cognitive strengths and weaknesses with specific learning disabilities. Rourke [1993] proposed a model for a specific learning disorder that he called the non-verbal learning disorder (NLD)[32]. This model was based on his finding that specific patterns of strengths and weaknesses in performance and in cognitive profiles could be systematically recognised within the learning disabled population. These specific cognitive profiles could be detected not only in patterns of learning disabilities, but also in behavioural consequences such as social dysfunctioning. Both learning and social functioning are therefore thought to rely, in part, on the same neurocognitive functions. In Rourke's model, the brain-behaviour relationship was explicitly defined and could be translated into age-specific observable behavioural profiles that acknowledged specific developmental implications. Additional behavioural profiles were defined for learning disabled children, e.g. based on Basic Phonological Processing Disabilities (BPPD). Subsequently, Pelletier et al. [2001] defined diagnostic rules for NLD and BPPD that encompass the various levels of behaviour and cognitive functioning and include models of cause, producing a sequential developmental impact that eventually leads to a specific behavioural presentation.

Although the validity of the above models can be questioned, one of their advantages is that they recognise the developmental impact of specific cognitive strengths and weaknesses on learning abilities. Recognising individual profiles of strengths and weaknesses in this way underlines the fact that individuals with learning disorders impose differing specific requirements on the educational environment. For example, if children meet the criteria for NLD,

37 The gene for catechol-O-methyl transferase, an enzyme involved in the inactivation of the catecholamine neurotransmitters (dopamine, epinephrine, and norepinephrine).

38 NLD is a broad category. Individuals with NLD are often also diagnosed with Aperger's syndrome or attention deficit disorder. It is called a 'nonverbal' disorder, since language functions are generally not affected, as is often the case with learning disabilities. For a definition, see gseacademic.harvard.edu/~daleysa/index.htm.

they have difficulty with visual processing and therefore need specific compensation to be able to progress adequately in their learning, especially with respect to arithmetic skills. Profiles of specific cognitive strengths and weaknesses are also very common within the normal population, although they do not necessarily lead to learning disabilities. These individual profiles furthermore reveal specific developmental patterns, making it clear that an individual learning environment can meet an individual's specific needs and optimise individual learning *if* the specific profile is known. A personalised learning environment can also help identify vulnerability factors at an early age so as to prevent negative developmental impact.

### Neurocognitive functions important for general learning abilities

The previous section showed that individual cognitive strengths and weaknesses have an impact on learning abilities and/or disabilities. One interesting question is *which* neuro-cognitive functions are considered important in relation to general learning behaviour. Such knowledge would allow us to monitor pupils' individual neurocognitive profiles and make appropriate adjustments to their personalised learning programmes.

So far, we know that attention and the executive aspects of attention are particularly important for controlling and processing incoming information, i.e. the basic and essential functions necessary for learning. The term 'executive functions' refers to those processes that control cognitive processing [Van Zomeren and Eling, 2004], for example inhibition, cognitive flexibility, planning and working memory [Lezak et al., 2004; Stuss and Levine, 2002]. In addition to attention and other executive functions, various aspects of memory are also important to general cognitive domains such as language development. These neurocognitive functions all develop rapidly during childhood and adolescence. Executive functioning only reaches maturity in early adulthood.

Individual neurocognitive profiles could therefore include the following domains of functioning: attention, executive functioning, memory functions, general intellectual functioning and language functioning (i.e. important indicators of global cognitive development), specific measures of social reasoning and ability to understand the motives of other people (see Box 6) and measures of personal well-being and self-evaluation (see also subsection 4.6.1). We can already assess these neurocognitive functions at different ages using neuropsychological test. These measurements are easy to perform, being computer-based and non-invasive. The neural correlates however, are generally not known yet, although neuroscientific research is making rapid progress in this respect. The question is whether neural measurements through imaging for example will provide more information on neurocognitive functions than

EXAMPLE XI

# Playing action video games improves visual skills

**Want to improve your visual skills and attention, plus your ability to mentally rotate objects? Start playing action video games. Students who play these games habitually tracked objects better, reacted faster and located visual targets better than non-players. What's more, these skills improved considerably in non-players who began to play action video games.**

Brain scientists from the University of Rochester in the United States studied the visual skills of two groups of students. The video game players had played action games like Grand Theft Auto, Crazy Taxi, Spider-Man, or Super Mario Cart at least one hour a day and at least four days a week in the previous six months. The non-players had little or no experience with such video games. The researchers tested four aspects of the participants' visual skills: attention resources, enumeration performance, attention over space, and attention over time. Habitual video game players performed better on all visual attention aspects than non-video game players.

In a fifth experiment, the scientists looked at what happened to the visual skills of non-players who played an action video game (Medal of Honor®) one hour per day for ten days. They compared their visual performance to those of students who had played a video game with a focused visual task (Tetris®) for the same period. The action video game players markedly improved their visual skills, unlike the group that had played Tetris.

The same scientists have shown in other experiments that playing action video games enhances the spatial resolution of visual processing, enabling players to tolerate smaller distances between a target and a distracting object than non-players. It also increases the number of objects that subjects can apprehend by changing visual short-term memory skills.

Recently, Canadian scientists have demonstrated that playing an action video game for only ten hours results in substantial improvements in spatial attention and mental rotation, with women benefiting more than men.

Whereas training usually induces improvements specifically in the relevant task, action video game playing alters a range of visual skills. It trains players to distribute their attention and perform various tasks simultaneously, which apparently results in brain changes that improve visual skills.

Original publications: Green and Bavelier (2003). *Nature*, 423, 534; Feng et al. (2007). *Psychological Science*, 18, 850

The findings offer opportunities for training programmes for visually handicapped people, or for people who have to perform demanding visual tasks, such as operating an air traffic control panel. Such programmes may also help to make mathematics and engineering more attractive to both men and women, as they offer a pleasant way to train the spatial skills necessary for these fields.

the currently available monitoring tasks. For the time being, neuro-imaging will remain a more invasive and time-consuming method of measuring neural functioning and will provide less information about individual performance.

**Box 6: Mirror neurons in relation to learning and social functioning**

Children at school learn within a social context. They are trained to read, write, do sums and practise other skills by a teacher, within the social setting of a peer group, using a methodology within the context of their own personalities. Social cognition – the ability to understand the dynamic and often changing and complex social environment – is therefore considered to be a very important domain of functioning that influences all information processing, including memory functions such as learning and selective retrieval, the selection of information, and consequently school-based learning. Recent findings suggest that the Mirror Neuron System (MNS) is important for social learning [Gallese, 2004, 2007]. Abnormal mirror neuron functioning has been found to correlate to underdeveloped mentalising abilities, i.e. those abilities necessary to be able to think from the perspective of the other person, which are, for example, dysfunctional in autism spectrum disorders [Martineau et al., 2008]. It is therefore important to evaluate the role of the MNS in normal development in relation to learning and social cognition.

The MNS is a mechanism that matches action and perception directly [Lepage and Theoret, 2007] and is thought to be related to such developmental domains as language acquisition, imitation and theory of mind[39]. This mechanism is not only activated by performing a given action, but also by observing someone who performs the specific action (see Figure 13). It therefore plays an important role in the representation of others [Rizzolatti and Craighero, 2004] and leads to learning without actual practice.

Research on the MNS so far has focused mainly on adult populations. It is assumed that the MNS develops gradually through experience, in other words through environmental stimulation. Adequate learning experiences are therefore important for gradual developmental refinement. Lepage and Theoret [2006] found evidence of the MNS in children; they measured nearly the same patterns of neural activation in fifteen developing children performing hand movements as when the children were observing hand movements .There is some evidence that the MNS is especially active if perception of intention is involved [Iacoboni, 2005]. This hypothesis is used to explain why the MNS appears to be more active in children than in adults: they are still learning about the implications of certain perceptions, again illustrating the environmental impact on learning.
Motor imitation is an early developmental phenomenon; The famous biologist Jean Piaget already included imitation as a major developmental issue in his model of

**39** The term theory of mind related here *"to the ability to attribute mental states – beliefs, intents, desires, pretending, knowledge, etcetera. – to oneself and others and to understand that others have beliefs, desires and intentions that are different from one's own."* (see www.wikipedia.org).

cognitive and social development. Newborns imitate facial movements by moving the same region of their face [Meltzoff and Moore, 1977]. Based on findings so far, Lepage and Theoret [2007] conclude that the motor programmes can be activated by observations of actions already a few months after birth, and that these motor representations can be elicited by different visual or auditory modalities. MNS activation is largely automatic. We can therefore conclude that a properly functioning MNS is an important prerequisite for learning during childhood and adolescence. The MNS is probably one of the factors that influences individual profiles of neurocognitive strengths and weaknesses involved in individual learning.

*Hanna Swaab*[40]

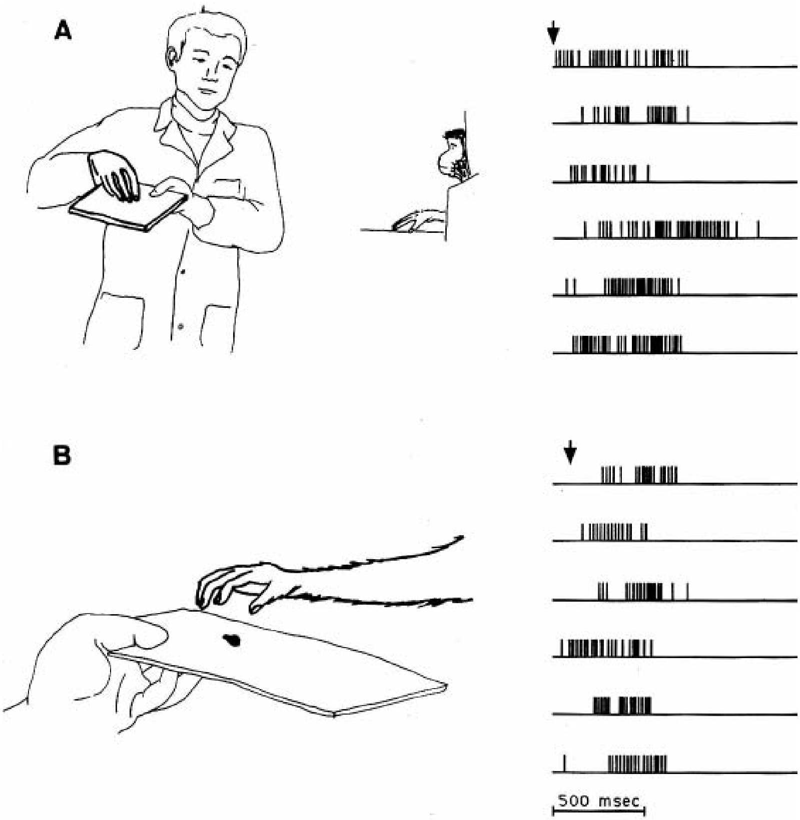



**Figure 13**
*Example of a F5 mirror neuron selectively discharging (A) during observation of a grasping movement done by the experimenter and (B) during monkey grasping movements. Arrows denote the onset of the movement. Six trials are shown for each condition. Source: www.scolarpedia.org/article/mirror_neurons.*

## Specific neurocognitive functions important for specific learning abilities

Unfortunately, not much is known about *specific* neurocognitive factors that are essential for *specific* aspects of learning. Some studies claim that profiles of strengths and weaknesses that include neurocognitive measures such as attention can differentiate between children with and without learning problems [Everatt et al., 2007]. Pavuluri [2006] evaluated the executive functioning

40 Professor of Neurodevelopmental Disorders, Department of Clinical Child and Adolescent Studies, Leiden University.

of children and adolescents between seven and seventeen years who had serious affective problems. Her research found that poor executive functioning (attention, working memory, verbal memory) was associated with reading difficulty. Another example is dyslexia, which is thought to be associated with problems in the working memory, inhibition and fluency [Reiter et al., 2005]. Visual spatial abilities are also found to be associated with the risk of dyslexia, however [Brosnan et al., 2002]. There has been even less research exploring the impact of interventions on these neurocognitive functions and their effect on general or specific aspects of learning. Although there have been some promising findings, further research on the relationship between specific learning abilities and neurocognitive functions is needed. Research should focus not only on the relationship between the two but also on the specificity of this relationship for each developmental stage and its predictive value.

#### Conclusion

Personalised learning is based largely on the monitoring of individual neurocognitive profiles. What are the individual cognitive strengths and weaknesses of the pupil and how can we adapt instruction to his or her profile? One of our key challenges is to learn more about the specific predictive value of candidate neurocognitive functions for the various aspects of learning. We also need to learn more about the educational strategies required to influence the development of those relevant neurocognitive functions. More specifically, we need to know more about the relationship between specific neurocognitive functions and the ability to master the different aspects of learning at school.

In terms of brain development, another important research question is how neurocognitive control functions develop over time in relation to learning behaviour. We need to learn more about the possibility of influencing the development of these functions and the effect this would have on learning. We also need to consider gender differences, specific aspects of development, and the combination of specific patterns of strengths and weaknesses within the individual profiles. In general, while aiming for personalised learning, neuroscientific and cognitive research strategies should focus on evaluating and monitoring individual developmental tracks more than on group effects.

### 4.5.2 A practitioner's view of sensitive periods

*Harry Gankema*[41]

It was Maria Montessori who popularised the term 'sensitive periods' in education. Her claim is that a child goes through many different stages of development and that the transition between one stage and the next can be

41 Advisor, KPC Group, educational innovation.

described as a sensitive period. Children in sensitive periods feel a tremendous urge to learn specific skills, the particular ones depending on the stage. Adults should tailor the support and instruction that they provide to these sensitive periods. In short, according to Montessori, sensitive periods are related to the child's stages of development. Jean Piaget subsequently became famous as the biologist who discovered the stages of cognitive development. He believed that a child goes through the various stages autonomously, and that education does not have much influence on them. Montessori's approach essentially keys into this idea: support a child who shows it is ready for the next stage.

The Russian psychologist Lev Vygotsky criticised this approach, stating that human beings live in a social environment. Through a process of internalisation, children master the human functions of the social system. They learn to read, tell time, but also to plan and prepare a meeting. The social system (and therefore the school) can influence the degree to which this happens by challenging the child. Education should therefore not *follow* the child – i.e. key into its current stage of development – but *challenge* it – i.e. stimulate it in what Vygotsky calls a 'zone of proximal development' (ZPD)[42], in essence a sensitive period. Vygotsky's approach differs from Montessori's in that it is the educator who must key into that sensitivity, and not the child. The educator must sense and comprehend that there's 'more to this child than meets the eye.'

### Brain maturation: cause or effect?

Cognitive development stages and 'learning sensitivity' were one of the most important themes of educational psychology and educational science in the 20th century. Remarkably, elements of the same discussion have been revived as neuroscientists study the plasticity of the brain in-depth. Neurobiologists have established that certain areas of the brain are more sensitive to change at certain periods in a child's development (the 'sensitive periods'). During these 'windows of opportunity', specific sensory input can optimise the development of specific brain areas (see section 4.4). Neuroscientists therefore view the stages of the brain's development in the same manner as the biologist Piaget: offer the brain something when it's ready for it.

This approach has its basis in the fact that the neurosciences are preoccupied with physiology: they view the brain cells, neurons and synapses as the basis of our knowledge system. Knowledge is seen as a function of that physiological basis, but in fact the two have at least some influence on each other, and it may even be that physiology is a function of knowledge. Connections between synapses appear or disappear depending on the individual's intelligent interaction with his or her environment. Intelligence therefore creates physiology.

**42** ZPD is the difference between what a learner can do without help and what he or she can do with help.

From a physiological point of view, the fact that we can see time-sequences in the human brain in which specific neural functions become more — or less — plastic with time does not necessarily mean that this is a result of the biological maturation of our brain, or that our educational system should be tailored to those stages of maturation.

It would be interesting for the cognitive sciences to explore whether there is a necessary time-sequence in the growing complexity of our knowledge structures, ultimately leading to the 'normal' behaviour of an adult human being. Then we could also test whether our brains are equipped to support an individual's socially determined cognitive development, and whether sensitive periods in brain development are the effect of that, and not the cause. Until now, the neurosciences have concentrated on establishing the cognitive stages empirically; they have not yet subjected the underlying logic to epistemological analysis.

### Time-sequencing in practice

Slash/21 and Wittering.nl[43] are two Dutch schools where learning is organised to fit in with the information processing principles of the brain and not, as is customary, the logic of teaching methodology. The two schools are based on the idea that traditional educational systems make demands on children's meta-cognitive skills too soon and are too linguistic in their approach to knowledge. Traditional teaching methodology is mainly based on one type of knowledge: formal, codified knowledge. The organisation and architecture of this methodology are not innate to the brain's approach to information processing. For example, virtually every child in the world has the ability to speak its native language correctly, without knowing any of the rules of grammar.

The model underlying these two schools describes the various forms of information processing in the brain, including the evolutionary dimension, i.e. the fundamental change that arose when human beings became capable of expressing sensory experience in language. Because the architecture of the two conceptualisation processes are basically incompatible[44], the model uses two different terms for them: genitive knowledge for 'natural' knowledge, based on direct sensory experience and the implicit meaning of phenomena; and cultural knowledge for the way in which human beings express felt meaning in the culturally determined laws of our language system and make that meaning consistent with those laws.

The model is based on the idea that the brain, which carries all of evolutionary history in it, builds up various 'knowledge' systems in stages before it can operate maturely as a unified whole[45]:

43 Respectively a secondary school and a primary school where innovative educational methods are used, based on a proprietary model describing the nature of various forms of knowledge and the implications for the design of learning processes. See www.slash21.nl and www.wittering.nl.

44 Examples are the extreme effort required to say in a foreign language what you feel naturally within, or the feeling that anything you say about an important emotional event, for example the birth of a child, can never express what you really felt and experienced on that day.

45 Piaget only described the first three systems: 'I am the world', 'Me and the world' and 'Me in the world'. As a developmental psychologist, he paid no attention to the fourth knowledge system, which is extrapersonal.

1. Controlling one's own physiology and tailoring it to the direct environment, for example the ability to swim. Memory and retrieval are embodied.
2. Learning what is not you: your environment and others. First through sensory experience, and later through language as a medium of communication. Memory and retrieval are linked to emotion, e.g. sensing that a small pebble will float when placed on a board.
3. Understanding the 'self', once language has developed to the point that the 'I' can be used as a distancing instrument.[46] Memory and retrieval are based on memorisation, e.g. being able to explain why a pebble floats on a board by referring to Archimedes' Principle.
4. Growing into a social being who uses the previous three integrated elements and the 'I' to contribute to the social context in which the 'I' operates. The meta-cognitive ability to manage knowledge in the future and knowledge beyond the 'self'. Memory and retrieval are linked to documentation e.g. having a team design and build a boat.

In the first two systems, knowledge is genitive, i.e. related directly to the biological basis of action and perception. In the final two systems, knowledge is cultural, i.e. it expresses knowledge in a logical linguistic unit separate from direct experience. Each stage is regulative with respect to the underlying stage. The second system uses the physiological skills of the first system (for example the coordination of the limbs) to develop new skills such as swimming. The third system expresses the felt knowledge of system 2 in language in order to achieve something in a human social environment, for example giving swimming lessons. The fourth system anticipates human behaviour (system three) in order to direct or influence social contexts, for example coming up with the sport of water polo.

This model of knowledge development is clearly cumulative in nature. It would be impossible to develop system 3 knowledge, for example, if we skip system 2. There are also the necessary cumulative developments within each of the systems. We see that in the joke 'I've learned to write and now I'm going to learn to read so that I can read what I'm writing now.' The curriculum at Wittering.nl is based on this knowledge hierarchy. For example, the school has done away with 'reading comprehension' as a subject because — certainly in the case of children — comprehension (system 2) does not develop by means of language (system 3); language is in fact an expression of comprehension. Wittering.nl first invests in genitive knowledge and only then in language as a means of expressing that knowledge. In the 3rd, 4th and 5th grades of primary school, we put a great deal of effort into phenomenology, such as the basics of chemistry (e.g. the difference between a mixture and a compound), physics (e.g. energy and the various transitional forms), sociology (e.g. why do I attach

46 'Self' is the person described in 2, and 'I' is de person who reflects on that self.

myself to some people and not to others?). Only in the upper grades do we communicate with one another about what we know. This means that at system 2 level we study things that pupils in mainstream education only start to explore in secondary school.

It also only makes sense to learn regulating skills — for example how to manage, monitor and evaluate one's own learning process — if there's something to actually regulate. The fact that girls are quick to pick up this skill may have nothing to do with brain maturation. It may simply be related to their reaching puberty earlier, which means that they grow into the social processes (system 4) that require distanced regulation. As soon as children perform the first cognitive regulative actions, the brain will follow; after all, that's what it was designed to do. We see a good example of this in children who are orphaned suddenly and forced to fend for themselves. Their rapid growth to maturity has everything to do with a new social context that requires regulation, and not with brain cells that have suddenly 'matured'.

In short, all this means that the education system should not wait until the brain has reached a particular critical stage of development. Instead, it should create contexts that the child cannot 'survive' if it does not regulate. It should create a need to learn — within the limits of pedagogical safety — and not merely facilitate the autonomous maturity of the brain.

### Conclusion

Our analysis indicates that brain maturity does not necessarily drive the process of cognitive development. The need to go through the sequence of cognitive stages means that different brain functions are activated at different times, something not contradicted by the fact that a sensitive period has both a starting date and an ending date. Cognitive models can also be used to demonstrate that, at a certain point, we cannot develop more lower-system knowledge after having moved to a higher system. To put it simply: we cannot return to childhood, even if we want to.

The implication of this reasoning is that the biological basis of brain maturation is not only physiological and empirical, but is likely also the result of a mental development process that is universal for all mankind. It will be clear that once a child is able to distinguish between itself and its environment, it enters an entirely new knowledge world. It is more logical to assume that that crucial mental step is the result of the cumulative effect of learning experiences (cognition) than to put it down to a genetic switch that is thrown after two years. No one would deny that the cognitive and the biological interact. However, our physical paradigm (i.e. the basic explains the more advanced) inclines us to value the biological over what is summoned by the biological: cognition. But it is very doubtful whether that is correct.[47]

The stages of the maturation process may therefore be more closely related to cognitive thresholds than to biological ones. The better a child understands complex phenomena, the more it will feel the need to express that understanding. The better it can make complex movements, the more it will be inclined to use those movements in its environment. Education therefore has two main tasks:

- To facilitate growth within each of the four systems and prevent a child being burdened with knowledge belonging in a higher system before it is finished growing in the lower system.
- To facilitate growth between systems and create the need to develop higher learning functions once the lower function is properly developed.

Our current system of education fails on both counts. Specifically, it neglects the differences between genitive and cultural knowledge. Children are asked to reflect and communicate on matters about which they have developed scarcely any genitive knowledge, if at all. They learn arithmetic rules before they have a sense of number or size. Doing sums then becomes a trick they perform with abstract figures, and they apply percentage rules without understanding what the rule actually 'does'. Children are asked to study independently and display regulative investigative behaviour about subjects for which they have no genitive, and therefore no emotional connection with their potential findings. Information science has shown us that information differs from data in that it is interpretive, has meaning. Something that counts as information in system 4 is not necessarily that in system 3 of a younger child. Something for which there is no interpretive framework of existing knowledge in system 2 may be stored as data and memorised for a test, but it will not have any meaning for the pupil. Data only becomes information, and then knowledge, if it can be integrated into the child's personal history of meaning, which becomes manifest mainly in system 2.

If we wish to transfer vital knowledge to children, then we must realise that such knowledge will not take on the shape in their minds that we have given it in our lesson or our book. Its shape ultimately arises from the child's ability to assign meaning at the time it receives the knowledge (perhaps the maturation stage) and the nature of what is being transferred.

47 It also contains an element of chaos theory: the processes elicited by the brain cells (information flows) have laws without a cellular equivalent.

## 4.6 Learning, scholastic achievement and motivational and emotional processes

*Jaap van Loon*[48]*, Ira van Keulen*

Teachers and developers of instructional materials devote much of their effort to motivating learners, and with good reasons, since motivation affects all teaching processes. It can influence how a child learns new behaviours and how it performs previously learned behaviours. Being aware of the importance of motivation is only the first step in improving the way individual pupils are taught. Teachers working in the field deal with motivation intuitively, based on their own experience and generally not on scientific evidence. Most of what we know about motivation is practice-based. We have some neuroscientific and cognitive scientific knowledge about how motivation works, but this mostly concerns basic motivational and emotional drives at group level. We know little about individual differences between motivational aspects, and even less about how they relate to educational settings. For example, one interesting research question is how to differentiate between lack of motivation and lack of challenge. There are infamous cases of highly talented children being bored to death in the classroom. If this situation goes unrecognised at a relatively early stage, the child may never achieve its full potential. It is therefore of great importance to personalised learning to identify the skills and abilities of individual children, to recognise differences in their motivation to learn, and to adapt instruction accordingly.

This section first looks at current neuroscientific and cognitive scientific insights into motivation from various perspectives pertinent to the development of personalised learning (i.e. biopsychology, developmental neuroscience and neuropsychology). Two authors active in educational practice, i.e. the KPC advice group and ThiemeMeulenhoff educational publishers, pose various questions for neuroscience and cognitive science, to begin with from the perspective of 'New Learning' and secondly from the viewpoint of gaming in educational settings as a tool for motivating pupils.

### 4.6.1 The neuroscientific perspective

*Jelle Jolles*[49 50]

The neurosciences and cognitive sciences, including developmental neuropsychology, have given us a better understanding of the motivational processes at work in the human brain, and of the way motivation, emotions and contextual factors (e.g. psychosocial environment, level of parental education)

48 Director of ThiemeMeulenhoff and chairman of the Group Educational Publishers of the Dutch Publishers Association.

49 Professor of Neuropsychology & Biopsychology, director Center for Brain & Learning, Maastricht University.

50 This contribution is partly based upon a paper written for an OECD-CERI workshop on brain, learning and motivation in Copenhagen, November 2004.

influence a child's performance, belief and attitudes. We also know that personal motivation and emotional engagement are essential prerequisites for proper information processing and learning. The human brain is equipped with the machinery that helps a child to judge the potential impact of sensory stimuli and motivational states of the body.

We will see below that the neurosciences and cognitive sciences have already produced major insights into the possible implications for educational practice and pedagogy, but in order to use this knowledge about motivation in educational settings, we must answer some important research questions, such as: how can this knowledge be used to improve the learning environment? Can better incentives be developed for encouraging motivation and learning attitudes? Could motivational factors related to hunger, thirst, sleep, sexual activity, etcetera impede efficient learning?

### The biopsychological perspective

Cognitive science and neuroscience have taught us that a human being can be regarded as 'an adaptive, information processing system'. 'Adaptive' means that the individual child, the adolescent, and the adult adapts to a changing environment. The term 'information processing' stands for the perception of stimuli via the senses, the selection of information to be consolidated or ignored, and the retrieval of information stored on previous occasions. In the case of pupils in educational settings, the external environment consists of all information deriving from teachers, parents, peers and others. But information also comes from books and electronic media, the noise of peers in the classroom, and the visual and audio signals produced by the computer. Much of this information not only has a cognitive content but is also emotionally or motivationally coloured: the deprecating attitude of the teacher, the beautiful eyes of the girl sitting in front, and the angry voice of the parent. All this information has to be processed by the senses and judged by the brain in terms of 'how important is this for me?', 'why should I do this?' and 'should I adapt my behaviour?' The pupil has to judge the emotional and motivational value of the stimuli that guide his or her behaviour.

The brain processes emotional information differently from motivational information. From biopsychological perspective motivations are seen as very basic determined entities related to internal states such as hunger, thirst, sex, care, sleep and the like. These are regulated by structures in the brain that evolved hundreds of millions of years ago. Emotions evolved somewhat later, and can be regarded as a biopsychological mechanism required to indicate the potential significance of a particular stimulus or state: they provide the organism with the information 'this is potentially dangerous, look out!' or 'this looks nice, move closer, you'll like it!' The following subsections look at the biopsychological mechanisms of motivation and emotion and their relevance for the educational system.

### The biopsychology of information selection

Judging stimuli on their emotional and motivational value is not an easy task, but human beings have evolved a large number of processes that help them filter incoming sensory and emotional information and decide which stimuli should be processed and stored and which should be discarded. The developing child adapts to the changing environment by changing the structure and function of its brain. The resulting biological maturation manifests itself in physical, social, emotional and cognitive development. The child's brain adapts by forming and changing the nature and efficiency of connections between its cells, and by reinforcing or weakening networks of brain cells. This process takes years and demonstrates the inherent plasticity of the brain. It turns out that the brain (or particular parts of it) continues to mature until well after the 20th year of life. At the same time, it remains plastic until quite an advanced age. Eventually, the brain is able to select relevant information and keep irrelevant information out. Motivational states and emotions are of the utmost importance in this selection process. They help the brain fend off particular stimuli and resist acting impulsively. Sometimes stimuli are so dominant that the brain has a hard time making the right choice: a very noisy class makes it difficult for a child to concentrate and to pay attention for a longer period of time. Attention and distraction are very important in the selection process, but so are working memory, planning, prioritising between conflicting actions, evaluating goals, self-evaluating and other higher-cognitive processes.

### The biopsychology of motivations and drives

The aim of the educational system is to transfer particular cognitive knowledge and experiences to pupils. Until recently, we have ignored the fact that a human being is a 'cognitive animal' guided by the same basic processes as his ancestors in the animal kingdom. In other words, much of our brain is still preoccupied with organising internal states that biopsychology describes in terms of motivation and emotion. These states involve the processing of basic stimuli, such as hunger, sleep, thirst, sex drive, interest in social interactions, novelty or newness, and even thermoregulation and related psychophysiological processes. Such stimuli may not be important in the instruction and knowledge transfer that lie at the heart of teaching, yet they do guide pupil behaviour. This means that emotions and motivations are also of particular importance for the didactic and pedagogical aspects of teaching. Some examples: hormones guide the attention span of the fifteen-year-old adolescent

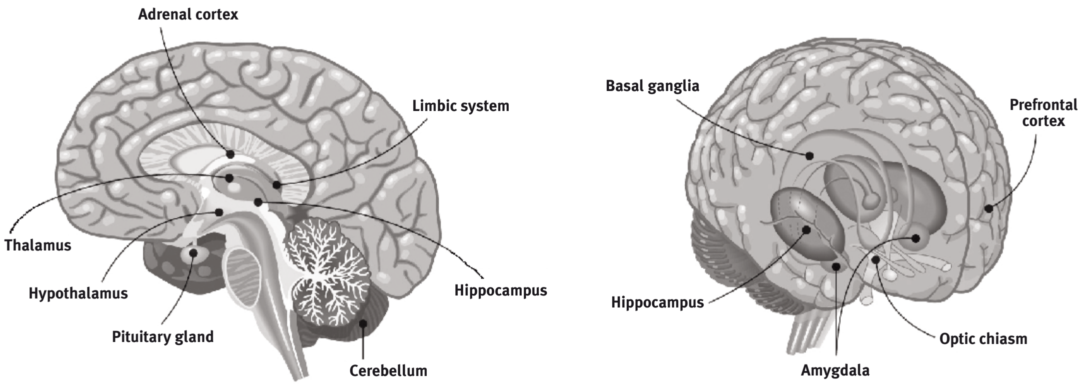



**Figure 14**
*Two brain models showing among other things, the limbic system, amygdala and prefrontal cortex: brain areas important in relation to motivational and emotional processes. By Paul Horn, www.cooljerk.com.*

who is in love; sleepiness is the source of distraction in the girl who went to bed at 1 a.m. last night; hunger motivates the twelve-year-old boy who did not have his breakfast. These fundamental biological drivers have not been paid much attention in education until now, and yet they deserve it. The fundamental biological mechanisms mentioned involve major brain structures consisting almost entirely of the subcortical structures. Very important structures in this respect are the thalamus and hypothalamus, which can be regarded as central processing units that integrate sensory information with bodily information. In their efforts to achieve homeostasis, these processes require a very potent brain-body interaction involving molecular factors, hormones, numerous neurotransmitters, food constituents, and both the central and peripheral nervous system.

## Biopsychological processes and emotions

While the motivational system is related primarily to basic drives essential to bodily survival (food, drink, homeostasis, sleep) or the survival of the species (sex drive, care, aggression), another system alerts the individual to potentially important stimuli. This is the limbic system, a phylogenetically[51] ancient system in the basic forebrain (see Figure 14). These brain circuits underlie emotions and are different from those underlying the primary motivations or drives, but they do overlap in anterior brain areas. The limbic system evolved early in evolution and is found in reptiles and amphibians as well. Its role is to apply an emotional value to sensory stimuli, ensuring that the organism recognises the importance of a particular stimulus later on. This may be because the stimulus is potentially threatening and thus requires the organism to fight or take flight; it may be a possible sexual contact; it may lead to food intake or to other reinforcers. The limbic system is therefore deeply involved in memory and in learning from experience. One part of it — the hippocampus (see Figure 11) — is a core structure with an essential role in memory consolidation,

51 Phylogenetics is the study of evolutionary relatedness among various groups of organisms (e.g. species or populations).

while another part — the amygdala — is a piece of brain machinery needed to decide whether a particular stimulus has a positive or negative emotional reward value.

### The biopsychological perspective: conclusion

Obviously, our ability to process information is challenged by situations that require us to shift our attention elsewhere. The traditional educational system is based on the premise that learning in school will take place when the information provided by the teacher is optimally structured and 'interesting' for the learner. Yet pupils will easily lose interest in stimuli and information when their attention shifts to executing acts that are more relevant to their internal states. We are wrong in denying the role played by these basic motivations and emotions, and also the role that emotional distress plays in psychosocial circumstances. Animal and brain research on the basic mechanisms underlying learning have shown that particular emotional stimuli and motivational factors are essential for optimal learning. Memory consolidation depends on a minimum level of emotional or motivational stimulation. Personalised learning is capable of creating these minimal levels of stimulation.

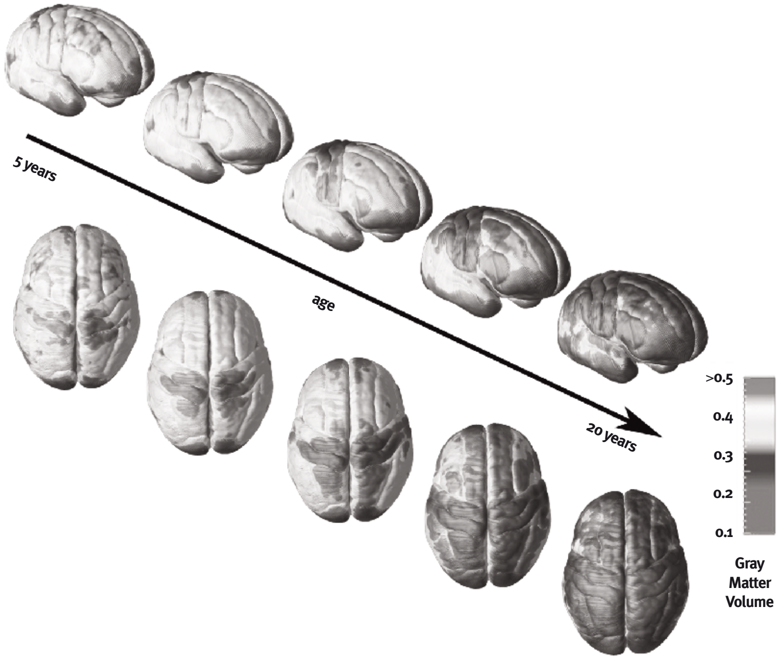
Biopsychological research also suggests that better incentives can be developed to stimulate motivation and a positive attitude to learning. It is not true that there is an inherent, biologically based 'schooldrive'. There is only a natural inborn curiosity directed at those stimuli that could, in one way or another, be of survival value to the individual. In addition, it has been suggested that negative emotions in particular must be avoided. The learning context should be altered such that learning and knowledge acquisition induce positive emotions in the learner. After all, individuals who are adept at handling relevant information and discarding non-relevant stimulation have an evolutionary advantage. Accordingly, we help a pupil's brain in this selection process when the information the teacher wants the student to learn is judged by the brain to be 'fun' or 'interesting'.

### The developmental perspective

Research carried out in recent years has shown that particular parts of the brain cortex develop in middle and late adolescence and do not fully mature until around the age of 25 in males and a few years earlier in females. Individuals vary in this respect, however, and it is highly probable that the psychosocial environment, including the learning context, guides the process of maturation (see also section 4.4 and subsection 4.5.1).[52] There are also strong indications that the brains of boys generally mature more slowly and reach full development some years later than those of girls. These findings come from developmental research conducted in the past five to seven years and involv-

52 More specifically, it is the quality of the learning environment in interaction with past life experiences and the present psychosocial environment that determines the optimal outgrowth of the brain, and thus the psychological development of child and adolescent.

Figure 15
*Right lateral and top views of the dynamic sequence of grey matter maturation over the cortical surface in the age from five till twenty years. Photo courtesy of Paul Thompson. UCLA Lab of Neuro-Imaging.*




ing structural and functional brain scans [Lenroot e.a., 2007; Giedd, 2004] (see Figure 15 as an example to show how the volume of grey matter in children change over a period of 15 years).

The neurocognitive functions that are the direct corollary of the functioning of the various brain networks pertinent to motivation and emotion regulation are related to the 'executive' functions[53], and it is precisely the brain areas underlying these executive functions that develop last, i.e. during middle and last adolescence. In general, our present system of education does not fully acknowledge the compelling role of the executive system. Much present-day teaching is based upon the premise that the pupil is able and motivated to state his own goals and act accordingly. Neuroscientific research shows that this premise might be false. Recent cognitive neuroscience research [Steinberg, 2005; Paus, 2005; Blakemore and Frith, 2005] shows that the medial prefrontal cortex matures from early to mid-adolescence until well into adulthood.

The structures responsible for executive functions in the prefrontal cortex (e.g. anterior cingulate area) are thought to be closely connected to the limbic areas and to areas of the hypothalamus and thalamus. Their role is to enable efficient behavioural planning in keeping with motivational and emotional processes. Self-evaluation and social monitoring are thought to be guided by these structures, making the medial prefrontal cortex of utmost importance to learning and the role of motivation.[54]

53 These executive functions enable the individual to act according to a plan, to prioritise on the basis of perceptual information, motivational states, and the social and emotional consequences in the short, medium and long term, and to use past experiences as efficiently as possible.

54 Note that the aspects of 'motivation' involved here have to do with the highest psychological and cognitive processes and, as such, are completely different from the basic motivational states mentioned earlier in relation to the core of the brain, i.e. the hypothalamus and thalamus.

The social support context (parents, teachers, peers and others), including the nature of the reward processes, emotional feedback, positive rewards, pain, etcetera, are primary factors guiding the development of this brain system. That development is certainly not an autonomous biological process. Indeed, it is only the very earliest stage of development that is guided by biological factors in which genes play a role. What guides proper development of brain networks, prunes the connections and optimises inter-neuronal communication is behaviour and sensory and motivational information. Environmental factors therefore determine the proper functioning of these brain structures and, consequently, higher cognitive, psychological and social functioning.

Educational reform really can make a difference thus, by laying down the conditions that will allow the motivational system to develop optimally. Environmental factors, including psychosocial processes, play a more important role here than genetics, because they determine the extent to which the individual reaches the theoretical boundaries set by genetic and biological constraints. Genes determine the theoretical maximum, but environment determines whether or not this maximum will be reached (see also section 4.4). Environment is a prime factor in 'talent development'. Reforms such as personalised learning are important in this respect, as there are major biological differences between children when it comes to the stages of brain development, social support (in both the positive and negative sense), psychological make-up (outgoing, sensation-seeking or introverted and even depressed).

### The developmental perspective: conclusion

Neuroscientific research on functional brain maturation up into the third decade of life indicates that the developing brain needs an 'external' motivator until adulthood. Such guidance should not stop at the age of eighteen, when the subject is legally an 'adult' in Western societies, but should continue for quite a few years. Of course, this does not mean that the child and adolescent should not be given any responsibility at all: the developing individual must be taught to take responsibility and experience the consequences of its actions as soon as possible. Nevertheless, teachers can help the child acquire the relevant knowledge and choose actions and directions that could be of major relevance in later stages, but which it cannot yet oversee or anticipate.[55]

This neuroscientific finding conflicts with educational concepts that state that the educator should retreat and that education should facilitate the autonomous learning process in students. We should reconsider what constitutes a good teacher, but also a good parent in the sense of an external motivator. Neuroscientific research suggests that an educator should not only be a passive facilitator who offers instruction when asked; he or she should also take a

55 This is especially the case for those tasks in which the executive functions are needed, i.e. in which social, cultural, emotional and motivational aspects are merged.

more pro-active attitude and motivate the pupil to engage in fields or domains that he would never have entered on his own. What we now require is more evidence-based research directly comparing self-initiated learning and learning based upon external motivators.

## The neuropsychosocial perspective

The period in which the brain is optimally suited for cognitive learning is adolescence. That is because the brain has, by then, acquired basic neuropsychological functions: its auditory, visual and haptic functions, language skills, perception, and psychomotor processes are all well developed and can be used for integrative activities. Likewise, a basic 'abstract attitude' is in place, meaning that the adolescent is able to think, plan ahead, and oversee similarities and differences between objects, actions, and situations. This is important for further intellectual and cognitive growth. However, the adolescent boy or girl is generally much more interested in social interactions with peers, i.e. social learning. This interest is a natural consequence of the physiological development of the brain. As mentioned earlier, there is a complex bidirectional influence between brain development and social development during adolescence. In other words, the adolescent becomes interested in social interaction because his brain enables him to, but the nature of that social interaction also helps further develop his brain. It is therefore quite easy for adolescents to develop negative attitudes and perceptions to learning, e.g. that 'learning is for nerds'. This is partly contingent on the rapidly growing importance of peers, and it has major implications for the pupil's learning trajectory and his motivation. For example, we can expect that learning will be optimal in settings that favour the kind of social interaction in which adolescents are interested.

## Negative emotions and stress can disrupt optimal learning

The foregoing makes clear that emotional development is of crucial importance when attempting to optimise a child or adolescent's information processing ability. Knowledge acquisition depends on an optimal rewarding atmosphere. We have known for decades that stress and negative associations disrupt learning.[56] It is particularly important to prevent negative emotional factors such as stress in individuals with a learning disability or brain dysfunction, but also in many adolescents for whom learning is not as 'automatic' as for younger pupils (see Figure 16).

The above is all the more interesting because there is a growing group of children who are developing a negative attitude towards learning. They are children who have had negative experiences with some aspect of cognitive learning (e.g. reading or arithmetic problems), motor learning (e.g. clumsiness,

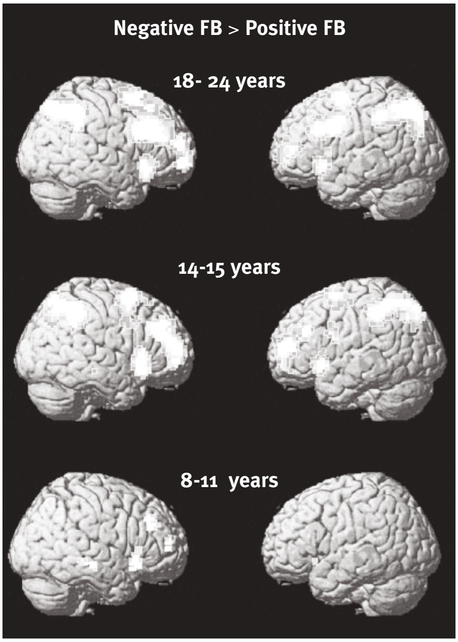



**Figure 16**
*While learning if we are on the right path, we typically make use of both positive and negative feedback on our behaviour. Different studies show that children still have a difficult time to adapt their behaviour after receiving negative feedback [Crone et al., 2008]. Photo courtesy of Eveline Crone, research Brain & Development laboratory, Leiden University.*

poor at sports) or social learning (e.g. unable to make friends). Such negative experiences can have a major impact on behaviour and attitudes. Many children are developing a phobia towards cognitive or motor learning or social interaction, and anxiety or depression is already prevalent among children. Such attitudes may have a major influence on their development and the type of school they attend, and therefore determine their whole life. Individual differences in brain and cognitive development makes this even more crucial; children who are 'late' in developing a particular brain function may reach an asymptote later, and even achieve a higher asymptote than children whose brain develops faster. All this once again underlines the importance of personalised learning.

### The neuropsychological perspective: conclusion

Early school-leavers are a problem in both secondary and tertiary education. In addition, many students make the wrong educational and career choices and end up with motivational problems. The anterior brain areas involved in planning, problem-solving, social learning, self-monitoring, social monitoring, self-initiation and impulse-management continue to develop until well into adulthood, as we found above. The choices made by an adolescent are therefore probably not based on rational arguments but rather on motivational and emotional factors, even a 'gut feeling' that might not be ideal. One way to prevent motivational problems in education is to consider the inherent motivation and interests of individual pupils and their psychosocial factors. Even such things as intellectual subculture, racial background, migrant status and

56 This is because 'self-control' and 'self-compassion', in which emotional factors play a major role, are of great importance for learning.

related cultural factors are highly relevant in this respect, as they have determined the past life experiences, i.e. the knowledge and experience base upon which new information rests.

### 4.6.2 A practitioners' view of motivation

*Harry Gankema*[57]

Suppose an intelligent person creates a robot with artificial intelligence. And suppose this robot passes the Turing test: a human being is unable to distinguish the robot from another human being while interacting with it. What are the basic programmes that make the robot behave as he does? First of all, of course, there is the programme that manages the technical parts. For a human being, this would be the brainstem, which causes the heart to beat and the lungs to breathe. It is the robot's basic power switch. But the next programme is even more intriguing. It is the programme that ensures that the robot does anything at all, that gives him basic reasons to act. It is what drives him to do something. The concept of drives as expressed by Maslow, for example, provides an adequate description of the second power switch: a set of parameters related to basic needs must be met at a certain level in order for the robot to act. Only if one of the parameters is unmet does the robot take action and leave the basic state of just 'being', e.g. when its battery is empty, it has to recharge it. All basic animal behaviour can be explained by this set of drives.

But within the context of such drives, only higher level animals — such as human beings — have the ability to make choices and express preferences. For example, when you are hungry — and lucky — you can choose what, when and where to eat. The concept of motivation offers us an adequate explanation for the personal preferences we observe in the variety of actions of such higher level animals. Motivation is related to intelligence because it reflects an attitude based on former learning experiences and the expectations extrapolated from those experiences. Emotions play an important role in establishing motivation. All mammals — and *only* mammals (who all share the same set of emotions) — have a playing phase early on in life during which they develop a personal set of experiences that provide the basis for motivation later on in adulthood.

Let us leave the metaphor of the robot; there is no such artificial intelligence at the moment, and we do not know if and when there ever will be. But the robot shows us that the two basic power switches — the brainstem and the drives — have nothing to do with what we call 'intelligence'. Both are merely necessary to make the robot and the human operational and to make both

57 Advisor, KPC Group, educational innovation.

of them act. Motivation, on the other hand, is the first sign of intelligence. Motivation creates choice.

The robot metaphor helps clarify the discussion about the role of motivation in education. The switch from traditional learning to New Learning[58] in the Netherlands is regarded as a paradigm shift. New Learning involves pupils actively constructing personalised, often informal, knowledge within the context of real-life problems, as opposed to the traditional idea of learning as an act of consuming formal knowledge provided by teachers and books. New Learning entails a shift from cultural, formal knowledge and information towards personal contextual knowledge and meaning. This shift has revived interest in how the brain works because educational psychology is more important in New Learning than pedagogy and didactics.

New Learning also emphasises the importance of motivation in the learning process. This is because many New Learning schools in the Netherlands are based on the social constructivist learning theory, which assumes that learners acquire knowledge and skills by actively constructing or building new ideas or concepts based upon their current and past knowledge. Learning has to start from the pupil's personal learning requirement and motivation. In the mainstream New Learning movement, pupils are therefore asked to reflect on their own learning requirements. Once they have expressed those requirements, they are made responsible for their own learning process.
The assumption is that it is motivating for pupils to work on their own learning requirement, and that they take responsibility for their learning process.[59] This is underlined in New Learning curricula in secondary vocational education, where 'motivation' is even identified as one of the competencies: the issue of motivation is placed squarely with the pupil. Traditional education does not address the issue of motivation specifically; in New Learning, the school's key requirement is that a pupil should be motivated, and he is explicitly held responsible in this respect.

In the New Learning approach at Slash/21 and Wittering.nl (see also subsection 4.5.2), motivation is linked to information theories about learning. Information is data that is interpreted, and knowledge is information that has relevance within a person's existing mindset. To turn data into information and subsequently into knowledge that makes sense for an individual, the data and the individual must be linked. The data should play a role in a problem-seeking process in which the individual is involved. If not, it remains data as such. For example, a textbook describing Ohm's law has no meaning for a child who reads it merely as a text and learns it by heart. The nature of that text changes dramatically when read by someone who is trying to solve a problem concern-

58 in Dutch Het Nieuwe Leren.

59 In the former subsection 2.6.1 this assumption is challenged by the author Jelle Jolles who argues that neuroscientific research on functional brain maturation indicates that the developing brain needs an 'external' motivator, i.e. a pro-active teacher, until adulthood. According to him these findings are in conflict with the concept of New Learning that states that education should facilitate the autonomous learning process in students.

**Figure 17**
*Gaming appears to motivate children by letting them compete with themselves and challenge themselves to reach a higher level just beyond their present ability. By Karel van Loon.*

ing the strength of an electrical field. He will be motivated to turn the data into information. In this approach, motivation is linked to the interaction between external stimuli or data and the individual's problem focus. New Learning therefore aims to get pupils thinking about problems instead of providing them with textbooks.

The need for real motivation — and emotion — is only relevant for learning situations where it is important to give personal meaning to a context or problem. If learning by heart suffices, then motivation is not vital. Repetition and rehearsal are important for building up routines such as welding or French conversation. Motivation will help, but it is probably not a decisive factor. The nature of the learning task determines the relevance of motivation.

All these considerations raise many questions for the neurosciences and cognitive sciences:

– It seems that without a drive, or with inappropriate drives, there is no motivation. What does that mean for children who start the day without breakfast, or for young adolescents who are entering a new world where they are influenced by hormones that draw their attention to the opposite sex?
– Is there a difference in learning outcomes — e.g. in terms of knowledge retention and matching neural changes — when the learning content is approached as information as such, as opposed to learning content within a problem based context?

– Is IQ more relevant when learning takes place without a relevant problem–based context?
– When is motivation important (i.e. in what kind of task) and when is it not?
– What is the effect or how big is the effect of fun or enjoyment on learning processes and learning outcomes, in terms of optimal neural strategies and changes?
– Within the context of problem-based education, when is learning more effective: when the problem arises from personal involvement in the context, or when studying a general case to which the problem is related?

**Box 8: The practitioner's questions about motivation in relation to gaming**

Attempts to inspire pupils nowadays focus merely on their intrinsic motivation[60], resulting over the past twenty years in teachers who favour methods that make learning fun. One of the most challenging problems facing teachers today is to hold the attention of their pupils in the classroom. In their efforts to solve this problem, they have caught on to the fact that computer gaming does what they are finding increasingly difficult to do: motivate children to learn (see Figure 17). But are games the solution? What do children really learn from gaming? Does learning need to be fun? There are other forms of motivation, for example extrinsic incentives.[61] In gaming, the extrinsic social reward of reaching a higher game level appears to be very important [Johnson, 2005]. We also see this in the motivation of children who are about to sit exams. Research could therefore explore the neural or mental mechanisms behind intrinsic and extrinsic motivation, and whether learners differ in their sensitivity to intrinsic or extrinsic motivation and to what extent.

Another important issue in relation to motivation is self-esteem or the mechanism of self-efficacy: the pupil's perception of his own competence. Gaming appears to motivate children by letting them compete with themselves and challenge themselves to reach a higher level just beyond their present ability. Children who perceive themselves as competent tend to have higher aspirations than children who judge their own abilities as poor. Consequently, the latter group needs to be challenged more. Is there a neural or cognitive basis for something like self-esteem and uncertainty? Can self-efficacy be measured? How can we use this knowledge to support able and self-confident children to make the best of themselves and to challenge learners who lack self-esteem? The answers to these questions could help us design personalised learning materials just beyond the students' current level of development, i.e. applying Vygotsky's concept of the 'zone of proximal development'.

*Jaap van Loon*[62]

**60** Intrinsic motivation refers to motivation to engage in an activity for its own sake. Participating in this activity is its own reward because it is enjoyable.

**61** Extrinsic motivation is the motivation to engage in an activity as a means to an end. We participate in this activity because we believe it will lead to desirable outcomes, such as a reward or avoidance of punishment. Further reading: [Schunk et al., 2008].

**62** Director of ThiemeMeulenhoff and Chairman of the Group Educational Publishers of the Dutch Publishers Association.

## 4.7 Conditions for the successful implementation of personalised learning

*Jan Rispens*[63]*, Frederik Riemersma*[64]

Personalised learning has been presented in previous sections as a particular direction for future neuroscientific and cognitive scientific research, the aim being to adapt evidence-based educational innovation to individual differences. The authors explored the need for personalised learning from the perspective of both science and educational practice. Now we would like to focus briefly on the ins and outs of introducing a personalised learning system for pupils aged four to eighteen.

Introducing personalised learning obviously implies a major change to standard instructional procedures. One of the effects is that differences between students will increase, as it is no longer the teacher alone but also the pupil who decides how much and how quickly he or she will learn. We can therefore expect to see obvious differences between pupils and their requirements. Class management will consequently become much more complicated, and new materials will be needed, geared to the differing interests of the pupils. Teachers and school managements will have to adapt to these new demands, something that will not only cost money — for example for training and to develop new instructional methods and materials — but will also require the cooperation of those involved in this innovation. Another reason why personalised learning might be especially hard to introduce is that the concept is still 'under construction'. Its precise meaning and expected results will be unclear for the time being; it is also not certain whether it may have unintended consequences, both relevant and irrelevant, or even detrimental to the intended results.

In short, introducing an innovation of this kind into a system requires a careful analysis of the pros and cons. In this final section, we would therefore like to consider:

- The *conditions* under which personalised learning should be elaborated, disseminated and implemented, i.e. evidence-based practice (subsection 4.7.1), a network organisation (subsection 4.7.2), a community of practice (subsection 4.7.3) and a long-term innovation agenda (subsection 4.7.4).
- The possible social and ethical *consequences* of introducing personalised learning, based on the neurocognitive monitoring of individual pupil abilities (subsection 4.7.5).

**63** Emeritus Professor of Pedagogy, Utrecht University.

**64** Council Officer, Education Council of the Netherlands.

### 4.7.1 The need for evidence-based practice

*Jan Rispens*[65]

As stated above, introducing an innovation into the current educational system requires us to analyse the potential gains and losses or costs in detail. One important question is the validity of the innovation: will the new approach live up to its promise, i.e. will it mean an improvement? The answer to this question requires careful empirical research. The claims made for a new approach must be validated empirically before a decision can be taken about its introduction. Many changes in the Dutch educational system — sometimes major ones such as New Learning — have been introduced without the benefit of empirical data. As a result, discussions about new procedures, materials, approaches, etcetera cannot be resolved because we lack empirical evidence about their effects. It is for that reason that we must know the facts about the effectiveness of personalised learning, and not only be able to explain the philosophy or the concepts that underlie this new approach.

About three decades ago, the notion of 'evidence-based practice' emerged in the fields of medicine and mental health care. This approach requires the claims made for a treatment to be subjected to a rigorous empirical test by answering the question: is there sufficient empirical proof supporting these claims? In most cases, an RCT (randomised controlled trial) paradigm is applied, in which an experimental group receives the new treatment and a control group is administered a placebo. Reviews of research reports suggest that this approach helps practitioners choose between various treatments, based on data about their effectiveness. But can this concept also be used in education to test the validity of the concept of personalised learning?

In 2006 the Dutch Education Council [Onderwijsraad, 2006] stated that evidence-based education is to be preferred in the case of future innovations. Evidence-based research should therefore be encouraged, although the report mentions a number of precautions, such as costs in relation to benefits.

One should not underestimate the problems of applying a sophisticated research design in field trials. For example, in order to guarantee that the experimental treatment or instructional material will be applied properly, manuals or protocols are provided that prescribe — often in painstaking detail — how the practitioner is to proceed. In many disciplines — including teaching — practitioners are not accustomed to adhering in detail to a manual. As a result, they often do not accept the new material and refuse to cooperate.

65 Emeritus Professor of Pedagogy, University of Utrecht.

The literature on evidence-based practice stresses how vital it is to incorporate the expertise of practitioners [Chambless and Ollendick, 2001; Kendall, 1998]. The report by the Dutch Education Council points out the importance of this conclusion by distinguishing between the use of hard scientific research designs, such as RCT, and 'softer' procedures, such as case studies, surveys and expert opinions. Both methods should be used. It is important to have field workers contribute to the research design of a new procedure, both in the initial phase of development and during field trials. Close cooperation between researchers and practitioners can help legitimise research.

Another important lesson pertains to the start of a research project. Research reviews indicate the necessity of performing an extensive search of the literature, including reports by practitioners about their experiences, resulting in a database describing all the available empirical evidence related to the methods and materials to be used.

Introducing the notion of personalised learning into our educational system requires research demonstrating the effectiveness of this concept. Any such introduction should therefore be the joint responsibility of researchers and practitioners. One option is for scientific institutes to assemble an interdisciplinary team of neuroscientific and cognitive scientists and experts in the field of learning and instruction and then set up a network with a number of schools. Development and testing of various applications of personalised learning in field trials should be a joint endeavour resulting in close cooperation between researchers and field experts. This network concept will be described in more detail in the following subsections.

### 4.7.2 The need for a network organisation

*Frederik Riemersma*[66]

One vital requirement for mobilising the scientific resources and evidence underpinning personalised learning is to introduce scientists — neuroscientists, cognitive scientists and educational scientists — to the concept of personalised learning. Practitioners in the educational system, i.e. teachers, school directors and policy-makers, will also have to be made aware of the importance of personalised learning. Raising consciousness within the educational system will require an information campaign promoting the idea of personalised learning. In fact, such a campaign has already been launched; some leading Dutch organisations – including the Netherlands Organisation for Scientific Research (NWO), the Royal Netherlands Academy of Arts and Sciences (KNAW), the Ministry of Education, Culture and Science (OCW) and

66 Council Officer, Dutch Education Council.

Maastricht University – are already turning the spotlight on the concept of neuro–evidence-based learning [e.g. Jolles, 2005].

What is needed to initiate such an awareness campaign is an acknowledged national organisation that advocates personalised learning-based practices. It could consist of a pressure group, i.e. a networking organisation that owns the concept of personalised learning. Its task would be to elaborate the concept and promote it within the educational community by introducing the idea and disseminating and implementing practices at a reasonable cost. At the same time it should be keen to share its ownership of personalised learning with other groups and organisations by sharing its knowledge, know-how and resources.

This personalised learning organisation may be a networking organisation uniting several existing institutions or parts of institutions — universities, research institutes, innovation groups, schools, etcetera — that care a great deal about the concept of personalised learning.

It is important that the members of this alliance between science, schools and government work together to launch evidence-based pilots in the first five years, intended to bring the concept of personalised learning from the 'laboratory' into the classroom. One good idea is to found a number of 'academic schools', i.e. schools that experiment with the concept of personalised learning in close cooperation with university departments.[67] This means that practitioners and scientists should collaborate closely at all levels, if evidence-based personalised learning is to be properly developed (see also the next subsection). These local pilots or academic schools must preserve the core of the personalised learning concept while respecting local characteristics.

The national network organisation should monitor and evaluate the pilots or practices based on personalised learning so that the concept can be disseminated to other schools and on a national scale.[68] Evidence concerning intended and unintended results and the process of implementation can be used to refine the concept, to support the implementation process and to make it possible to learn from good practices.

Personalised learning can be disseminated and implemented in various situations, for example in different school populations or in different geographical situations, but also in various relevant 'cognitive' subjects such as reading, languages or arithmetic.

**67** In 2005, ZonMW launched a programme initiating 'academic workplaces' in the Dutch health care system, a concept similar to the 'academic schools'. The programme received an overall positive evaluation. One important insight was that academic thinking takes time to develop; a financial investment of more than four years per 'academic workplace' is therefore essential.

**68** Although from time to time an independent evaluation will be needed.

### 4.7.3 The need for a community of practice

As stated in the previous subsection, the concept of personalised learning and practices should be developed at local level, with external innovators, supporters and internal practitioners cooperating closely. Such close cooperation is indispensable for several reasons, as lessons of the past demonstrate. For example, most recent innovations were regarded as having been imposed from outside the system. Practitioners easily felt that they had lost control over their individual situation and had no sense of ownership concerning the intended innovation. Furthermore, outsiders, staff and school principals often have differing attitudes towards the intended innovation. In most cases of large-scale innovation, staff and school principals do not see any reason to change their existing practices. Instead, they argue that they lack the right conditions, the time and the money, or the knowledge to do so. Most of the time they are right, as innovators from outside the school often neglect to create the necessary conditions to implement new ideas.

Other inherent features of the educational system may also impede implementation of personalised learning. For example: educational practitioners are accustomed to working autonomously in their primary task, and that makes it difficult for them to cooperate with others in the primary process of teaching. Most of them are also 'non-interventionist', meaning that it is hard for them to see how something new fits into their specific situation [Fullan, 2001].

These considerations underline the need for local communities of practice in personalised learning in addition to a national network organisation. Such a community should consist of persons from inside the school system (i.e. school principals, teachers, administrators) and from outside the system, i.e. scientists, policy-makers, consultants, etcetera. The community should take it upon itself to enlarge the knowledge base of personalised learning on three levels: personalised learning as a concept (propositional level), personalised learning as a technology (application level) and personalised learning as education (level of specific educational activities). This would allow the practitioners' knowledge to be used to direct neuroscientific and cognitive research. The network referred to before should play a stimulating and supporting role in such local communities of practice. For this to happen, several conditions must to be satisfied.

#### Time

The process of introducing innovations at school level is neither easy nor fast. There is a constant push from the outside to reform, which leads to a certain amount of fatigue and disillusionment with people who work in educational practice. Although change will as a rule be met with resistance, such resis-

**Example XII**

**There is no single best way to memorise a series of objects. In fact, there are four main strategies, and two of them are more effective than the others: visual inspection and verbal elaboration. They each use a different network of brain regions.**

American psychologists wanted to know why some people are better at learning than others. They suspected that the individual differences in performance could be traced to differences in learning strategies. To study this, they selected 29 right-handed students of 18 to 31 years of age. They familiarised the students with 240 pictures of living and non-living single objects, and got them used to lying in a functional magnetic resonance imaging (fMRI) brain scanner.

# Memorisation takes on many forms

Following the familiarisation session, the psychologists showed the students 120 images pairing two of the single objects. For example, they saw a turkey sitting on a horse, a pig on top of a large key, or an oversized banana on a small truck. The students were told to study these pair images for a memory test. Meanwhile, their brains were scanned.

After scanning, the volunteers were asked to pair single objects to test their memory for associations, and to indicate how often they had used each of ten possible memorisation strategies. The subjects used four of the ten strategies more often than the rest: visual inspection, verbal elaboration, mental imagery, and memory retrieval.

The participants using the visual inspection strategy looked carefully at the content of images. Those using the verbal elaboration strategy made up sentences about the objects they saw. The subjects working with a mental imagery strategy imagined cartoon-like images, and those using a memory retrieval strategy associated the meaning of the objects with their personal memories.

The participants reported using multiple strategies during learning. Those who used the largest number of different strategies were better at remembering object associations. Those who mainly used the verbal or visual learning strategies had better overall memory performance than those who did not.

Original publication: Kirchhoff al.(2006). *Neuron*, 51, 263

The brain scans revealed that the participants who used the verbal elaboration strategy often had significantly more brain activity in a network of brain regions in the left-frontal area of the brain. This area plays an important role in thinking about words and processing them. Students who used the visual inspection strategy had specific brain activity in the left-rear area of the brain, which is involved in viewing and retrieving visual information.

The study shows that not every person memorises information in the same way. These individual learning strategies appear to be based in different areas of the brain, each of which may influence memory performance separately. Findings such as these can be useful to teachers who want to help their students study more effectively. They may also be helpful in creating more effective behavioural therapies for people with memory impairment, for example due to Alzheimer's disease.

tance can also be a source of information for further improvement [Thomson, 2007]. The timescale for introducing personalised learning will differ from one group to the next, i.e. students, teachers, policy-makers, bureaucrats, etcetera Introducing it at school level will require commitment, especially from the teachers, but commitment alone is not enough: everyone involved will need time to explore, to reflect on their individual activities and ongoing processes, and to adapt their routines to the new concept. Moreover, most innovations require additional funding to be set aside to give teachers and other persons involved time to adjust, most certainly in the experimental phases.

### Support

Besides setting aside the necessary time, a support system is also required. We have already mentioned the community of practice. In addition, the personalised learning organisation described above can deliver expert knowledge, emotional support and funding. The school can also organise its own support system, for example a School Improvement Group (SIG) for personalised learning, consisting of four to eight persons including the school principal. The members of this group should represent all the people involved in the school. As a steering committee, it should discuss, modify and plan the priorities areas defined by participating in the personalised learning programme, communicate openly and frequently with everyone involved, and collect data to enable an ongoing evaluation, so that personalised learning can be converted into evidence-based innovation.

It is important to make the move towards personalised learning high profile within the school organisation, and to share findings internally and with other schools interested in personalised learning [Thompson, 2007]. The community of practice should therefore create a platform for discussing new ideas, progress and the results of monitoring and evaluation. Open communication is important for ensuring a broad basis of support for the innovation and for reinforcing a sense of ownership.

In conclusion, the time perspective is very important. We must avoid the pitfall of trying to change too much too fast; the danger then is that there will be a brief burst of activity followed by a relapse into long-established ways. That is why we need a long-term innovation agenda.

### 4.7.4 The need for a long-term agenda for personalised learning

It is difficult to introduce changes in the educational system because there are so many factors resisting change. It is therefore very important to begin deliberately and 'slowly', giving both external parties and insiders time to understand each other, clarify their mutual intentions and consider carefully all the implications of the innovation they intend to introduce. People must become aware of personalised learning and envision how they might use it. What is required is a long-term innovation agenda of fifteen to twenty years that gradually builds a sustainable implementation strategy (in addition to a research agenda, see section 4.8).

A long-term agenda can also prevent unintended side-effects (see next subsection). For example, there is the risk that personalised learning will become individualised learning, and that social development of pupils will be neglected. Another 'doomsday scenario' is that the concept will be adopted by only a small number of highly competitive schools that claim ownership and prevent further development.

In summary, a long-term innovation agenda based on personalised learning is needed in order to:

- Build up a national functioning organisation to promote and monitor the concept and build learning circles of networking organisations at local level. Both are needed to continue developing the concept of personalised learning, i.e. to develop learning materials and assessment instruments.
- Relate personalised learning to the national policy on teachers and teacher education. Teacher development and professional growth are needed to successfully implement this innovation, but so far the policy on teachers and teaching has had its own dynamic and has been kept more or less separate from other policy domains [McDaniel et al., 2007]. The necessary condition of coherence between educational innovation and teacher policy has therefore not been met. It will take time to get the policy-makers concerned involved in the concept of personalised learning.
- Connect personalised learning with other developments at local and national level, for example the increasing use of information and communication technology or competency-based vocational education.[69]

After several years of experimenting with the concept of personalised learning, an evaluation should be performed at national level in order to collect more solid evidence for the intended results [e.g. Onderwijsraad, 2006]. Last but not least, sustainable innovation requires a firm financial basis.

**69** Vocational education is increasingly directed at developing competencies and not just at acquiring a diploma in order to improve the link between education and the labour market.

## 4.7.5 Social and ethical aspects of personalised learning

*Sandy Litjens*[70]

The preceding subsections will have made clear that the goal of personalised learning is to optimise a child's development. In contrast to the current situation, all children will be appropriately challenged, according to their specific needs, capacities and motivation. This method of education should be beneficial for both the individual and society: children's abilities will be recognised early on and the child will be highly motivated and eager to learn, thereby getting the most out of himself. Society will benefit by having optimally educated members, thereby boosting the knowledge economy. But there are also down sides to personalised learning, both for the individual and for society. What are they and are we willing to accept them for the sake of the benefits that personalised learning will bring? This subsection will point out, but not address in detail, some of the social and ethical questions related to personalised learning.

### Investment in the future

Innovations and new technologies are often more expensive than current practice, especially in the first few years after implementation. Personal learning will require changes to the way education is organised, information technology (i.e. adaptive cognitive systems) and possible neuro-imaging technology (i.e. monitoring individual learning abilities) — and all of these things are costly. Who will pay these costs? Is the government ready and able to take responsibility for making personalised education accessible to all? Equality in good quality care and education has always been highly valued in the Netherlands, but rising costs are altering this belief. Nowadays, people are willing to accept the fact that money can buy more and better quality of care and education, provided that everyone has access to sufficient quality. Will personalised learning be reserved for the rich, possibly resulting in more social inequality? Or will we be able to make personalised learning affordable and therefore accessible to everybody?

### Confidentiality

Like genetic screening, monitoring someone's learning abilities (in the future perhaps through brain imaging) produces sensitive information about that individual. In the case of brain imaging, it not only provides the information that we want at that time, but also other knowledge about that person's brain. For instance, brain imaging may allow us in the future to capture the emotional status of a respondent while he is performing a task. In time, it will likely be possible to analyse much more than his psychological state, e.g. whether he is

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susceptible to addiction or stress. It is therefore important to consider who is entitled to this information. Like a person's medical details, a pupil's brain and cognitive profile should be kept confidential and not be handed over to third parties, such as insurance companies or future employers, who may want to use — or abuse — such information. On the other hand, some information may be relevant when applying for life insurance or disability insurance. What facts can a person withhold and which ones should be disclosed? The issue of confidentiality raises many more questions. How do we handle the risk of stigmatisation and social exclusion of pupils whose brain and cognitive profile has become public? Is confidentiality feasible in a public domain such as education? Since it may not be easy to maintain strict confidentiality, it is important to think about how wrongful use and abuse of brain and cognitive profiles can be prevented.

### Individual risks

Another important ethical question is what to do if a pathology or a pathological risk is detected when monitoring individual students' learning abilities. The Stanford Centre for Biomedical Ethics has published various papers on the incidental detection of brain anomalies in the MRI scans of healthy volunteers. For example, of a group of 225 neurologically healthy children aged one month to eighteen years, 21% were found to have an incidental brain abnormality [Kim et al., 2002]. Not all of these anomalies will be serious or clinically relevant. For instance, an MRI scan cannot distinguish between a malignant tumour and a harmless cyst, making further diagnostic procedures necessary. Of the aforementioned children with incidental brain abnormalities, for example, 38% required clinical referral. Some brain cysts may never cause problems, in which case alarming the person causes unnecessary anguish. False-positive scans or untreatable pathologies may also result in needless anxiety. Moreover, MRI screening followed by additional — possibly unnecessary — diagnostic interventions will put further pressure on the health care system. These considerations raise many questions: who is responsible for deciding whether a pupil should be notified and treated for an assumed pathology? Who is responsible for actually informing the pupil? Do pupils or their parents have the right not to know? And how do we deal with the potential increasing burden on our health care system? To a certain extent some of these issues are the same as those raised as a result of medical screening of the population. An important difference, however, is that the purpose of medical screening is early diagnosis and prevention of diseases, whereas in this case monitoring is meant to optimise a child's education, with medical information being merely a by-product. Our appreciation of the goal — what value do we place on optimal education? — is therefore important in answering the above questions. In any case, if society accepts personalised learning, it also needs to accept its side effects. In fact, every pupil being monitored (or their parents) should be informed of the possible by-products, especially in the case of brain imaging. The principle of informed consent is hence one of the requirements for the responsible implementation of personalised learning.

### Medicalisation

The concept of medicalisation is hard to define. The term is often used to denote the increasing medical interference with 'natural' life-events such as having children, menopause, ageing and dying. From a broader perspective, medicalisation means solving societal issues by a medical approach. One example is that women today who have passed their fertile period can still have children owing to various new kinds of medical interventions. It is important to note that the term medicalisation is normative and that its use depends largely on our views of society and mankind. In this case, the question is: can personalised learning be regarded as the medicalisation of education? The concept of personalised learning involves monitoring the cognitive and brain profiles of pupils — possibly by imaging children's brains with such techniques as fMRI and EEG. Techniques that currently belong in the medical domain will be used for a purpose outside that domain, i.e. effective and efficient learning, and that indicates a tendency towards medicalisation. In addition, children's competencies or their lack thereof will be measured, resulting in a cognitive profile. It is conceivable that some of these profiles, e.g. the ones lacking specific abilities regarded as indispensable in our current society, will be regarded as disorders. Human characteristics or behaviour previously considered normal will thus become abnormal. A trend of this kind also indicates a tendency towards medicalisation. However, as we have already said, one's view of society determines whether or not some profiles will be considered undesirable and therefore medicalised.

### Conclusion

In addition to its obvious benefits, personalised learning may also have disadvantages. In the end, it will only be acceptable if the benefits outweigh the adverse effects. One important precaution that we should take before implementing personalised learning is to investigate society's values and opinions on such issues as the integrity of our brains, the costs and benefits of brain or cognitive profiling — including the potential use and abuse of the information — and the importance of getting the most out of ourselves and our children. The result of such a debate will predict whether or not personalised learning will be embraced as a worthy method to educate our children. It is important to note that social opinion can change over time. If society is not ready for personalised learning now, it may very well be in the future.

## 4.8 Discussion

*Jan Rispens*[71]*, Ira van Keulen*

This chapter explores how learning might benefit from progress made in the neurosciences and cognitive sciences in the next few decades. It looks in particular at personalised learning. We argue that new neuroscientific and cognitive scientific findings will help solve a basic educational problem, namely how to adapt instruction to individual differences. Customised learning has always been a distant dream. Despite many attempts during the past century — for example in the Reform movement of the nineteen twenties or, more recently, the development of such systems as adaptive instruction — gearing instruction to individual needs remains a challenging problem for a classroom teacher. The main reason is that we still lack insights into the various strategies and procedures of learning that children apply during a learning task. Due to that lack of knowledge, our instructional materials and the traditional teaching methods do not take account of these differences. Children are confronted with forms of instruction that in many cases do not invite them to participate, are not stimulating enough, and do not fit in with their type of learning.

We speculate in this chapter that in the next few decades, neuroscientists, cognitive scientists and educational researchers will together make considerable progress on solving this problem. The basic and cognitive neurosciences are giving the cognitive sciences a solid biological basis for developing theories about learning and individual differences. As a result, cognitive theories can test — on a fundamental level — notions as to which parts of the brain are involved in various types of information processing. That means that we will be able to validate theories about information processing in relation to various types of learning tasks and about individual differences in information processes. Likewise, neuroscience can provide behavioural measures or measures of learning outcomes for individual students. This in turn allows educational researchers to develop and test various strategies for adapting instruction to these differences. As a consequence, instruction can be geared to the individual needs and preferences of children, resulting in personalised learning.

Personalised learning represents a notion of learning that is not compatible with the traditional view of how children should learn. It is more than just another label for a method of adapting instruction to individual needs. Personalised learning is primarily a challenge to the educational system. It requires a school (or an environment) that creates the opportunity to learn in

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a way that is determined by the individual child. His or her needs, interests, ways of exploring, curiosity, prior knowledge, and speed of information processing are of paramount importance to the learning process that takes place in this system. This is not to imply that children determine the learning content. On the contrary, personalised learning supposes a learning environment based on a careful analysis of what children should be learning at a given time. Learning materials are designed in such a way that children can take different alternative routes and vary in the speed and depth of their processing, but in the end they must have learned the content prescribed by the curriculum.

Personalised learning requires a solid body of knowledge about how children learn and how a teacher should start, support, sustain and, if necessary, correct and improve the individual child's learning process. We expect to see significant advances in this knowledge in the next few decades, especially if the neurosciences and cognitive sciences take individual learning differences as a starting point for research. However, we are still far from knowing all we need to know. There are still many gaps in our knowledge.

Firstly, this chapter illustrates that, while our knowledge of the brain is growing rapidly, it is limited at the moment. Although we know a lot about the various (molecular, cellular, network) levels of the brain, we do not know much about its structure in relation to how we function in everyday life or even in relation to our behaviour. As we saw in section 4.4 on basic neuroscience, we also need much more micro-level research to understand the growth and development of the human brain. Since a considerable amount of our knowledge has been derived from animal experiments, the question is whether these insights hold true for humans. Another issue that we need to address pertains to individual differences, for example varying patterns in early brain development. As a result, the actual contribution of the basic neurosciences to cognitive theories is still limited. Findings from cognitive neuroscience revealing brain activation patterns in specific learning tasks are more enlightening because they link brain activity to specific cognitive processes (see example XII). In general, however, cognitive theories still lack a solid biological basis, although we are slowly and gradually discovering neurophysiological evidence for behaviour (see examples I, III and XVI), e.g. the mirror neuron system as a basis for social learning.

Secondly, we must improve the connection between cognitive science and educational research. For example, section 4.3 argues that cognitive science can contribute significantly to instructional procedures if we properly apply empirical data available on the way memory plays a role in learning, or on the effects of feedback on learning, in teaching materials and procedures. It is difficult to unlock knowledge from the cognitive sciences and neurosciences for educational scientists and practitioners. Each discipline has its own terminology, making it hard for each other to keep track of scientific progress in other fields. Once the various concepts have been clarified and aligned as a common ground, a professional dialogue between the various stakeholders is of paramount importance [Jolles, 2006].

Thirdly, we must avoid the tendency in educational practice to implement new ideas and procedures without data about their effectiveness (see subsection 4.7.1). Better teaching implies evidence-based practices. Adaptive cognitive systems, an essential element of personalised learning, are inherently evidence based, for example. As instructional tools, these systems themselves collect the data on the neurocognitive profiles and progress of individual students needed to evaluate the effectiveness and applicability of personalised learning. In general, it is important to understand the consequences of innovations — such as personalised learning — before launching them on a large scale.

### 4.8.1 Outline of a research and development agenda

Introducing personalised learning and instruction within fifteen to twenty years will require research. In this last subsection, we briefly outline a research programme for the coming decades. It includes various topics mentioned in the previous sections.

#### Brain development and sensitive periods

We concluded in various sections of this chapter that our knowledge of brain development is limited in three different ways: on the detailed micro level, in relation to cognition function and psychological processes, and in relation to individual patterns. We need to know much more about how the brain develops anatomically, in order to answer important questions about patterns and phases of growth. We also require a detailed understanding of how the brain develops — in terms of its flexibility, sequences of development, potentially adverse conditions, and positive conditions for growth — in order to connect the outcome of brain research to cognitive theories.

Of special interest to educational practice are the ‘sensitive periods’ in brain development. These are specific periods of neural plasticity, restricted periods of time in which certain brain areas or functions develop. There is still much debate in the neurosciences and cognitive sciences about the existence of these periods and their importance, as will have been clear in the various sections of this chapter: each author approaches the concept differently. All agree, however, that the developing individual cannot learn everything in every developmental phase. A child cannot learn certain skills if it has not yet mastered the basic, underlying skill. The OECD was very reluctant in its report to admit the existence of these specific windows of opportunities in brain development. Unlike binocular vision, there is little high-quality research supporting the existence of such periods for a specific brain or cognitive function. If we stretch the concept a bit more, we can give more examples that can be classified as sensitive periods. One is that a lack of maternal care in the first year of life leads to introversion and negatively influences learning performance. We *do* know that there is no sensitive period for some abilities, for example learning from experience in an enriched environment. The period during which the brain is positively susceptible to an enriched and challenging environment is not restricted. This kind of plasticity does not stop in adulthood, although it does decline with the years.

Still, the concept of sensitive periods of plasticity could be relevant for the evidence-based innovation in education represented by personalised learning. If it turns out that sensitive periods do exist for various brain or cognitive functions, we would be able to facilitate brain development by adapting instruction to such sensitive periods and optimising the material to make it challenging.

### Individual differences

Brain development and the development of cognitive abilities influence each other. As the brain develops, it permits cognitive abilities to develop; and the use of cognitive abilities allows further brain development. We saw in section 4.4 that both genetic and environmental influences are decisive in brain as well as in cognitive development. Genes determine the minimum and maximum boundaries of the brain's structural and functional characteristics. Ultimately, however, brain development is influenced by environmental factors. For example, during the first years of life — including during pregnancy — dramatic environmental influences such as isolation, stress and alcohol and drug use can play a particularly decisive role in language, social and intellectual functions. Psychosocial factors (parenting, the physical environment, educational opportunities) may also underlie differences between children.

The influence of both genes and environment results in considerable individual differences in children's ability to learn, and in how and how efficiently, they acquire information and experiences. Unfortunately, the neurosciences basically have no tradition of researching individual differences. If we want to introduce the notion of personalised learning, we need more insights into individual differences, and especially at the basic neurobiological level: we need to know about differences in perception and information processing. The potential contribution of the neurosciences to validating theories and ideas developed in the cognitive sciences depends on such anatomical and neurobiological data. The developmental neurosciences must also focus more on evaluating and monitoring individual developmental tracks — more than on group effects. Such knowledge is needed for the neurocognitive profiling of individual students, one of the conditions for developing personalised instruction. Over the next few decades, we need to explore psychosocial factors in greater detail, so that we have a better idea of how to handle individual differences caused by these factors in instruction. To summarise, we must address the development of personalised learning from many different angles and force the representatives of the various disciplines to communicate and bridge the many gaps between their fields.

### Relationship between neurocognitive functions and learning

Research findings show that specific developmental problems in neurocognitive functions result in an individual being susceptible to specific disorders and also to learning disabilities. For example, problems in motor functioning, language abilities and attention regulation in early childhood are associated with a susceptibility to psychosis. Other research shows that specific cognitive profiles identified within a learning-disabled population can result in specific learning disabilities and social dysfunctioning. These findings demonstrate a relationship between specific neurocognitive strengths and weaknesses on the one hand and learning abilities on the other. Although we know something about the relationship between neurocognitive functions and general learning ability, we know virtually nothing about the relationship between specific functions and specific aspects of learning. For example, we know that attention and the executive aspects of attention are relevant to controlling and processing incoming information, but we do not know which neurocognitive functions — for example attention, executive functioning, memory, social reasoning, etcetera — contribute to a child's ability to master various different aspects of learning at school, such as reading, writing, algebra and geometry. It is particularly important in personalised learning to be able to predict how a child handles (commands) different aspects of learning on the basis of its neurocognitive functional development. Of course, we would also like to know which interventions, when applied to relevant neurocognitive functions, have a positive effect on specific aspects of learning.

### Motivational processes and learning attitudes[72]

One of the major issues in the educational world today is how to motivate pupils. One of many complaints is that the educational system does not engage children's natural curiosity, or at least not to optimal effect. Children's

72 This subsection is based on the main results of a workshop held during the NWO invitational conference 'Brain, Learning and Education' in 2006, as described in the publication 'Brain Lessons' [2006].

curiosity is probably linked to the human brain's responsiveness to novelty or new stimuli, an essential evolutionary factor that enabled our ancestors to cope with a changing environment. It is vital for us to study this inborn tendency to react to novelty in order to improve our understanding of its potency for the learning process. Children's eagerness must be stimulated as much as possible (e.g. by gearing instruction more towards individual interests), and their learning experiences must be positive ones, as this helps the brain to process information more effectively. At the same time, research indicates that particular negative experiences and their emotional connotations could have a major impact on learning.

Research should monitor the educational situation closely and address the various aspects of motivation. Our current knowledge of the brain and of the neurocognitive and biopsychological mechanisms that form the basis of motivational processes could be used to understand these various aspects. We should also pay particular attention to the role played by those regions of the brain that regulate emotion and motivation and their integration with sensory and motor functions. Certain parts of the prefrontal cortex appear to be of major importance in that respect, and these brain structures develop until well into the twentieth year of life.

It is essential to investigate in greater depth how children's emotional problems and their attitudes to learning and school affect their performance. Many children are regularly upset or anxious, have 'arithmetic phobia' or wrestle with other emotional learning problems. These problems can have a dramatic impact on their motivation to learn. Likewise, cognitive learning strategies should be more closely linked to children's emotional and motivational development and its stages.

### Intervention studies

Before introducing an educational innovation, we must collect data on its potential effects. Evidence-based instruction implies collecting empirical evidence about the effects of that instruction. We therefore require intervention studies in which we carefully test new procedures, materials, and changes in the organisation of the educational system. Innovation should not be implemented without data about its potential effects, in terms of both gains and losses. This will require close cooperation between researchers and educational practice. What we need to do in the next decade is to establish networks connecting research centres — in most cases, universities — to a number of schools. These networks will give researchers an opportunity to test their theories, and practitioners an opportunity to influence research by suggesting ideas, summarising practical experiences, and criticising research proposals.

We already mentioned the need for close, interdisciplinary cooperation between brain scientists, cognitive scientists and educational researchers. Such cooperation is a necessary condition for success, resulting in intense interaction with respect to the choice and description of research topics. The connection between these three domains is necessary because they are mutually dependent when it comes to applying knowledge in the field.

### A technology agenda

Educational technology — in terms of hardware and software — will play an extremely important role in introducing a far-reaching concept such as personalised learning into the educational system. Personalised learning requires all kinds of materials and tools. We have already proposed cognitive learning systems as a key element of personalised learning (see section 4.3). A cognitive system is an adaptive system that monitors various parameters of a pupil's learning process, resulting in an individual cognitive profile. The system then presents the instructional material in such a way that it matches the profile. Current insights in the field of cognitive science into meta-cognitive methods (how to learn) can also be applied in support of the learner. Although such cognitive systems already exist, they have rarely been used in educational settings. A technology agenda is therefore needed to determine what must be constructed and tested in the next few decades to facilitate personalised learning. In addition to the development of cognitive learning systems, that agenda might include the use of computer gaming to improve individual pupil involvement, easy-to-use imaging technology designed for use in educational settings or imaging techniques for diagnosing learning problems.

### Teacher training

Even after the introduction of personalised learning, teachers will remain of utmost importance. If we want to change the system, we must be sure that teachers not only accept and support the relevant changes but also act as change agents. They therefore need to be trained. Teacher training is an important issue in the process of innovation. Interestingly, Pickering and Howard-Jones [2007] studied how British teachers view the link between neuroscience and education. They found that teachers see information about the brain as highly relevant to a wide range of educational activities, including the design and delivery of educational programmes. Practitioners are also more interested in results directly relevant to classroom practice than theoretical developments, but at the same time they want to understand how and why certain brain-informed practices are useful. Moreover, they already rely on a variety of different information sources about the brain. The study concludes, however, that it is important to help teachers develop critical skills that allow them to question the sort of dubious brain-based practices and methods that are often offered to teachers in the United States and the United Kingdom. Teacher training of this kind may soon turn out to be of relevance to teachers in the Netherlands as well. As Pickering and Howard-Jones suggest that: *"Communication with practitioners may become a key factor influencing the success of attempts to enrich classroom practice with scientific understanding about the brain and mind."*

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# 5

# Evidence-based Judicial Practice

## 5.1 Introduction

*Ira van Keulen*[1]

Like in the domain of education, cooperation between neurosciences, cognitive sciences and law may improve judicial practice on the basis of scientific evidence, resulting in evidence-based practices. Indeed, current and future insights in the brain can inform criminal investigation, judicial process, detention and treatment of delinquents in many different ways. For example neuroscientific research can help legal specialists to understand a suspect when it comes to addictive or antisocial behaviour. There is also much to be expected of insights in the effect of punishment or proper treatment for delinquents: better diagnostics, different treatment strategies, determination of accountability, etcetera. This chapter focuses mainly on the contribution of the brain sciences to investigation and the judicial process, however. As a consequence the emphasis lies on the judicial impact of neuroscientific findings on the workings of memory, decision-making, lying and free will.

According to American neuroscientist Michael Gazzaniga, brain research findings are already beginning to leave their mark on the legal system. At the end of 2007 there were 912 cases before American courts in which brain sciences played a role. At the same time a research and outreach project was launched in the USA in October 2007, called The Law and Neuroscience Project[2].

1 Projectmanager, STT.

2 See www.lawandneuroscienceproject.org.

The initiators of this project are convinced that with a cautious and proper integration of the neurosciences, *"our justice system could have more accurate predictions, more effective interventions, and less bias."* An important aim of the project is therefore education and outreach: brain scientists need to understand the law and legal specialists need to understand the neurosciences.

In the Netherlands, there is no such project yet. Nonetheless, there was a conference 'Justice and Cognition', held in Zeist in November 2007, with the same aim as The Law and Neuroscience Project. The conference gave neuroscientists and cognitive scientists a platform to share their knowledge with legal practitioners and vice versa. The conference was organised by the Study Centre for Technology Trends (STT), the Rathenau Institute, the Netherlands Organisation for Scientific Research (NWO), study centre Kerckebosch and the Dutch Ministry of Justice and the Dutch Ministry of the Interior and Kingdom Relations. This chapter consists of summaries of the lectures at the conference by journalist Niki Korteweg (see section 5.2 to 5.10) and two essays on false memory detection through functional magnetic resonance imaging (fMRI) (see section 5.11) and the neuroscientific perspective on free will (see section 5.12). Latter essays were published earlier on in the journal 'Justitiële Verkenningen' (in English: Judicial Explorations) of the Research and Documentation Centre of the Dutch Ministry of Justice.[3] Hopefully these different initiatives will lead to a better match between the neurosciences, cognitive sciences and legal practice resulting in socially relevant research and the successful application of brain research in judicial process.

## 5.2 Did my brain make me do that?

*Lecture Michael Gazzaniga*[4]

The neurosciences — the branch of biological research that explores the functioning of the brain — are a growing field of research. Brain research findings are beginning to leave their mark on the legal system, and their impact will only increase, said renowned American neuroscientist Michael Gazzaniga. As the first speaker, he reviewed the present state of affairs in brain research and described what role research can play in the judicial process. "On the one hand, our knowledge of the brain helps to understand the thought processes and behaviour of a suspect, or to solve a case. On the other, legal specialists tend to overestimate the value of research data, for example brain scans, or they are presented in an overly simplified form. In that sense, brain science should not play a role in judicial process," said Gazzaniga.

3 After the conference, the journal 'Justitiele Verkenningen' published in cooperation with STT an issue on the subject of (neuro)science and the law in Februari 2008 (volume 34). See english.wodc.nl/publicaties/justitiele-verkenningen.

4 Professor of Psychology, Director of the SAGE Center for the Study of the Mind, University of California, Santa Barbara.

**Figure 1**
*Michael Gazzaniga at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

The law is entirely at odds with brain research in many respects, he said. The law focuses on individuals and divides matters into two categories: guilty or not, of sound mind or not. Brain research, on the other hand, often studies groups of people, and has repeatedly revealed the many shades of grey separating black and white. In order to integrate the neurosciences into judicial process, brain researchers must understand the law, and lawyers must understand the neurosciences. We are now taking the first steps in that direction.

## The Law and Neuroscience Project

Gazzaniga is the director of the earlier mentioned 'The Law and Neuroscience Project'. "The purpose of this project is to be able to identify what brain research specifically can and cannot do in judicial process and to stay abreast of developments in this area," he related. "We have judges, lawyers, brain researchers and philosophers involved in the project." The project consists of three research networks focusing on three major topics in criminal responsibility: Differing Brains, Addiction and Antisocial Behaviour, and Decision-making. Criminals often have problems in one of these three areas: they are addicted to alcohol or drugs; they are psychopathic; or they take decisions that a normal person would not take. Brain research has made major advances in these three areas. Once we fill in the gaps in our knowledge, we can apply our new understanding of the brain within the context of the law. "The project addresses countless issues," said Gazzaniga. "Should brain scans be used as evidence showing whether a defendant was accountable for his actions if merely seeing the scans already prejudices those present in the courtroom? How are brain research results changing the way we think of ourselves as people? When is someone responsible for his actions?"

## Free will and responsibility

Copernicus (1473-1543) claimed long ago that the sun — and not the earth — was the centre of the universe. Since then, the insights of such major minds as Galileo, Descartes, Darwin and Freud have made it ever clearer that man is not at the centre of all being. Today's researchers describe the brain as an automatic mechanism that controls our perception, attention, emotions, judgements and decisions. The general thinking is that the laws of nature decide what nerves look like and how they function. Nerves steer our behaviour and control what we do. Are there no other forces we can blame when things go wrong?

Our brain is a 'decision machine'. It is constantly taking decisions, day after day, second after second, every single moment of our lives. The brain collects information over the course of time, processes it, and ensures that we display behaviour appropriate to its observations. All of that very likely takes place even before we are aware of it. It takes approximately half a second (300 tot 500 milliseconds) for a decision taken by the brain to reach our consciousness. It was the pioneering American researcher Benjamin Libet (1916-2007) who discovered that delay in consciousness. He applied direct stimulation to the cerebral cortex and measured how long it took before the subject became aware of it. "If we accept the findings of modern brain research," said Gazzaniga, "then we must conclude that our brain makes us what and who we are. That means that by the time you become aware of something, your brain has in fact already done it."

It is possible to see what someone intends to do 300 to 500 milliseconds before they act. A group of researchers published an article in early 2007 describing how they could predict which of two buttons a subject in an fMRI brain scanner would press. The brain activity picked up by the scanner betrayed the subject's intentions. The causal chain theory advocated by some scientists and philosophers is as follows. If our mind is produced by the brain — a physical and determined entity — then the thoughts produced by our mind must also be determined. Viewed in this way, free will is an illusion. That means that we must reconsider the concept of what constitutes personal responsibility for one's actions. The legal system would then have to alter its assumptions. The question, according to Gazzaniga, is whether it should in fact do so.

## Interpreter

If free will is an illusion, why do people *believe* that they have a free will and are responsible for their actions? Studies involving split brain patients (which Gazzaniga himself carried out as a young researcher) have shed some light on the topic.

Split brain patients are epileptics who — in a last-ditch attempt to control major seizures — have undergone surgery cutting off the connection between the left and right hemispheres of the brain (i.e. the corpus callosum). Although they function normally in everyday life, things become interesting when a researcher shows them two different objects, one on the left side of their field of vision and one on their right side. The right side of the brain takes in what is on the left, and vice versa. In split brain patients, neither hemisphere knows what the other has observed, because the corpus callosum — the communication channel — has been severed. And only the left hemisphere can describe what it has seen, because that is where the speech control centre is located.

"In one of our first experiments, we showed the left hemisphere a chicken claw and the right hemisphere a snowy landscape," Gazzaniga related. "We asked the patient to select a picture from a series of images that most resembled what he had seen, first with one hand and then with the other. The right hand, controlled by the left hemisphere (the seat of conscious observation),

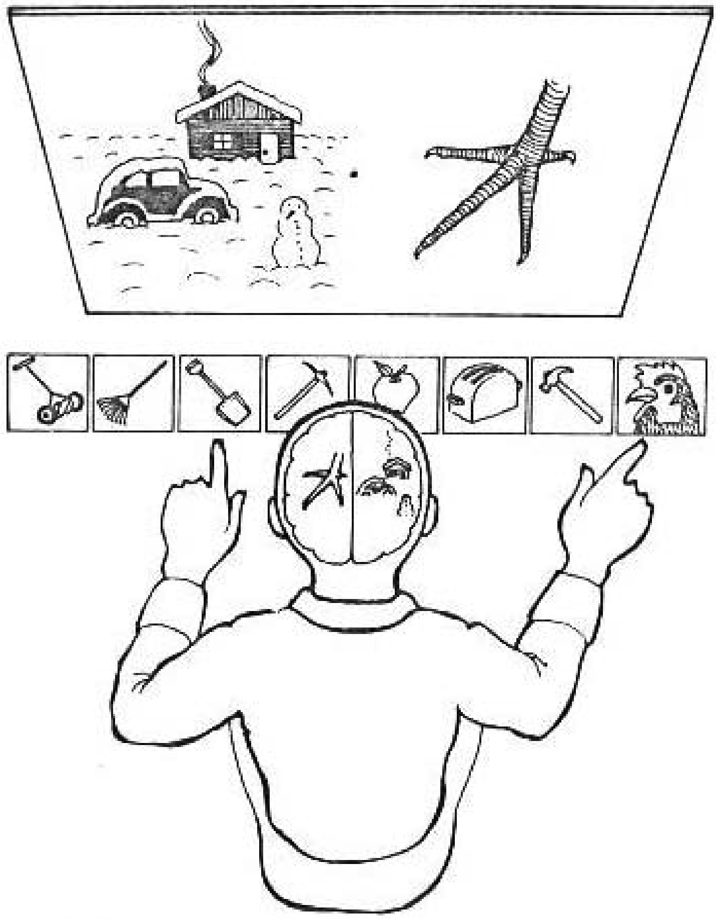


**Figure 2**
*Gazzaniga's chicken claw experiment with a split brain patient.*

selected a picture of a chicken, and the left hand chose a picture of a snow shovel. When asked to explain his choices, the patient said: 'Oh, that's easy. The chicken claw belongs with the chicken, and you need a shovel to clean out the chicken coop (see Figure 2).'"

Gazzaniga's split brain experiments revealed that the left hemisphere has the ability to explain our observations and our own and other people's behaviour and emotions. This 'interpreter' is constantly looking for patterns and relationships between perceptions in order to concoct a plausible story. "That's why none of us believe the theory of the automatic brain," said Gazzaniga. "The interpreter is telling us that we're in control of ourselves. So we may *feel* free — but our brains are automatic nevertheless."

### Free will no, responsibility yes

As contradictory as it may seem, the law's current approach to the workings of the brain is not at odds with what brain researchers now believe about free will, said Gazzaniga. The law regards personal responsibility as the product of a normally functioning brain. But what about someone with a brain disorder, brain damage, or an abnormal neurotransmitter system? What about someone who has had poor early training, something that may cause the brain to function abnormally? There are currently 912 cases before the American courts in which the brain sciences play a role. In some of these cases, the lawyers have presented brain scans of the suspect showing that he is suffering a disorder, for example a tumour. The defence then argues that the suspect cannot be held responsible for his actions because of the disorder, or indeed should be acquitted on the grounds of insanity.

"It's true that brain damage can alter people's behaviour," said Gazzaniga. "For example, damage to the prefrontal cortex may make someone more aggressive, but not *everyone* who suffers damage there becomes uncontrollably aggressive — in fact, some people don't become aggressive at all. So we can't say that damage to a particular part of the brain indemnifies someone. In fact, that wouldn't be wise, because if the law held that people with a particular brain abnormality were not responsible for their actions, everyone with a brain abnormality would be free to harm others. It's a tricky problem and the Law and Neuroscience Project will be studying it in-depth."

Gazzaniga also described how he personally thinks responsibility should be viewed. "To date, no one has discovered a region of the brain or brain circuit where responsibility is located. Responsibility is therefore a social construct, a set of rules that operate within a social group. Just about everyone can follow the rules, so people are always responsible for their own deeds."

### Individual variation and prejudices

The second problem with using brain scans in judicial process is the huge individual variation in the way the brain is organised. If we take the average brain scan of sixteen different individuals, for example, it will show a region of the brain that is retrieving something from memory. But the active regions on individual scans may differ considerably from the region indicated on the average scan, Gazzaniga showed. The connections between regions within a brain can differ considerably from one person to the next. “Brain scans do not offer the certainty required in judicial process, and should therefore be used with great care,” Gazzaniga concluded.

The brain sciences may play a more significant role in fields other than judicial process, Gazzaniga related. One example is to test whether someone is brain dead so that his organs can be used as transplants. A skilled neurologist would be able to establish the diagnosis. What is more difficult is to determine whether someone is in a persistent vegetative state or in a state of minimal consciousness. Neurologists cannot say which patients will and will not recover, or which treatments are or are not permissible in such cases. The neurosciences can also answer questions relating to the beginning of life. Does a fourteen-day-old embryo have a brain? No — in fact, it does not even have the cells yet that will become the brain. That is a scientific fact of enormous significance in the ethical debate about the use of embryos.

Psychological research can also play a role in the courtroom. For example, we have known for ninety years now that people are biased in favour of their own race. A Japanese person has more trouble evaluating the behaviour and facial expressions of a white person than of another Japanese person, and the reverse is also true. Brain scans have also shown that the emotional system of the brain does not react when a person encounters someone who is not in his or her own social group or class, for example a drug addict. So when an investigator, a jury member, or a judge sees a suspect from a different social group to his own, and he attempts to pass judgement on that person, his decision is influenced by his psychological bias.

### The neuroscience of morality

Cognitive brain researchers have begun to focus on an entirely new area in recent years: morality. Are universal moral principles built into our brains at birth, or do we learn them? In 2004, psychologist Mark Hauser of Harvard University described how people around the world view moral dilemmas. For example: an out-of-control train is heading straight for five people who are crossing the tracks. You are standing near a switch that you can throw to turn the train on to another track. Unfortunately, there is someone standing on that other track. Is it right for you to throw the switch? What if you were standing on a footbridge above the speeding train and saw that you could save the lives of the five people on the track by shoving one fat man off the footbridge and on to the track?

"People around the world and from many different cultures, some religious and some not, answer this type of question in about the same way," Gazzaniga relates. "The majority by far (89%) believe that it is morally acceptable to throw the switch in the first instance in order to minimise the number of victims. But an equally large percentage believe it is immoral to murder someone for the same reason."

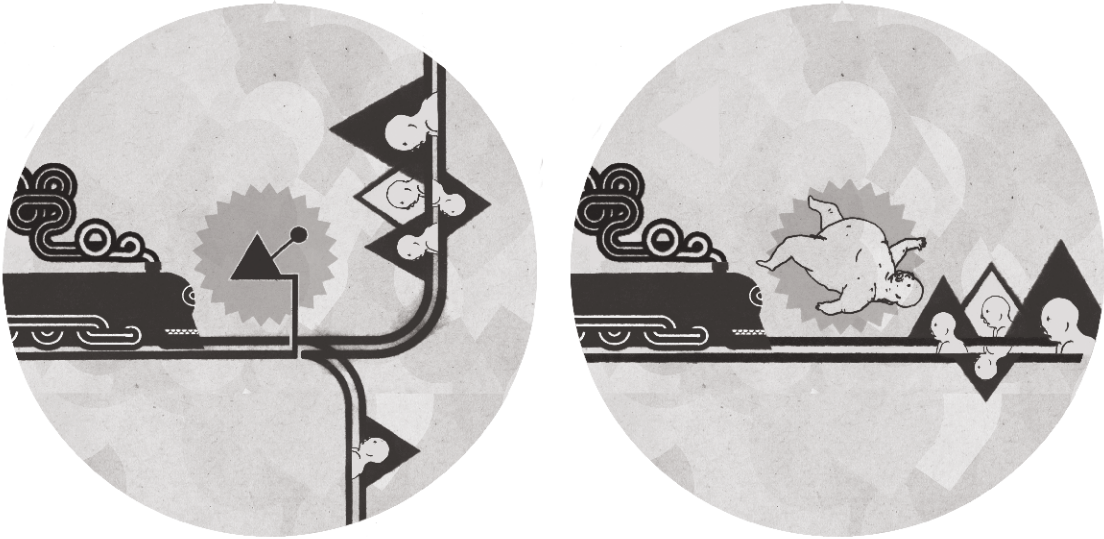


**Figure 3**
*Moral dilemma: an out-of-control train is heading straight for five people who are crossing the tracks. "You are standing near a switch that you can throw to turn the train on to another track. Unfortunately, there is someone standing on that other track. Is it right for you to throw the switch? What if you were standing on a footbridge above the speeding train and saw that you could save the lives of the five people on the track by shoving one fat man off the footbridge and on to the track?" By Yarek Waszul.*

In 2001, brain researchers at Princeton University published fMRI brain scans of people struggling with the moral dilemmas just described. Where the situation called for a man to be pushed in front of the train, their scans showed activity in their emotional brain circuits, which seemingly operate as a mental brake. "It looks like we have a built-in moral reflex in our brains," Gazzaniga concluded.

"People around the world all gave different reasons for not pushing the fat man on to the track," said Gazzaniga. "But no matter what their reason was, the point is that they simply wouldn't *do* it." It may be that the moral reaction is automatic and unconscious, and that the interpreter concocts a reason to back it up later. Studies such as this one support Gazzaniga's theory that there is a universal set of biological reactions to moral dilemmas. Just like the brain's language and mathematics systems, there is presumably also a built-in ethical system that helps us to distinguish intuitively between good and evil.

### Revenge or forgiveness?

Gazzaniga believes that brain research findings will eventually influence our concepts of justice, revenge and forgiveness. Our knowledge of the human brain and how it generates emotion, behaviour, morality and thought is increasing rapidly, as is our understanding of the effects of drug abuse and early training on the way the brain develops. Thanks to brain research, we will be able to make more accurate diagnoses of psychiatric and neurological disorders and develop better treatment programmes.

It is possible that new insights into the brain will shift the emphasis in judicial process from punishment and revenge to treatment and forgiveness. Gazzaniga refers to British philosopher Janet Radcliffe Richards on this topic. "Do we want revenge, does society need it to function properly, and is it important? Or is the view of forgiveness preached by Jesus in his Sermon on the Mount realistic: not to revenge a crime, but offer the perpetrator the other cheek instead?" Richards proposes rising above our own thirst for vengeance and reconsidering our attitudes towards punishment.[5] Whether that is possible only time will tell. Gazzaniga and other scientists involved in The Law and Neuroscience Project and similar research will look at such questions in-depth. "The answers that emerge are important to us all," said Gazzaniga in conclusion.

## 5.3 What lawyers can learn from neuroscientists

*Lecture Prof. Ybo Buruma*[6]

After Gazzaniga had described how brain researchers regard the law, it was up to a renowned Dutch professor of criminal law to explain the lawyer's view of brain science. Ybo Buruma of Radboud University Nijmegen did not mince words. "Many lawyers are interested in developments in brain research, but know very little about it. Judicial process may eventually benefit hugely from a better understanding of the brain, and not only in the taking of evidence, but also in other phases of criminal procedure: investigation, prosecution and punishment." Like Gazzaniga, Buruma warned that brain science must be introduced very gradually in judicial process, and with great care.

5 *"If we understand that there are good evolutionary reasons for our wanting people to suffer when they have done direct or indirect harm to us, then we can account for our strong feelings about the appropriateness of retribution without presuming they are a guide to moral truth... We may be able to recognize our retributivist feelings as a deep and important aspect of our character – and take them seriously to that extent – without endorsing them as a guide to truth, and start rethinking our attitudes toward punishment on that basis."* [Richards, 2000, p. 210].

6 Professor of Criminal Law and Criminal Procedure, Radboud University.

Figure 4
*Ybo Buruma at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

## Investigation

Before 1985, criminal investigation in the Netherlands involved searching for an offender after a crime had been committed. Since that year, however, all Dutch police forces have had criminal intelligence units, and they do precisely the opposite: they use profiles and analyses to predict who will commit a crime so that that person can be caught red-handed. There is growing pressure to apply this strategy, fuelled by the importance of catching terrorists before they act.

Other police units have adopted the same approach. They investigate risk indicators and buffers, i.e. data showing that someone is highly likely to commit a crime, or, conversely, reducing the risk that they will do so. “It’s well known that someone who feels little loyalty to his neighbourhood, has a father in prison, or suffers from ADHD runs a greater risk of becoming a criminal,” said Buruma. Our growing knowledge of the brain will contribute to the list of risk indicators. “As soon as brain researchers can say for certain that, for example, a large amygdala or small frontal lobes make people more aggressive, we will be asking whether we shouldn’t monitor people with these features,” said Buruma.

The greater the role of investigative risk analyses, the greater the potential role of biological data. Buruma does not expect biological risk to replace the criminal act (or attempted act) any time soon as the deciding factor for taking pre-emptive measures. The purpose of such measures is to prevent the risk factors with which some individuals are saddled from being expressed in criminal behaviour.

**Figure 5**
*There are currently 912 cases before the American courts in which the brain sciences play a role. In some of these cases, the lawyers have presented brain scans of the suspect showing that he is suffering a disorder, for example a tumour. The defence then argues that the suspect cannot be held responsible for his actions because of the disorder, or indeed should be acquitted on the grounds of insanity. Adapted by Mirjana Vrbaski.*

When deciding whether a situation calls for pre-emptive measures, intelligence units consider five points: how grave is the danger (are we talking about a nuclear reactor blowing, or a shoplifter?), how strong is the warning (has someone actually overheard that a building is going to be bombed, or does he just have a feeling?), how likely is it to occur (is it certain to take place, or only probable), how urgent is it (will it take place 'some time' or 'tomorrow'?), and what impact will intervening have on the perpetrator (will he go to prison, or is a warning more appropriate in his situation?).
In the case of biological risk factors, the gravity of the anticipated criminal offences and the likelihood that they will actually occur are too uncertain, Buruma found. "The indication and the urgency are not strong enough, and the personal impact quickly becomes too severe. A brain disorder alone does not give us the right to throw someone into prison."

## Prosecution: public health or criminal law?

The prevailing notion is that we can distinguish dangerous people from the rest. Traditional approaches are based on the injury suffered and the dangerousness of the act. The risk now is that we will adopt an approach based on the dangerous person, warned Buruma. "Research shows that we can predict with a fair amount of accuracy which child will be drawn into a life of crime later, for example. Dutch child psychologist Theo Doreleijers believes it is a moral obligation to treat children who are at risk before they are in their teens.[7] I agree with him, but it's a questionable line of thought," said Buruma. "Can we justify applying pre-emptive criminal law and convict a child who has yet to commit a crime?"

7 For more info on Theo Doreleijers's research, see www.capvumca.nl.

Buruma drew attention to a 2002 World Health Organisation report that argues for a 'Public Health Approach to Violence'. "It's an interesting notion," he recalled. "Why shouldn't we consider violent crime the symptom of a disease?" We can establish risk factors for that disease and then develop preventive strategies relieving society of that particular 'burden of illness'.
The 'medicalised' approach to criminal behaviour exposes the problem immediately. "Objective health does not exist," said Buruma. "Health is subject to social norms. Illness is a state that deviates from the relevant person's ideal or from a statistical average."

Approaching crime as a public health problem could have bleak consequences. Buruma sketched a 'Brave New World' scenario in which social risk determines who is healthy and who is not, with the latter group being subject to preventive treatment, prosecution or incarceration. Another approach would be to accept deviations from an average as long as the relevant individual is capable of dealing with his latent risks and satisfies the requirements of his social environment. Buruma considered it improper and undesirable to use mental health care as a furtive form of preventive criminal justice.

### Evidence

Judges in the Netherlands are almost completely at liberty to consider or not consider evidence in their decision. What are they supposed to do with new technologies such as brain scans? They could be important in future as evidence for behaviour (criminal acts). Buruma had the audience perform a thought experiment. "Imagine that a woman is being tried for the murder of her two children, and there is only one witness who heard the mother badmouth her children prior to the murder. The meagre evidence means that the woman will probably be acquitted. But how will the court rule if the Public Prosecution Service brings in an expert witness and presents a brain scan that shows someone who is fearless, impulsive and aggressive? No judge should accept a brain scan like that as evidence for murder."

"What is even more dangerous is the train of thought that that brain scan sets off in the judge," he said. "It might just be the final push that removes his last doubt. For example, if it also turns out that the mother bought arsenic, and the children died of arsenic poisoning."

Judges, lawyers and public prosecutors are all tempted to believe in the hard data of a brain scan. "Researchers must be aware that their interpretation can have a major impact on the taking of evidence," said Buruma. "Can they reach a specific conclusion about an individual from the test results, or are their conclusions applicable to a large, general group?" Evidence of intent appears to

**Example XIII**

**Did the person in the brain scanner see a picture of a cow or a garden gnome? Data from a brain scan makes it possible to determine which one. American scientists have demonstrated that they can infer which category out of ten different ones their participants had been seeing. Their study shows that there is more information present in fMRI brain scans than is often appreciated.**

Three men and one woman were placed in a functional magnetic resonance imaging (fMRI) scanner. For twenty seconds at a time, they each looked at ten different pictures of objects belonging to the same category. They saw, for example, ten different baskets, or ten chairs, horses, garden gnomes or teapots. They had to look at the pictures and covertly name the object category. In this way, ten different categories were presented, with a wide variety of object types: living, not living, small, big, common or uncommon.

# Brain scans can reveal what you were thinking

After the training session, the blocks of ten pictures per category were presented again in a later session.

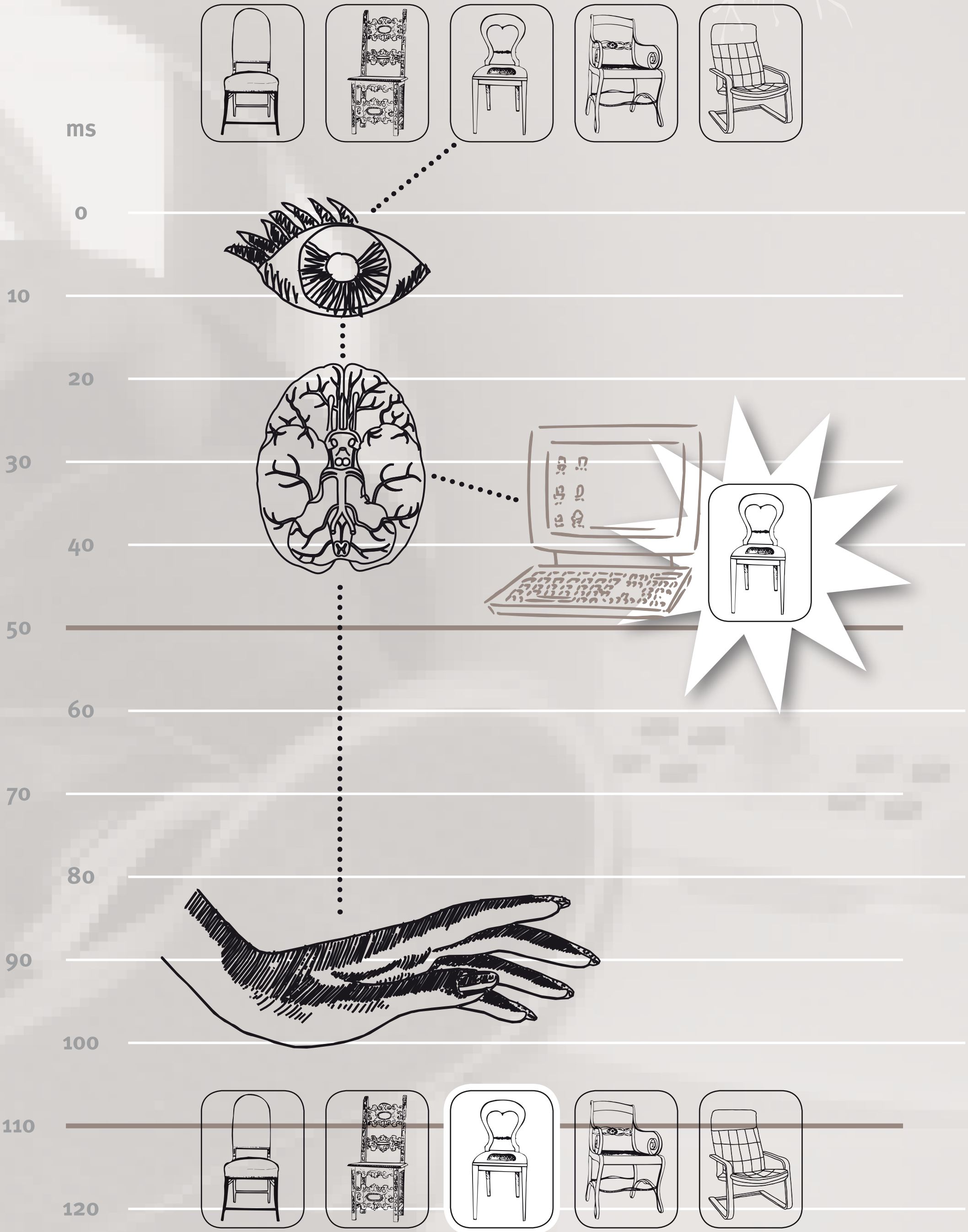
The brain scan information from each participant was fed to a computer to train a data processing paradigm, or “classifier”, to recognise the brain activity evoked in this individual by looking at the pictures. Unlike traditional fMRI brain scan analysis, in this study multivariate statistical pattern recognition methods were used to classify patterns of brain activity not only over time but also across space. The scientists tested several different classifying paradigms.

With accuracies far above chance, it was possible to determine from just twenty seconds of fMRI data which objects a participant had been looking at. Two different classifiers could determine correctly which picture had been viewed in up to 97 percent of the cases. The classifiers could distinguish between objects as similar as horses and cows, or birds and butterflies. This was the case even when there were several days or weeks between collection of the training data and the test data, and also when the pictures in the test run were not exactly the same as the ones seen during training.

The technique provides a framework for detecting other types of information, in other areas than the visual cortex. In a recent study, similar predictions could even be made based on large sets of novel, complex images. Further, a group of British brain researchers were able to read hidden intentions in the decision-making brain area just behind the forehead: the prefrontal cortex.

Original publications: Cox and Savoy (2003), *NeuroImage*, 19, 261; Kay et al. (2008). *Nature advance online publ.*, 5 March; Haynes et al. (2007). *Current Biology*, 17, 323; Haynes and Rees (2006). *Nature Reviews Neuroscience*, 7, 523

Such classifiers have even been shown to be able to infer what a person had seen unconsciously. However, in all studies, mental content could only be read from brain activity when the participants had first fed the classifiers with their own brain imaging data. One challenge for researchers is to investigate whether and how this technique can be used for lie detection or face recognition.



be at odds with the notions of free will proposed by cognitive brain research. According to cognitive neuroscientists such as Michael Gazzanniga, a person feels free but his brain is automatic. Free will does not exist. Buruma agrees with what Gazzaniga said earlier about the legal profession's view of responsibility and free will. "Whether or not the brain works automatically, people themselves decide how to interpret their deeds, their brain's reaction. That's why the law regards a person as someone with a free will, who can be held responsible for his actions."

"Legal specialists tend to base a judgement of intent — exercising one's free will — on the circumstances in which a person acted, and not so much on his psychological state," said Buruma. "There is the example of a person in a pub fight who pulled a pistol and fired a shot, hitting someone he didn't know in the leg. The judge considered that acting with intent and convicted the fellow for attempted murder, because someone who deliberately shoots off a pistol in a crowded pub must have the intention of hitting someone."

### Punishment

"Due to abnormalities, the control process in some people's brains is not as good as in other people's. Some people have more control over their fate than others," said Buruma. "But that doesn't mean that everyone with a demonstratable brain-related mental disorder should be excluded from punishment." According to Buruma, we can expect most people to learn to deal with their limitations, control their impulses, and realise that they themselves are responsible for their own deeds and the company they keep. "We can continue to hold people liable under criminal law. The criterion is whether they could have acted differently than they did."

In extreme cases, brain scans can serve to support a psychiatric assessment. But they should never be used as more than supporting evidence. Buruma warned against presenting brain scans in the courtroom too easily. "You can always find a peculiarity if you look hard enough." Our understanding of the brain does not preclude our holding perpetrators accountable under criminal law, Buruma concludes. "But that same understanding should make us show more compassion for excessively aggressive persons or ADHD sufferers who received the wrong treatment, because such people have less control over their fate than others."

## 5.4 Memory detection

*Lecture Ewout Meijer* [8]

Caution is required when interpreting test results in judicial process. But which research techniques are already reliable enough to use in investigations and examinations? Can brain scanners be used as lie detectors? No, said Ewout Meijer of the Faculty of Experimental Psychology at Maastricht University, where he conducts research into lie detection techniques. "Of all the available lie detection devices, the polygraph dating from the 1930s is still the most reliable," he said. "Not as a lie detector per se, but as a memory detector."

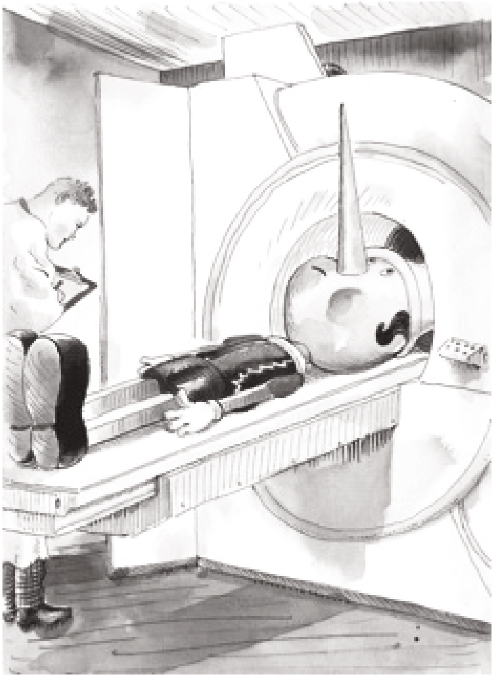
A polygraph measures the skin conductivity on the fingers. The more people perspire, the more conductive their skin. Almost no one who is asked an incriminating question concerning criminal knowledge can stop themselves perspiring. More than one hundred studies have shown that the polygraph can correctly pick out the innocent in 83% to 99% of cases. In the case of the guilty, that percentage is between 76% and 86%.

Two more modern techniques currently under study are fMRI and the electro-encephalogram (EEG). "The fMRI test is not suitable for lie detection yet, even though two American companies are already marketing it," said Meijer. The technique shows which region of the brain is using a relatively large amount of oxygen, indicating that it is active. The brain's 'lie centre' cannot be shown because it does not exist, but fMRI can visualise cognitive processes associated indirectly with lying. According to Meijer, the fMRI findings are patchy,

**Figure 6**
*Ewout Meijer, Researcher of Experimental Psychology at Maastricht University.*

8 Researcher, Experimental Psychology Capacity Group, Maastricht University.

**Figure 7**
*The fMRI test is not suitable for lie detection yet, even though two American companies are already marketing it. By Barry Blitt, barryblitt.com.*



ambiguous, and usually describe a group average that can not be applied to an individual. In the three studies that did focus on individuals, fMRI classified between 78% and 90% of the subjects correctly.

It is difficult to reach conclusions about lying from a brain scan, said Meijer. According to British professor Sean Spence, the standard setting of the brain is to tell the truth. That setting has to be consciously switched off to lie. That involves a region of the brain known as the prefrontal cortex, right behind the forehead. If that region becomes active when someone answers 'yes' to questions concerning the charges ("Did you kill him?"), then that 'yes' is a lie and the defendant is innocent. "But how does the brain of a guilty person work who has gradually come to believe in his own innocence?" Meijer wondered out loud. "Perhaps the lie is the standard setting for him, and the scan would lead to the wrong conclusion. The power of brain scans is overestimated," concluded Meijer, echoing Buruma and Gazzaniga. The mere presence in a text of trivial sentences starting with "Brain scans show that..." make a scientific claim more credible for lay persons *and* brain science students, as recently demonstrated by psychologist Deena Skolnick Weisberg at Yale University.

A much more promising research method is the electroencephalogram or EEG — also known as brain fingerprinting — which measures the brain's electrical activity. The EEG recording shows a brain wave that occurs 300 milliseconds after something unusual has happened; this is known as the P300. Seeing his

**Figure 8**
*A much more promising research method is the electroencephalogram or EEG - also known as brain fingerprinting - which measures the brain's electrical activity. By Rolffimages, dreamstime.com.*

get-away car in a line-up of random cars is enough to evoke a P300 peak in an offender. Some 25 studies have been conducted with this technique, and the findings are uniform. In a study by Meijer, the P300 peak correctly showed in 92% of cases that the subject had seen a familiar face. "That can help determine whether someone is a member of a criminal organisation but is trying to hide it," said Meijer. But like fMRI and the polygraph, the P300 test can also measure the presence of criminal knowledge, he emphasised. "It reveals a cognitive process related indirectly to lying."

The polygraph is as good a way of demonstrating criminal knowledge, and it is cheaper and easier to operate, concluded Meijer. "It too is an indirect measure of criminal knowledge, but the results of a hundred studies are clear and the technique is already in widespread use."

## 5.5 The practical side of lie detection

*Lecture Thinka Bethlem*[9]

The work of researchers such as Meijer is highly relevant to investigators. In fact, they are dying for reliable lie detectors, said investigative specialist Thinka Bethlem of the Amsterdam-Amstelland Police Force, because unmasking liars is anything but easy. "Investigators, customs officers, judges and lay people are shown to be right in little more than half of all cases," said Bethlem. The laboratory work described by Meijer is highly promising, but

9 Investigative Specialist, Amsterdam-Amstelland Police Force.

**Figure 9**
*Thinka Bethlem, Investigative Specialist at the Amsterdam-Amstelland Police Force.*

Bethlem immediately pointed out a practical problem when it comes to lie detection equipment: "The legal context limits its use; besides the right to remain silent, suspects also have the right to refuse a scan or other lie detection method."

She said there was no direct connection between lying and verbal, non-verbal or physical behaviour. She also confirmed Meijer's claim that there is no 'lie centre' in the brain. "Lying is associated with psychological processes that influence behaviour. Those processes, in their turn, are influenced by the lie itself, the liar, the person who detects the lie, and the interaction between those two."

The Amsterdam-Amstelland police launched a credibility analysis project in 2006 entitled 'Wanted: the Truth'. The first stage involved test-running a verbal analysis method known as Scientific Content Analysis (SCAN). False statements made in writing differ linguistically and content-wise from truthful statements. SCAN may show, for example, that the husband of a missing woman is already writing about her in the past tense. Could it be that he knows she's already dead? Or a woman describing her violent kidnapping by three men writes "We went outside by the back door." The word 'we' attests to a group feeling that is unlikely after such a brutal crime.

Although the results cannot be used as evidence, the pilot showed that SCAN can help to collect information and therefore to uncover the truth in investigations. "One big advantage is that we don't have to depend on the suspect's cooperation," reported Bethlem. "We can also analyse letters, e-mails, diaries and transcriptions of interrogations."

The second project step will involve test-running a memory detector based on skin conductivity and the criminal knowledge test described by Meijer.
We need more knowledge of the working of the brain and psychological processes to understand how those processes influence verbal and nonverbal untruthful behaviour, Bethlem concluded. She emphasised that there is a pressing need for laboratory research simulating the circumstances of a police interrogation more accurately. In-depth research in the field should also demonstrate the practical and legal value of verbal analysis methods and the memory detector, for example. “Ultimately, this will make it easier for investigators to expose more liars,” according to Bethlem.

## 5.6 Simple truths from memory research

*Lecture Willem A. Wagenaar*[10]

While modern techniques derived from brain research can help police investigators to uncover the truth, they are not yet suitable as evidence. And it’s a good thing too, according to memory researcher Willem Wagenaar, emeritus professor of Experimental Psychology. Brain researchers should be careful about passing on their insights to legal specialists, he thought. “Until the knowledge of the brain that *can* be used in the administration of justice has penetrated through to judicial process, it makes no sense to tell lawyers and judges about the latest neuroscientific discoveries.”

**Figure 10**
*Willem Wagenaar at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

10 Emeritus Professor, Experimental Psychology, Leiden and Utrecht University.

“Judges tend to believe a later suspect statement more than the first one,” he explained. “But brain researchers have known for a long time that our memories don’t become more accurate in time. The farther back in the past something happened, the *less* accurately we recall it.” Brain research has also shown that our memory is inconsistent, fills in gaps, and makes up stories and reconstructions. If a witness suddenly claims that he recalls more than he did before, or only reports a crime to the police weeks after the event, the judge must investigate who the witness has spoken to in the meantime or what he has seen.

Wagenaar explained that when a witness has only a vague recollection of an offender, his merely glancing at a photograph of a suspect is enough to replace that vague recollection with the subject’s face. Asking a witness to identify a suspect is therefore a one-off affair, and should always give the witness a representative series of potential offenders to choose from. In one case, after a robbery by a dark-skinned man, the line-up consisted of one black man among eleven white ones. “According to the authorities it was an administrative error, but it’s not one that can be put right,” Wagenaar emphasised. “You can’t redo the witness line-up. Based on the results, the judge should not have convicted the dark-skinned man.”

A report made to the police is also not reliable evidence, according to Wagenaar. A mentally handicapped girl who only nods in agreement to her father’s suggestive questions may dig a story up out of her memory weeks later about events that have not in fact taken place. “Judges have an obligation to make enquiries, but in some cases they don’t make them,” said Wagenaar.

“There are about two hundred cases worldwide in which later and more accurate DNA analysis revealed that the wrong person was convicted,” said Wagenaar. “In 70% of those cases, the conviction was based on wrong identification by eye-witnesses. The authorities ignored the identification procedures. It happens in the Netherlands too, despite a ministerial decree. Only a small percentage of cases are involved, but that’s why we have judges, for those few difficult cases.”

## 5.7 A judge considers

*Lecture Frans Bauduin*[11]

In his rejoinder to Wagenaar's critical comments, Frans Bauduin, coordinating vice-president of the Amsterdam District Court, described the circumstances in which judges reach their verdict.

"Criminal judges play a special role in judicial process," said Bauduin. "It's up to them to decide whether or not a defendant is guilty, and that's a very difficult decision. It isn't up to the witnesses, or the experts, or the media, or the victims, or the politicians. It's up to the judge." Criminal judges hand down verdicts many thousands of times. The single-judge chamber of the Amsterdam District Court ruled in 11,500 cases in the first nine months of 2007. Added to that were almost 2,000 sentences passed by the multiple-judge chamber, four thousand arraignments, more than a 1,000 sittings in camera related to pre-trial detention orders, and so forth.

"The criminal code dictates what judges can use as legal evidence, and in what way," Bauduin related. "The judge has to base his decision on that evidence. Judges consider an expert's report reliable when it is made by a competent professional who has remained within the boundaries of his discipline, based himself on generally accepted insights, and has supported his statement with sound arguments." Witness statements should always be considered with the greatest circumspection. Our memories are fallible, Bauduin admitted. "Suspects sometimes make false statements, deliberately or not. Judges look at the circumstances in which the statement was made and try to link witness statements to the other case documents."

A good criminal judge enters the courtroom with an open mind. "He has to bear his own opinions in mind, but only let them come into play when it's time to reach a verdict. He has to learn as much as he needs to know to be *able* to reach a verdict. So if he's got the feeling that something isn't quite kosher, he has to ask more questions. Judges also have to be open to alternative interpretations of the facts." What Bauduin considered most important was for a judge to maintain his belief in humanity and not treat everything with deep suspicion from the start. "Criminal law is interesting because things happen that you couldn't have imagined, but you're still required to reach a verdict," said Bauduin. Neuroscience can help judges in their work, for example by determining the boundary between self-defence and excessive self-defence. The Dutch criminal code says the following about excessive self-defence:
It is not an offence to exceed the limits of necessary self-defence if such is

11 Vice-President, Amsterdam District Court.

**EXAMPLE XIV**

**Simply moving one's eyes from left to right for thirty seconds seems in some circumstances to increase true memory and decrease false memory. People are better able to recognise which word was not on the list of words they learned before the eye exercise.**

Studies into false memories make use of lists of words that all converge or relate to a critical word that is not listed. If a list contains words such as 'thread', 'pin', 'eye', 'sew', and 'sharp', a participant often falsely recalls and recognises the word 'needle' as being part of the list. These false memory errors often outnumber the true memory, and they are hard to reduce. Even when participants are told the nature of the experiment, they still make many mistakes.

# Moving the eyes reduces false memories

Lists of words are thought to be memorised in two ways: via a verbatim memory trace, which focuses on the details of the word, and via a gist-based memory trace, which focuses on the general meaning. False memories are recalled and recognised better when emphasis is placed on the gist trace.

False recall is reduced when the words are more distinctive, for example by having them being spoken out loud, or pairing them with pictures. Remarkably, it is also reduced when participants perform bilateral eye movements for thirty seconds after learning the list of words.

False recognition is also reduced by bilateral eye movements, British psychologists have found. Vertical eye movements and no eye movements had no effect.

A hundred participants were divided into three groups and learned ten lists of fifteen words. After learning they followed a black circle on a computer screen to guide their eye movements for thirty seconds. The circle appeared every half second, either alternating positions on the right and left side of the screen, on the top and the bottom, or on and off in the centre of the screen.

The participants then looked at lists of ninety words containing ten non-studied critical words (like 'needle' in the above example), forty studied words, and forty unrelated words.

Original publication: Parker and Dagnall (2007). *Brain and Cognition*, 63, 221

The group of people who made bilateral eye movements identified significantly more learned words, and made significantly fewer mistakes in identifying non-learned critical words and non-related words compared to people in the other two groups. Bilateral eye movements seem to enhance the true verbatim memory, and decrease the extent to which people rely on gist-based false recognition.

The effect of bilateral eye movements on memory processes is still under debate, and the explanation for it is not yet definitive. One theory is that it improves communication between the two brain hemispheres, as such facilitating processes make use of both hemispheres. If future research is able to reveal how eye movements can influence memory components, these insights may become useful in court, for instance when questioning witnesses.

the immediate consequence of an *emotional outburst* caused by an assault. “Should teenagers — whose frontal lobes are still underdeveloped — be allowed more time for that ‘emotional outburst’ than adults?”, Bauduin wondered out loud. “Judges should consult others, but the choices they make are their own and their responsibility,” Bauduin emphasised again. “It’s up to the judge.”

## 5.8 Nature and nurture

*Lecture René S. Kahn*[12]

Judges have to take very difficult decisions: yes *or* no, guilty *or* not guilty? But brain specialists can rarely give them clear-cut answers, according to René Kahn, professor of Biological and Clinical Psychiatry in Utrecht. “The question is not whether nature *or* nurture is to blame for someone’s actions or behaviour — the fact is, both genes *and* environment play a role.” Kahn illustrated this by describing the origins of schizophrenia and the course of this illness.

Schizophrenia is a devastating, life-long mental illness that affects one in a hundred people, usually at about the age of twenty. Schizophrenics often have psychotic episodes in which they confuse fantasy and reality, believe they are being controlled by external forces, and hear voices. Heredity, in other words DNA, accounts for about 50% to 75% of the likelihood of developing schizophrenia. The closer a person’s biological relationship with a schizophrenic, the greater the risk of him too developing the illness. “But the chance of identical

**Figure 11**
*René Kahn at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

12 Professor of Biological and Clinical Psychiatry, Utrecht University.

twins with identical genes both developing schizophrenia is only 50%, not 100%," related Kahn. "The brain of one child may have larger cerebral ventricles — the fluid-filled spaces in the brain — than the other, an abnormality typical of schizophrenia. So environmental factors also play a role."

Immigration, for example, is a risk factor for schizophrenia. In the Netherlands, the incidence of schizophrenia is ten times greater among Caribbean, Surinamese and Moroccan immigrants than among the native Dutch population. That cannot be attributed to genetic differences, because the incidence of schizophrenia in the countries of origin is about the same as in the Netherlands, according to Kahn. Cannabis is another risk factor. "People with a certain genetic disposition are four times more likely to develop schizophrenia if they use cannabis," said Kahn. "The illness manifests itself sooner and more severely and the brain abnormalities are exacerbated." So there are many different factors that can influence normal and abnormal human behaviour, Kahn concluded. The question of guilt is a difficult one, both for judges and for experts.

## 5.9 Room for interpretation

*Lecture Inez N. Weski*[13]

The same range of factors that control our behaviour also play a role in how we *interpret* the person behind the suspect and the charges made against him. That is the claim made by Inez N. Weski, criminal lawyer at Weski Heinrici Advocaten in Rotterdam, in defence of suspects under investigation. "There can be an unbridgeable gap between the suspect, the charges made against him, and the judge's opinion of his culpability and accountability," she said.

The judge's verdict is based on a reconstruction of the facts and circumstances of the case, drawn from the information collected and selected by the reporting police officers and the Public Prosecution Service, according to Weski. The way in which suspects are described, the impression they make on the judge, the witnesses selected, and the use of an interpreter may all influence that reconstruction of the facts. It is also coloured by the psychological profile of the behavioural specialists and the judge, as well as by their fears, their world view and/or their prejudices.

Nevertheless, the judge's verdict must be as objective as possible. "A lot of people criticise the fact that judges are free to select which evidence they will use to support their verdict," said Weski. There is also the risk that judges

13 Criminal Lawyer, Weski Heinrici Advocaten.

Figure 12

*Inez Weski at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

will bow to the public's call for harsher sentences in order to protect society. "But no punishment should exceed the crime," Weski said. "Unfortunately, the Dutch Supreme Court has rejected that principle until now."

Even in the case of neurological and scientific measurement data, there is room for interpretation within the limits of probability. Like the previous speakers, Weski thought that, similar to DNA testing, neurobiological testing — for example EEG brain fingerprinting, fMRI scans, memory recovery techniques — must be used with great care in investigations.

Persons can be compelled by law to provide fingerprints, blood, tissue for DNA tests, and photographs. But the brain, its chemistry and its thoughts, are a legal private domain, said Weski. "An individual sitting in a courtroom is more than a power failure in the brain."

Weski expected that legal reality will increasingly be based on the brain's fine mechanics. "But that will always be supplemented by interpretation, intangible patterns of expectations, and the attitudes of all those involved in a case towards humanity."

## 5.10 Discussion

*Debate between Willem H. Woelders[14], Hans Nijboer[15], Huibert J. Donker[16], Inez N. Weski[17], René S. Kahn[18] and the conference attendants*

If anything was made clear to the conference participants, it was that new insights derived from brain research must be used with the utmost caution in the courtroom. Much of the data produced by brain research cannot be used as evidence, but it still exerts a subconscious influence on judges. The debate therefore concerned the role of the experts consulted. They must be acutely aware of the impact of their expert opinions.

### The expert in judicial process

No matter what the view of the Public Prosecution Service, the defence team or even the judge is an expert can be found who will support it. “That is a huge danger,” said Huibert J. Donker, investigative public prosecutor for the Public Prosecutor’s Office in Breda. “Fortunately, more and more judges in criminal proceedings are insisting that experts meet specific requirements.” An experts register is being compiled, Donker added. “The people — including brain researchers — who are listed there as having a particular expertise will base their reports on the science, and not on a specific interest. That way, all the parties involved will listen to them and decide for themselves.”

Someone from the Ministry of Justice in the audience said that starting 1 January 2008, the experts register would be available to everyone involved in a trial: the lawyers, the judges and the public prosecutors. At the time of the symposium, the Ministry was defining the criteria that experts would have to meet to be included in the register.

Not every expert belongs in the courtroom. “The search for an expert should be more fine-tuned; they need to be up to date on the latest scientific and clinical literature. That isn’t always taken seriously enough,” psychiatrist René Kahn found. “An expert should know precisely how the discipline views a particular illness these days, how to diagnose it, and how likely recidivism is if the patient is left untreated. After all, the expert’s opinion impacts matters of vital interest to the suspect. It is crucially important for the judge to know whether someone has a short-term, treatable illness or whether he already had a personality disorder before the crime took place and is not treatable. So you must have the very best people in the courtroom.”

“What is often a problem is knowing what category of expert should be consulted in a particular case,” added criminal lawyer Inez Weski. “There should

14 Deputy Chief of Police, Utrecht Regional Police Force.

15 Judge, Amsterdam Court of Appeal, Director of the Seminary of Evidence Law, Leiden University.

16 Investigative Public Prosecutor, Breda Public Prosecutor’s Office.

17 Criminal Lawyer, Weski Heinrici Advocaten.

18 Professor of Biological and Clinical Psychiatry, Utrecht University.

**Figure 13**
*Huibert Jonker (right), Hans Nijboer (middle) and Willem Woelders (left) at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

be some mechanism for analysing what form of expertise is required."

Another problem is that the top people in the field are often *unwilling*," said Frans van Dijk, head Development at the Dutch Council for the Judiciary. "A lot of scientists just don't want to appear in court, either out of fear, or modesty, or lack of time."

## Expertise

But the search for the best expert and the compilation of a register should not make judges overconfident, Donker said. "One person cannot be an expert in everything. Experts should state what they are good at. We have to document that information and make use of it when a particular problem arises. It's up to those involved in the case — the public prosecutor, the lawyer or indeed the judge — to make sure that the right person appears in the courtroom at the right time."

It would be better at times for the Public Prosecution Service and the defence to consult at an earlier stage in complex criminal cases, thought Donker. Then they would be able to select an expert together. It would indeed be better for the two sides to consult, agreed a representative of the Pieter Baan Centre, the Ministry of Justice's psychiatric observation clinic, and not only about the choice of expert but also about the question he will be asked to consider. "In the Netherlands, expert reports are often provided by institutes that practically have a monopoly, such as the Pieter Baan Centre. The unintentional effect is that information can be one-sided."

Besides possessing the right and most accurate expertise and a willingness to appear in court, an expert must also be familiar with judicial process. “Unfortunately, not all scientists know what to do for their report to be useful as evidence or to help a judge decide whether a defendant was accountable for his actions,” said judge Hans Nijboer. “Experts sometimes overestimate the importance of their explanations in legal proceedings. That was recently demonstrated once again by statisticians who believe that legal questions can be described in terms of the laws of statistics.”

Celine van Asperen de Boer of Amsterdam University responded from the audience. “I’ve studied the future of statistics in criminal law. Experts know nothing more than their area of expertise. We can’t expect a statistician to know everything about criminal law, the rules pertaining to evidence and all the associated problems,” she said. “What’s most important is for judges to learn which questions they should ask a particular expert, and for them to be aware of the pitfalls at the start of the whole procedure and in their interpretation.” Van Asperen de Boer argued for more mutual understanding between judges and experts.

### The judge and the expert

The debate made clear that judges face quite a job in that respect. They are, after all, responsible not only for the legal side of the process, but also for the results of the expert’s report, if included in their verdict. But even before all that, a judge must first understand that report. Judges need to know more about science in general, and the neurosciences in particular.

The judiciary is already working on that. “We have a programme now to improve our level of expertise,” related Frans van Dijk of the Dutch Council for the Judiciary. “The question is what general level of knowledge judges ought to have. How can a judge keep up with the expert’s level of knowledge? That isn’t easy, given the enormous range of expertise that is called in. It should be common practice for judges to ask experts critical questions. Why are you here, and what makes you an expert? We can compensate for that to some extent with a register, but never entirely.”

Weski believed judges should receive extra training in a variety of different fields to keep them up to date on developments. In her experience, some judges do not even know much about digitising files, let alone other technological advances.

Van Asperen de Boer suggested that judges, lawyers and public prosecutors could specialise in particular areas, such as statistics or psychology. “The national and functional public prosecutor's offices have people who are knowledgeable in specific fields," said Donker. "I think that the judiciary should do the same, so that we have judges with an above-average understanding of particular subjects. It would improve the quality of our criminal justice system." A representative of the Netherlands Forensic Institute (NFI) reported that the NFI organises courses for judges and public prosecutors on technical forensic and statistical subjects.

### Investigation

Before neuroscientists can be called in routinely to testify as experts, judges and the Public Prosecution Service should have a better understanding of scientific advances, their implications and their practical application. Our knowledge of the brain will not produce any suitable evidence in most criminal cases, but brain research findings already serve a practical purpose in investigations.

"The police can benefit in two ways by our knowledge of the brain," said Willem Woelders, Deputy Chief of Police in Utrecht. "On the one hand, it can help them make *choices* in their investigative work, and on the other, it can help them determine *the initial action* they take towards people. That's why it's important for police officers to have that knowledge."

"Knowing about the brain can help police officers get to the truth, for example because they have a better idea of how to tackle an interrogation," explained Woelders. "It can help an officer on the beat decide what action he should take towards someone. For example, if he recognises the behavioural signs of schizophrenia aggravated by cannabis use, he can respond accordingly and take steps to keep the situation under control."

### The future

It was only when asked what they wanted from neuroscience in specific terms that the legal specialists on the panel and in the audience really got going. Frans van Dijk said that the conference had not persuaded him that the neurosciences already had a lot to offer the judiciary. "I'm sure the future will open new doors, but in the short term the neurosciences cannot really help us solve problems in the field yet," said Van Dijk. Donker agreed. "I'm interested in fMRI and EEG and polygraphs as lie detection methods, but with accuracy scores of only 80% for guilty parties, they're useless as evidence."

"There may well be a role for the neurosciences, but one that is less directly related to actual investigative practice and the courtroom," proposed Peter Hagoort, brain researcher and director of the F.C. Donders Centre for Cognitive

**Figure 14**
*Neuroscientist Peter Hagoort asking a question to the panel at the conference Justice and Cognition, 20th November 2007, Zeist. By Kelle Schouten.*

Neuroimaging, from the audience. “The general public is getting to know more about the brain too, so legal practice will benefit from a world view that matches that of scientific practice. How do concepts, attitudes towards humanity and world views inspired by the neurosciences fit in with the thinking in legal practice?”

Katy de Kogel of the Ministry of Justice’s Research and Documentation Centre (WODC) summed up a series of questions that she wanted to see legal specialists and neuroscientists consider together, for example about such topics as accountability and sanctions. “What does punishment mean to delinquents? What effect does it have on them, and how do those effects differ from one delinquent to the next? What does impulsiveness mean for someone’s behaviour, and what are the best courses of treatment?”

Inez Weski wanted a checklist for recognising certain symptoms. “So that I have an easier time categorising a client I’m counselling in criminal proceedings. If he exhibits behaviour A, then perhaps I should examine point B in more detail.”

“It would be a good idea to collaborate not only on evidence and in criminal trials, but also within the context of hospital orders,” added Theo Doreleijers, professor of Child Psychiatry at the VU University of Amsterdam. “No one knows what the impact is of court-ordered treatment. That lack of knowledge cries out for multidisciplinary research by psychiatrists, behavioural specialists, legal specialists and social workers. We spend many millions of euros right now on the criminal justice system, in stark contrast to the miserly sums spent on treating young delinquents. Legal specialists and brain researchers ought to take a long, hard look at that together.”

**Example XV**

# Erasing traumatic experiences by re-recording memories

**People who have had to deal with violence or abuse can suffer from a post-traumatic stress disorder. They relive the horrible event over and over, experiencing strong emotions and physical symptoms such as a pounding heart and sweaty palms. Only recently, neuroscientists have discovered a way to ease such traumatic memories.**

For over a hundred years, brain scientists have thought that memories are labile when they are formed, but become consolidated when they are stowed in the long-term memory. This process requires new protein synthesis in nerve cells.

In 2000, American psychologists discovered that when a memory is being recalled, its brain networks become instable again. After the recollection, the memory is re-installed in a stable form. During this process, memories can be manipulated.

The psychologists trained rats to associate a tone with a mild but unpleasant foot shock. After the learning phase, the mere sound of the tone elicited fear in the rats. It was already known that injection of an agent that inhibits protein synthesis in the brain immediately after this fear conditioning would block fear memory. But the Americans played the tone and at the same time injected the rats with the agent after 24 hours and after 14 days, when the fear memory already had been formed. One day later, the rat's fearful behaviour upon hearing the tone had clearly diminished. This was not the case when the tone was not played before the agent was administered, and as such the memory was not relived. This indicates that the fear component of the memory had become unstable during retrieval.

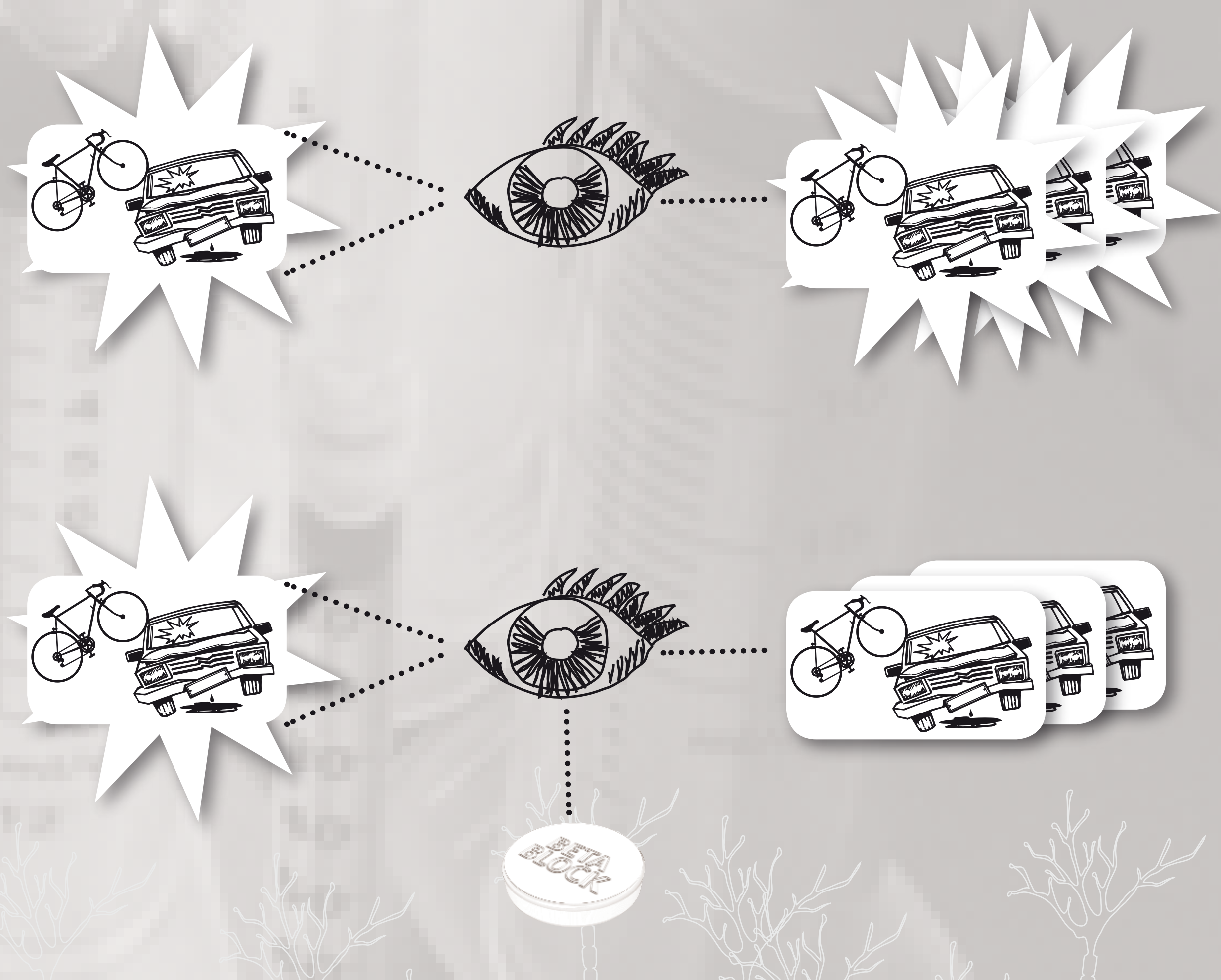
A similar process takes place in people. Psychiatrists from Canada studied participants with chronic post-traumatic stress disorder. These people had suffered childhood sexual abuse, vehicle accidents, physical assault, severe death threats or a house fire ten years before.

Previous studies had shown that administering propanolol, a drug normally used to lower blood pressure, within six hours after a traumatic experience dampens physical responses during recall of the event. Now, either propanolol or a placebo was given after recollection of the event ten years later.

Original publications: Nader et al. (2000). *Nature*, 406, 722; Brunet et al. (2007). *Journal of Psychiatric Research*, June 21 (ePub ahead of print)

After they had written up their traumatic event, they received either propanolol, or a placebo. One week later, the memory of people in the propanolol group recalling the terrifying memory had less emotional weight, and their physical response was softened as compared to the placebo group.

The use of drugs that affect memory raises ethical questions about their use in courtroom trials. What if, in future, memory-diminishing drugs are given to victims of trauma or violent assault as a matter of routine? Those memories may be needed in order to testify. And can the sole eyewitness to a crime be forced to take a memory-enhancing drug to identify the perpetrator? These issues require careful consideration of individual rights, moral responsibility and the common good.



Donker was in complete agreement. “We could perhaps offer young people and adults much more effective treatment. We certainly aren’t going to solve any social problems through criminal procedure.”

For the time being, brain science has more questions than answers for judicial process. The conference and follow-up debate provided a good launching pad for aligning supply (science) and demand (legal practice) when it comes to investigation and judicial process. That should lead to research of greater relevance and interest to society and, ultimately, to successful practical applications.

## 5.11 Detecting false memories with brain scans: a long way off, for now

*Marko Jelicic, Maarten Peters, Tom Smeets*[19]

Some time ago, the Australian memory expert Donald Thomson was arrested on suspicion of rape. In the line-up, the victim immediately picked him out as the rapist. Thomson had a watertight alibi, however: at the time of the crime, he was appearing in a live television interview — ironically enough on errors in eyewitness statements. It turned out later that a television had been on while the woman was being raped, and that she had confused her memory of Thomson’s face with that of the rapist [Baddeley, 1997].

This anecdote not only shows how susceptible our memories are to distortion, but it also illustrates the legal implications of false memory. According to Doyle [2005], many miscarriages of justice — at least in the United States — are the result of flawed eyewitness’s memory. He argues as follows. DNA profiling was first introduced in forensic medicine in the 1980s. This technique makes it possible to accurately determine who has been in contact with a crime victim or at the scene of a crime. In the United States, many of the prisoners who were later released because their DNA did not turn out to match that of the offender had originally been convicted solely on the basis of eyewitness testimony. Because the wrong people had been imprisoned, it stands to reason that the eyewitnesses’ memories were incorrect.

Doyle’s ideas about the grave legal ramifications of flawed memory concur with psychological research showing that false memories are easily created even in intelligent test subjects [Loftus, 2003]. Our memories are not like DVD recorders that store events and then play them back to us with absolute fidelity. Recent findings from cognitive neuroscience offer an explanation for

19 Marko Jelicic is a university professor and a member of the Experimental Clinical Psychology capacity group at Maastricht University. Maarten Peters and Tom Smeets are post-graduate members of the same group.

flawed memories. Whatever we experience leaves traces behind in our brain. These traces are chopped up into bits and saved in various different parts of the cerebral cortex (the visual elements in the occipital lobe, the auditory elements in the temporal lobe, and so forth). When our brain retrieves information, it has to reassemble all these various elements of memory, and quite easily gets things wrong [Schacter and Slotnick, 2004].

Research shows that false memories are very difficult to distinguish from correct ones [Roediger and McDermott, 2000]. People will even insist that they remember things that they have not seen ("I know for sure that this word was on the list you showed me earlier"). According to Schacter and Slotnick, modern imaging techniques such as Positron Emission Tomography (PET) and fMRI may help to solve this problem. These authors suggest that the brain activity associated with correct memories differs from that associated with false ones; correct memories are more likely to involve perceptual details, for example hearing a voice or seeing vivid images. Therefore when someone has a correct memory, he is not only activating those parts of the brain that play a key role in recollection, but also the areas responsible for processing and integrating perceptual information. The latter areas are not activated at all, or only to a minimal extent when the memories are false.

This section reviews various techniques for inducing false memories. It then considers false memory research conducted with modern imaging techniques such as PET and fMRI. The section ends with a discussion of whether these techniques can be used to detect false memories outside the laboratory.

### Inducing false memories

There are various techniques for inducing false memories in the laboratory. The American memory expert Elizabeth Loftus has played a pioneering role when it comes to memory flaws. In the 1970s, she began a series of experiments in which she induced false memories in student subjects. In one of her experiments, she showed her subjects a slide show in which a pedestrian is hit by a car [Loftus et al., 1978]. After the slide show, she posed suggestive questions to give some of the subjects misleading information, for example "Did you see the car stop at the Stop sign?", even though the sign in question was a Yield sign. The memories of the subjects given misleading information were more likely to contain erroneous elements than the memories of the control group subjects. In another experiment, Loftus [1993] showed that it is possible to implant entire pseudo-memories in people. Loftus told her research participants that they had been lost in a large shopping mall when they were small. She led the subjects to think that she had received this information from their parents. Loftus had indeed contacted the parents, but only to check whether their child had in fact ever been lost while on a shopping trip. That was not the case for any of the subjects. When the subjects returned to Loftus's laboratory after a time, a considerable number reported that they had indeed got lost in a shopping mall as children. Some of them even had vivid memories of this fictitious event.

Inspired by Loftus, Crombag [1996] developed the 'crashing memories' method. In October 1992, an El Al aircraft crashed into a block of flats in a suburb of Amsterdam. Crombag and his colleagues asked the subjects (including medical doctors and lawyers) whether they could recall the amateur video images of the moment of the crash. Although no videos of the crash existed, more than 60 percent of the subjects said they could recall such images. This study was recently repeated. Subjects were asked whether they could recall a non-existent amateur video of the assassination of Dutch politician Pim Fortuyn. A large number of them said that they had indeed seen these images [Smeets et al., 2006], and some could even 'remember' all sorts of details that had been in the video [Jelicic et al., 2006].

Another method for inducing false memory is the Deese-Roediger-McDermott (DRM) paradigm [Roediger and McDermott, 2000]. Here, the subjects listen to various lists of words (for example: dream, rest, night, bed, yawn, and so on) all having to do with a particular theme word (in this case, sleep). The theme word (sometimes called the 'critical lure') itself is not mentioned. When the subjects are asked to reproduce the words later, approximately 40 percent recall the theme word — a word that was not presented in the learning phase. When they are asked to listen to a list of old and new words (including the theme word) and decide which ones they had heard in the learning phase, approximately 75 percent say that they had heard the theme word before, even though they had not. The DRM paradigm is popular among memory researchers, who have conducted dozens of experiments with this method to induce memory flaws in various research populations (see [Peters, 2007] for an overview).

### Theories

Researchers have proposed two theoretical explanations for false memories. The 'source monitoring' theory suggests that people may have trouble distinguishing between real and imagined events [Johnson et al., 1993]. The non-existent video of Pim Fortuyn's murder is a good example. Some people may have reconstructed the circumstances of Fortuyn's murder 'in their heads'. Source confusion — an error in ascribing the source of a memory — may then have led them to recall their own reconstruction as video images that they had seen on television. According to the 'fuzzy trace' theory, false memories result from an erroneous sense of familiarity [Reyna and Brainerd, 1995]. Proponents of this theory believe that events are stored in the brain in two different ways. On the one hand, the brain stores all kinds of details about an event; on the other, it stores only the gist. After a while, the details fade and only the gist remains. In subjective terms, when we recall the gist of an event, we feel a sense of familiarity. When a highly distorted or fictitious event incorrectly induces that sense of familiarity, people may believe that the false event is true. If suggesting that there are amateur videos of Pim Fortuyn's murder rouses our sense of familiarity, then we may believe that we have seen those images.

### Research using brain scans

A number of researchers have studied the possibility of using brain scans to distinguish false memories from correct ones. Because almost all of them made use of the DRM paradigm, we will restrict our discussion here to studies based on that method.

Schacter et al. [1996] were the first to use the DRM paradigm to induce false memories in subjects while their brains were scanned. Before taking their place in the scanner, the subjects listened to a list of words being read out loud. The words were all related to a theme word, but the theme word itself was not mentioned. Once in the scanner, the subjects were given another list of words. Some of these words they had heard before, whereas others — including theme words — were new. While PET scanning was under way, the subjects were asked to indicate whether they had heard the words on the new list in the learning phase of the experiment. There was some overlap between

**Figure 15**
*When Schacter et al. [1997] replicated this study using fMRI instead of PET, they found that both correct and false memories activated the same network in the brain. Photo courtesy of Duke University Medical Center, Scott Huettel.*

the areas of brain activated by words they had heard before and areas activated by the new theme words. Both types of word activated areas involved in learning and retrieving verbal information (the left medial temporal lobe). The subject's brain activity also differed depending on the type of memory: only in the case of a correct memory were the brain areas involved in auditory and phonological information processing activated (areas between the temporal and parietal lobes). This study thus supported the hypothesis that correct memories differ from false ones in that they are associated with extra activity in the brain areas responsible for processing and integrating perceptual information.

When Schacter et al. [1997] replicated this study using fMRI instead of PET, they found that both correct and false memories activated the same network in the brain (in addition to the medial temporal lobe, this included other areas such as the frontal cortex, see Figure 15). The replication experiment did not find any areas of the brain that were activated only by correct or false memories. Cabeza et al. [2001] also used the DRM paradigm in their fMRI research into the neural correlate of correct and false memories. In order to activate perceptual aspects of the words during the learning phase, the subjects were shown a video of someone saying the words out loud, rather than listening to them on tape. As in previous studies, the subjects were asked to carry out a recollection task while in the scanner. Once again, there was a reasonable amount of overlap between the brain areas activated upon hearing old words again and those activated upon hearing the new theme words. In this case, however, relative to false ones, correct memories were associated with heightened activity in the brain areas involved in processing and integrating perceptual information (the posterior parts of the medial temporal lobe).

Slotnick and Schacter [2004] used a visual variation on the DRM paradigm in their fMRI research on brain activity associated with retrieving correct and false memories. Subjects were shown a number of abstract figures in the learning phase. In the test phase, while their brains were scanned, they were once more given a series of abstract figures and had to indicate which ones they recognised. They had seen some of the figures in the learning phase, but others were new. The new figures were divided into two groups: figures that resembled those shown before, and figures that did not. The subjects tended in particular to 'recognise' the figures resembling those they had been shown in the learning phase, although they had not seen these figures before. Once again, there was an overlap between the brain areas activated by correct and false memories. In this experiment, the researchers only considered false recognition of figures resembling figures shown to the subjects earlier. Both types of memory activated brain areas involved in the late processing of visual information (anterior areas of the occipital lobe), but only correct memories were associated with activity in those areas responsible for early processing of visual information (posterior areas of the occipital lobe).

In replication research using fMRI and the same stimuli, Garoff-Eaton et al. [2006] also studied brain activity induced by false memories of new figures that did *not* resemble figures presented earlier. In both cases, recognition of figures presented earlier and of figures resembling earlier figures induced activity in a huge network in the brain (the medial temporal lobe, the parietal lobe, and the frontal regions). Unlike previous research, fMRI was unable to distinguish between these two types of memory. Recognition of figures that did *not* resemble earlier figures, however, induced unique activity in the brain. This type of false memory tended to activate the areas of the brain involved in language processing (parts of the lateral temporal lobe).

### Discussion

As mentioned above, Schacter and Slotnick believe that correct memories differ at neural level from false memories because they uniquely activate areas of the brain involved in processing perceptual details. Several studies support this hypothesis. Three of the five experiments described above show that correct memories induce more activity in those areas of the brain involved in processing perceptual information than false memories do. The precise areas activated by correct memories differ considerably, however. That is partly owing to the nature of the stimulus material (visual information is processed by the occipital lobe; auditory information by the temporal lobe), but even in studies that use the same material, correct memories activated differing areas of the brain. For example, Schacter [1996] found that correct memories of auditory information were associated with the unique activation of brain areas between the temporal and parietal lobes, while Cabeza [2001] reported that such memories activated the posterior parts of the medial temporal lobe.

There are researchers who claim that false memories induced by the DRM paradigm say little about false memories in reality [Pezdek and Lam, 2007]. In the DRM paradigm, words such as dream, rest, and night activate the theme word sleep semantically. In the real world, false memories are induced in other ways, for example by fantasies about fictitious events. Critics of the DRM paradigm say that methods in which subjects recall non-existent amateur videos of public events or fictitious incidents from their childhood bear a closer resemblance to actual false memories. It is therefore important to know whether the false memories induced by these methods activate other areas of the brain than do real memories.

**Example XVI**

**It has long been known that people are better at recognising faces of their own race than of other races, and that people are biased in their evaluation of individuals from other races. Recent studies have identified the brain regions that may underlie these behaviours.**

American psychologists tested ten black Americans and ten white Americans in their functional magnetic resonance imaging (fMRI) brain scanner. The participants viewed pictures of unfamiliar black and white faces, and of antique radios, and had to try and memorise the pictures.

# Detecting prejudices in the brain

They were then given a memory test with previously presented pictures and new ones. All the participants, in particular the white respondents, remembered more faces of the same race than of the other race. Furthermore, the brain area specialised in face recognition, the fusiform face area, was more active when participants looked at same-race faces compared to other-race faces. The better participants could remember whether they had seen a face before, the more activity was measured.

Another study described the neural basis for race-evaluation biases. During brain imaging, white participants viewed unfamiliar black and white faces and had to indicate when they saw the same picture again. They then completed an explicit test about racial attitudes, and two indirect assessments of racial bias.

The white Americans had a pro-black bias on the explicit test, but an anti-black bias on the implicit tests. Furthermore, the participants who had a greater indirect negative racial bias also had a more active amygdala upon seeing unfamiliar black faces compared to white ones. There was no activation in the amygdala of the participants though when they viewed the faces of familiar, positively regarded blacks like Michael Jordon or Martin Luther King, Jr.

The amygdala is important for the implicit, physiological expression of a learned emotional evaluation, for example increased sweating as a response to something fearful. The amygdala response seems to be predictive of implicit race bias. That means that even people who consciously believe that they have no biased attitude may be influenced by experiences and cultural stereotypes in such a way that implicit tests still reveal an unconscious bias.

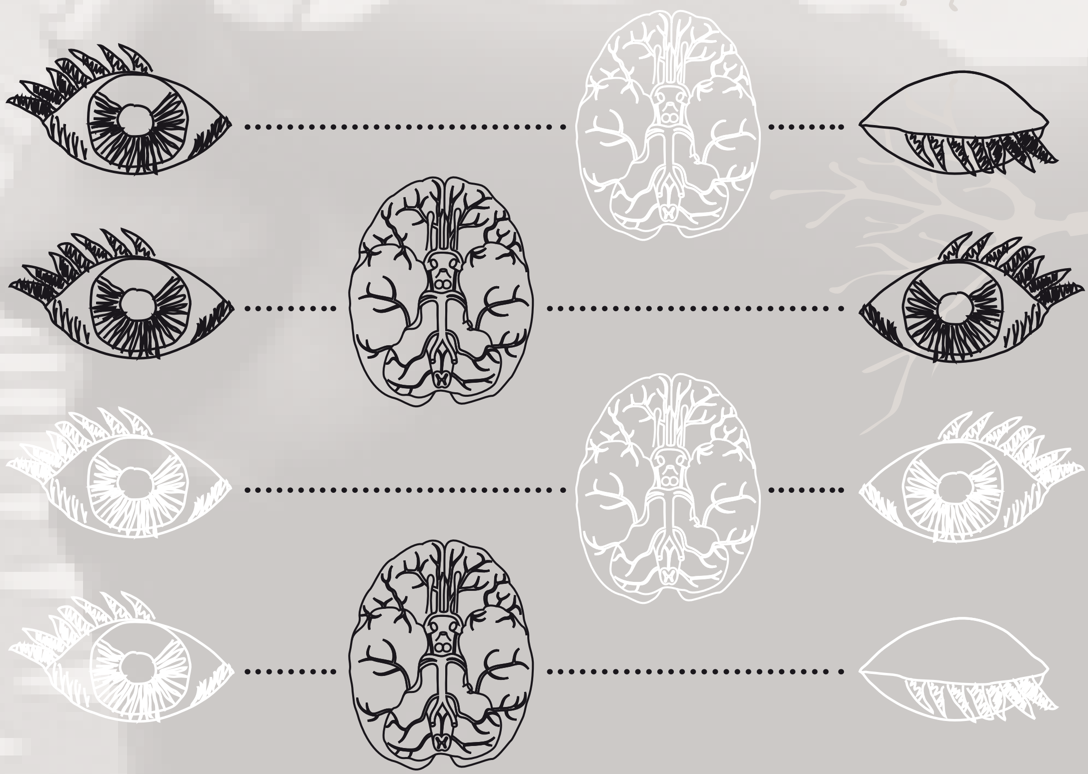
A third fMRI study demonstrated that when students see pictures of members of groups with a low social economic status, such as drug addicts and homeless people, this does not elicit brain activity in a region that is neces-

Original publications: Golby et al. (2001). *Nature Neuroscience*, 4, 845; Phelps et al. (2000). *Journal of Cognitive Neuroscience*, 12, 729; Harris and Fiske (2006). *Psychological Science*, 17, 847

sary for social cognition. Pictures of other social groups do activate this area. Extremely marginalised groups appear to be regarded as less than human by the brain.

An interesting question for further research is to what extent familiarity and exposure to certain facial types nullifies the above mentioned neural responses. For example, black people might show a less active amygdala since they spend more time – especially in child hood – looking at white faces. The same might count for people who grew up in mixed race families.

In conclusion, these results of neuro-imaging research have to be carefully interpreted. In his book 'The Ethical Brain' neuroscientist Michael Gazzaniga phrases it as follows: "*It appears that a process in the brain makes it likely that people will categorize others on the basis of race. Yet this is not the same as being racist. Our ability to make such a categorization is probably necessary for racism but does not necessarily lead to it.*" Still the neuro-imaging data underline that prejudice can influence the decisions of judges, police, and other participants in the judicial process involuntarily. Although such neurobiological findings improve our knowledge of social behaviour, basic behavioural science can still predict human behaviour with the same certainty.



In our opinion, it is not yet possible to use brain scans to distinguish false memories from correct ones outside the laboratory. Take the unfortunate woman who thought she had been raped by Donald Thomson. Would a scan have revealed that she was confusing her memory of Thomson's face with that of the rapist? We do not believe it would have. What we need is research in which subjects recall true and fictitious life events while in the scanner. If research of this kind systematically shows that correct memories activate other areas of the brain than false memories do, and that those areas activated by correct memories are always the same ones, then there may well be a place for brain scans in determining the veracity of an eyewitness's or suspect's memories. Until then, using scans in this way is — at best — still a long way off.

## 5.12 Control, free will and other humbug

*Victor A.F. Lamme*[20]

It's 23 May 1987. Kenneth Parks has had an awful day. He is struggling with debt and out of work. He hasn't had more than two or three hours of sleep a night in several weeks. Completely exhausted, he flops down on the couch to watch 'Saturday Night Live'. He can't concentrate on the show, however, and quickly dozes off. When he wakes up with a start, he is in his in-laws' living room. His father-in-law is lying in front of him, gasping for air. He sees his mother-in-law a few feet away, lying lifeless in a pool of blood. Parks looks around in confusion. Suddenly he sees that he too is covered with blood. He has a large kitchen knife in his hands that is dripping with red.

What happened? Sometime in the course of that night, Ken Parks got up from his couch and wandered out of his house. He got into his car, drove 23 kilometres to his parents-in-law's house, and, almost immediately upon arriving, attacked his mother-in-law with a kitchen knife that was lying about. She died at the crime scene. His father-in-law barely survived.

Ken Parks saw no reason to deny anything. The evidence was irrefutable: his car was parked in front of the door; there was blood on his hands; his father-in-law witnessed the whole thing. But there was one slight problem: Ken Parks was unable to remember anything. His memory 'blacked out' between watching 'Saturday Night Live' and waking up amidst the carnage at his in-law's house. No matter how hard he tried, he could recall nothing of what had happened that night. As a matter of fact, he did it all while sleepwalking.

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Parks's lawyers latched on to this fact and constructed a heroic defence. A sleep expert conducted EEG tests on Parks and discovered that he did indeed suffer from sleepwalking. The expert also argued plausibly that Parks had sleepwalked that very night, as he would have been likely to do so in a stressful period. The expert explained that people sleepwalk in the deepest stages of sleep, when it is scarcely possible to awaken them. A sleepwalker is as unconscious as a healthy (and living) person can be. In short, the events of that night resulted from a sequence of involuntary, automatic actions over which Parks had no conscious control. That is why, his lawyers argued, he should be acquitted. And in fact he was.[21]

Only in the USA, you probably scoff. But in fact, this particular case took place in Canada. France has the phenomenon of the 'crime passionel', and the Dutch criminal justice system recognises the concepts of 'met voorbedachten rade' (with malice aforethought) and 'ontoerekeningsvatbaar' (to be not responsible for one's actions). The justice system of every Western culture has a similar concept indicating diminished responsibility for one's actions, a sign of how deeply ingrained ideas such as consciousness, control, intention and free will are embedded in our society and in the way we think about humanity. They are the qualities that make us human, more or less the diametrical opposites of the unconscious, instinct, automatism and reflex. We come across these concepts in every aspect of our lives. In fact, it starts back in childhood, when we are told that we haven't acted wrongly if we 'didn't do it on purpose'.

But what is the difference between an unconscious and a conscious act? In the case of Parks, the dividing line is difficult to draw. He was evidently capable of driving a car without being conscious, and yet that is something that required him to process complex sensory information and to carry out an intricate series of actions. Parks's brain had clearly not 'switched off'. So why was he acquitted? Because it wasn't the *real* Parks who committed murder? Is there a 'creature' inside of him that he cannot control and for which he is therefore not responsible? Where in his brain is that creature? And where is the real Parks then? Does conscious control even exist, or did Parks's defence lawyers pull the wool over the jury's eyes? Aren't we all simply fooling ourselves?

In the first place, we have to understand that our ideas about free will and control are largely culturally determined. Human beings have always been fascinated by the distinction between body and mind, especially when they discovered the terrible things that happened to the body after death. The Egyptians tried to do something about it; the Christians let the worms have the body and concentrated on the soul. After Descartes and *"I think, therefore I am"*, and after Freud and the id, ego and superego, we now believe that

21 Lawrence Martin's internetpage 'Can sleepwalking be a murder defense?' describes a number of such cases. See www.lakesidepress.com/pulmonary/Sleep/sleep-murder.htm.

there is a control centre somewhere in our minds that not only rules our bodies but can even suppress morally reprehensible primeval instincts implanted deep in our brains.

What do psychologists and brain scientists say about this idea? If anyone knows the truth, they should. Do we really have any control over our behaviour? And is there really a control centre in our brains? It's a difficult question, so let us first look at what the lower orders of animals can teach us.

### The toad and the cricket

When a toad spies a cricket in front of it, it sticks out its tongue and gulps it down. That is very useful behaviour for a toad. If the cricket is not directly in front of it, the toad may leap or turn to one side first, so that the cricket still ends up on its tongue. It looks as if the toad knows where the cricket is, but behavioural biologists say that what we are seeing is a set of inbred or learned reflexes [Ewert, 1970].

Research into the brains of toads shows how the reflexes work. The toad sees an insect that is right in front of it as a moving spot in the upper half of its retina. The moving spot sends a signal to a kind of switching station, the tectum, which in turn controls the muscles that cause the toad to gulp.

**Figure 16**
*The toad sees a moving spot which sends a signal to a kind of switching station that in turn controls the muscles that cause the toad to gulp. Photo courtesy of Young-Ho Jeon.*

The tectum connects other parts of the retina to the leaping and turning muscles. The toad responds correctly depending on *where* in the retina the nerve cells are stimulated. These simple reflexes cause the toad to catch crickets entirely automatically [Ingle, 1970].

But what if there's an obstacle between the toad and the cricket, a large rock for example? If the toad goes through its standard repertoire, it'll bump its nose. What the toad should do is hop around the rock, but that is asking a lot of simple reflexes. It would mean that the toad would have to move away from its prey in order to get closer to it in the end. The tectum reflexes have to be overruled for a moment, and then allowed to resume dominance.

What happens is this: if you put an obstacle between a toad and a cricket, the toad will move sideways — in other words, away from its prey — and then attack from a better angle. It looks as if the toad is able to project the consequences of its actions into the future. It seems to have what in human beings psychologists refer to as 'cognitive control'. But how does a simple toad brain manage that?

The toad's brain has another structure in front of the tectum called the pre-tectum. This too receives signals from the eye, but only responds if a large area of the retina is activated all at once. In other words, it responds when the toad sees a large spot. The pre-tectum then sets off characteristic behaviour known as avoidance behaviour, which consists of hopping to one side [Ingle, 1973].

So the tectum sees to it that the toad catches crickets, and the pre-tectum makes the toad hop around obstacles. Does that solve the toad's problem? Not really. If the two systems worked independently, the toad would hop sideways and then back each time. One reflex would get it hopping towards the cricket, and the other away from it, ad infinitum. A type of supervisor system is seemingly still required to monitor which system should be active at any given moment, to grasp the overall situation and to take a judicious decision. But there really isn't much more to a toad's brain than a tectum and pre-tectum. So what is going on?

The answer is that the two systems — the cricket-catcher and the obstacle-avoider — keep each other in check. The tectum and pre-tectum's neurons are so closely associated that they can never be active at the same time. If a toad is seated before an obstacle and sees a cricket, both its tectum and its pre-tectum will be activated at first. But then one group of cells will repress the other. This mutual inhibition is based on the 'winner-take-all' principle: the winning system is fully active, and the other entirely inactive. The idea is not for one system to weaken the other: an all-or-nothing decision is required. It's no good to the toad to stick out its tongue only halfway or make half a hop sideways.

Nothing and no one in the brain decides who wins; the systems decide themselves, based on the extent to which they are activated by external stimuli. The tectum wins if it's a big cricket behind a small rock. The toad will leap forward or gulp. The pre-tectum wins if it's a small cricket behind a large rock. The toad will then hop sideways [Ingle, 1973; Collet, 1982].

The insight that we can draw from this example is noteworthy. When two systems with opposing interests keep each other in check, they appear to give rise, automatically, to an extra function. In this case, it is a function that closely resembles a 'decision module', at least on the surface of things. It really does seem as if the toad is making a decision. It is as if it is lying in wait of its prey; you can almost hear the toad thinking 'Do I attack now or should I hop sideways first?' But it isn't thinking at all. A toad psychologist who only observes the toad's behaviour might conclude that it is 'able to optimise its behaviour by considering the long-term effects of moving forward or moving sideways'. That is the ostensible effect of the toad's choices, but it is giving the underlying mechanism more credit than it deserves. In other words, it's easy to see something 'on the surface' as cognition when it is not. There is no control unit in the toad's brain. The real answer is infinitely more efficient. And dazzlingly simple.

### A prince is still a toad

Can we apply this insight to human beings? Do human beings, like toads, appear to be more than they actually are? It may be going a bit far to compare humans, who write books and fly to the moon, with a toad that catches crickets with its tongue. A human being does not see every moving spot as a bite of food. He can tell the difference between his car and his neighbour's. He knows which child is his in a classroom of toddlers. He is capable of recognising a rare postage stamp at a fair. And for every stimulus, he displays a different appropriate behaviour. The human stimulus response repertoire is much richer, but in essence it is the same as that of the toad. And much of that repertoire is controlled by the environment.

Higher-order animals are no different than toads when it comes to choosing between one stimulus and another. They are also subject to competing alternatives. Extensive research with monkeys has borne this out. For example, you can teach a monkey to instantly move its eyes to the right when he sees something moving to the right, and to the left when something moves to the left. If you look at its brain during this exercise, you see how a weak signal is amplified at each station along the way in the structures that detect motion, until the signal finally reaches the structure that controls eye movement. By then it has become a powerful 'left' or 'right' signal, regardless of how slight the motion was in the first instance. Things really get interesting in the case of 'noise', i.e. multiple dots moving every which way. The chimpanzee can then choose 'freely'; both left and right are 'correct'. What happens then? Is its 'free will' module activated? Not really. A slight difference in the brain cells' activity coding for 'right' compared to those coding for 'left' is amplified to the point where 'right' wins out over 'left'. In other words, it's the same winner-take-all competition as in the toad [Huk and Shadlen, 2005].

Where does that slight difference come from? Does the monkey decide? Is that its 'decision-making scope'? No, not really. One brain cell just happens to be slightly ahead of the other or more active than the other. That might be because the other cell had just been active and was 'recovering'. Repeated stimuli tend to 'ingrain' favourite pathways in the brain, so that they automatically induce a stronger signal. If the animal looks 'left' more often than 'right', that in itself will influence its 'free' choice [Platt and Glimcher, 1999]. That also applies to stimuli that we come across in everyday life. We automatically find things we have seen before beautiful, a phenomenon known as the 'mere exposure effect'. Certain types of stimuli also draw our attention because evolution has hard-wired them into our brains; for social animals such as humans and monkeys, one such stimulus is faces [Theeuwes and Van der Stigchel, 2006].

Does this mechanism apply to all sorts of choices that we make in life? Don't things work differently if we think carefully about our decisions beforehand? I'm afraid not. When we go to vote and have to choose between Labour and the Conservative, the same thing probably happens. Some people will have an ingrained Conservative pathway. It's an easy decision for them. Undecided voters will probably go through something similar to what happened to the chimpanzee when confronted by the 'noise' pattern. A slight difference will be amplified until the voter knows for sure: "I'm voting Labour." Where does that slight difference come from? Did he see the Labour candidate on TV more often? Or too often, so that his neurons are suffering Labour fatigue? There are no hard data, but that is probably how it works. Research on the American presidential and congressional races have shown that all kinds of unconscious factors play an important role in voters' choices. These include how tall the candidate is (tall is better than short), the shape of his face (a square or rectangular face wins more often than a round one), or the tone of his voice (a lower voice is better than a higher one).

No one is going to admit that they voted for Arnold Schwarzenegger because he has a square face and a low voice, of course. Not that they are lying; it's just that people don't know why they choose what they do. They think they know, but that is not the same as actually knowing. That has been shown in Libet's classic series of experiments. He had people press buttons spontaneously. They were allowed to press them as soon as they felt the urge to do so. In other words, they were given a free choice. And what did Libet find? He found that the subjects' brains decided to press a button a second or two *before* the subjects actually did so [Libet, 1985]. That clearly suggests that 'free will' does not precede an act, but in fact follows it.

The fact is, our brains decide to do something, and we come up with a reason for it. That has been demonstrated by research into split-brain patients showing that the left hemisphere has a module, called the 'brain interpreter' by researchers [Gazzaniga, 2000], that comes up with reasons for our behaviour (and probably the behaviour of others). Normally, that reason matches the actual determinant of the behaviour. All day long, our brain interpreter produces reasons for our behaviour. When we take decisions, the mechanism is not essentially different from the toad's. The only difference, in fact, is that we have a module that comes up with 'linguistic' reasons for that decision. That is why we believe that our thoughts influence our choices. But in fact, it's the other way around (see also section 5.2 on split-brain patients).

### Wanting and knowing by design

So where does the brain interpreter come from? And what use is it to us? Social animals — such as monkeys, apes, and human beings — are constantly asking themselves "Who's going to do what, and when?" We need to know that to acquire food, status, a mate, the best bed for the night, and all sorts of other things. Such species have therefore developed a remarkable function that we call the 'Theory Of Mind', or ToM for short. ToM is our ability to project ourselves into someone else's mind. More accurately: it's the ability to predict another person's behaviour based on what he wants and knows. Children, for example, come to understand at a certain point that they can prevent another child from taking their toys by hiding them. By projecting yourself into someone else's mind, you know what he knows and can predict his behaviour [Premack and Woodruff, 1978].

ToM is often described as a uniquely human ability, but that is nonsense. Ethological studies have given splendid examples of ToM behaviour. A wildebeast usually flees when a lion approaches, but if the lion is too far away to attack, the wildebeast will move towards the lion. The wildebeast is saying "I see you, and I know you can't get to me." And the wildebeast is assuming that the lion knows this too, because otherwise it is only running an extra risk. By making use of ToM, the wildebeast is saving itself — and the lion — a whole lot of effort [Griffin, 2005]. Behavioural biologists will explain this in terms of conditioned or inbred behaviour, the result of having to deal efficiently with energy.

When a person makes use of ToM, he predicts someone else's behaviour in terms of that other person's motivation, knowledge and abilities. He wants this, he knows that, he can do these things. These are handy operational terms within the context of predictions, but that does not mean that concepts such as wanting or knowing actually determine the other person's behaviour.

Let's go back to the toad one last time. Anyone watching a toad hop around a rock will describe that in the following terms: "The toad wants to catch the cricket, but it knows that it can't reach it. So it decides to hop around the rock." We now know that what is actually going on inside the toad does not resemble this description in any way whatsoever. Nevertheless, it is an entirely appropriate description within the context of ToM. It is an appropriate way of predicting the toad's behaviour, but not an appropriate description of the actual determinants of the toad's behaviour.

Gradually, human beings began to apply ToM to themselves, and the concept deteriorated into the brain interpreter. Somewhere in the course of evolution, human beings began to think that predicting their own behaviour according to such concepts as 'wanting' and 'knowing' actually caused that behaviour [Gopnik, 1993]. That is because the predictions often seemed to be accurate, in part because they are not predictions at all; they are attributions after the fact. Human beings survey the situation before they act and the situation after they act and fantasise a whole chain of mental causality to link the two. And that chain naturally tends to seem correct. It is only under clever experimental circumstances (such as with split-brain patients) that we can demonstrate that people may give entirely false reasons for their behaviour. There have been many instructive and amusing social psychological studies on this subject [Wegner, 2004; Gladwell, 2005].

### Crime and punishment

In the light of what I have said so far, we are forced to say that control does not exist. More precisely put, it's an illusion to think that we control our actions with our thoughts. Anyone who has ever tried to lose weight will know what I am talking about. Nowadays, control comes in a jar. The dairy firm Campina has captured the *zeitgeist* and named its latest hunger-suppressing yoghurt drink Optimel Control®. Our actions are controlled by the brain, of course. But the fact that the brain at the same time also produces all kinds of thoughts doesn't really matter all that much. Those thoughts serve to predict our own behaviour, to apply the ToM to ourselves. But in fact, our behaviour is as much of a mystery to us as the behaviour of others.

Does that mean that no one can be held responsible for his actions? "But Your Honour, it's my brain that did it, not me!" Defence lawyers in the United States recently used this argument. They evidently did not understand: people are what they do, no matter what they say or think about their actions later on or beforehand. Someone's character is the sum total of all stimulus-response connections laid down in his brain, whether that be genetically or by ingrained experience. Someone's personality, his real 'me', is located all throughout the brain, and not only in some control module. And if that brain does something wrong, it has to be punished as a whole, including the person in which it is encased.

So it seems to me that we would be better off scrapping such notions as intention and control from our view of humanity, and, logically, from our criminal justice system. The traditional view of humanity is based on scientific insights that the past fifty years of research have made obsolete. If we throw out Descartes and Freud and take modern psychological and neuroscientific findings on board instead, we will be forced to conclude that the distinction made in Western law between 'free will' and 'impulsiveness' doesn't cut much ice [Denno, 2003].

The concept of diminished responsibility proposes that a suspect's free will may have been so restricted at the time of the crime that he cannot be held accountable for his actions. It is an argument often used in obviously pathological cases, such as Parks, who murdered his mother-in-law. At the fatal moment, sleepwalking 'deactivated' parts of his brain, and the stimulus-response connections in the rest of his brain prevailed. Unfortunately, those connections were of the less sympathetic kind. But Parks was helpless: he could do nothing more than what he did, and is therefore not accountable for his actions. But this is a specious argument, because it applies to every one of us (the 'winner-take-all' mechanism simply does what it does).

More important in my view is that Parks's remaining stimulus-response connections should be corrected. It is very odd that lighter sentences are generally meted out for 'impulsive' acts than for premeditated ones. It is precisely the acts we commit on first impulse that represent the stimulus-response connections lodged deepest in our brain. They tend to win the winner-take-all competition between the various alternative responses and reveal someone's most deeply ingrained stimulus-response repertoire. They are what reveals a truly nasty disposition. Strong stimulus-response connections of this kind must either be inbred or have been developed after very severe training — something like a drill sergeant who trains his soldiers to respond properly even when they can't think straight. It takes just as long to remove such ingrained paths from the brain. In the criminal justice system, that training tends to consist of prison sentences. So my advice is: longer sentences for crimes committed on impulse.

Some stimulus-response repertoires are so ingrained that they will probably never disappear, for example in cases involving sexual offences or extremely violent murder. In the Netherlands, oddly enough, these are precisely the cases that are given the most expensive form of 'training': detention in a hospital or youth custody centre. As we know, the effect of this sentence is minimal — not surprising in the light of what we now know. We cannot really remove the traces by talking and other forms of psychotherapy. Rigorous behavioural therapy, pharmaceutical intervention or even psychosurgery are what is required. The situation becomes truly dangerous when we start to predict an offender's future behaviour based on what someone thinks or says. That will be clear enough to the readers by now.

So what *can* we do? I think that modern brain-imaging techniques can give us quite a good idea of the wrong stimulus-response connections in, for example, sexual offenders. Based on the results, it might be possible to predict their future behaviour more accurately. The criminal justice system should do less talking and take more action.

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# Summary

*Ira van Keulen*[1]

The brain is one of the most complex systems known to mankind and certainly one of the most intriguing systems. That much is clear from the media attention brain research receives nowadays. The reason why we are so fascinated by neuroscientific research is because never before — not even with genetics — did scientific research get so personal. Research on the brain and mind deals with our very selves, our conscious and unconscious behaviour that make our identities and personalities. If we come to fully understand the workings of the brain and mind, we will understand how we ourselves think and behave, with potential relevance in every domain of life.

1 Projectmanager, STT.

So far neuroscientific research has been largely technologically driven. Every new (research) technology has been pushing the field forward with large steps. For example, the inventions that allowed non-invasive imaging of activity in the functioning brain (finally opening up the possibility to couple higher functions in the brain with activity in the underlying neural substrate), the patch-clamp technology in neurophysiology (allowing researchers to record the activity from identified individual neurons in the central nervous system) and the multitude of tools provided by genetics (linking function to molecules at all possible levels of brain functioning). All these technologies have resulted in great knowledge about the anatomy of the brain, about the way individual neurons process information and how they communicate with each other, how the major sensory input systems collect and represent information and how output systems (such as muscles, glands, etc.) are addressed. We still face major challenges in understanding the brain and mind though. We lack the right concepts on how to analyse such a huge complex system and on how to handle the strong dynamics of the brain. We are short of computational approaches to integrate the huge amount of data from the different branches of the brain sciences. And there is still a lot of research to do in order to understand the relation between molecular aspects and different higher cognitive functions.

However, it is not necessary to understand everything about the brain and its mechanisms in order to be able to think about current and future application possibilities of the growing knowledge of the brain. Even minor neuroscientific findings can be of relevance in product development and in applied sciences (e.g. educational or food). In fact, it is becoming more and more clear that — as the prominent neuroscientist Michael Gazzaniga once put it — “the neurosciences have much to comment in dozens of areas of social concern and invention”. Besides making rapid progress in fundamental research, the neurosciences and cognitive sciences should not forget to focus as well on links between their basic research and societal issues, not only within health care, but also outside this domain. Most of the existing applied neuroscientific research is related to health care, simply because most brain research seeks to understand neurological and psychiatric disorders. It is exactly this challenge — how society can benefit from the mounting scientific insights in the brain and the mind beyond the area of health care — that the STT project Brain Visions has been taken up. In three transdisciplinary[2] expert groups and one large-scale conference, STT has explored the application possibilities in the areas of food, man-machine interfaces (MMI), education and judicial practice. The ideas and discussions of the expert groups and the speakers at the conference are reflected in this STT publication.

2 Each expert group consisted of about thirteen people from different backgrounds: academia, industry, government and other stakeholders. See also ‘Project Organisation’, in the back of the book.

## Results

The results of the STT project are a collection of ideas — or 'brain visions' as we call them — on how to apply brain scientific knowledge in four different areas. In addition, the project offers some clues to the conditions that will allow the neurosciences and cognitive sciences to develop to the benefit of society.

### *Nutricognition*

There are two ways to think about the relationship between food and the brain, or 'nutricognition', as we refer to it in this book. First, there is growing research on the effect of diet and individual nutrients on brain development and cognitive functions. Examples are the positive effects of fish oils on children with ADHD and elderly people with mild cognitive decline or the negative effects of arsenic in groundwater on the developing brain of children in Bangladesh and India. Secondly, researchers are learning more and more about the neural mechanisms behind eating behaviour, e.g. satiety, food perception and liking, hunger, food addiction or buying patterns. Recent neurocognitive research has demonstrated, for instance, that the response of the food reward system in the brain to food cues such as food advertisements varies widely between individuals. People with a strong tendency to overeat have a high reward sensitivity and are therefore more susceptible to appetizing food cues.

The growing mound of nutricognitive research may lead to the introduction of various food products now and in the future: 'brain food' (i.e. products that can affect brain development and performance), weight-control products (i.e. high satiety products that reduce the consumer's appetite) or products based on cross-modal compensation strategies (i.e. replacing different sensory stimuli like taste, odour, texture or colour with one another to achieve the same effect in liking while preventing potentially harmful effects). But it is not only the food industry that will profit from the increasing research on brain-food interdependency. The public will also receive better nutritional advice, with, for example, the elderly being advised to consume folic acid to slow the mental decline of aging and vitamin D to alleviate depression. Scientific research into the neural mechanisms behind overeating may also lead to more effective policy measures to fight the obesity epidemic.

In nutricognitive research, neuro-imaging techniques will be particularly crucial. They can provide sensitive and specific test methodologies to help us understand sensory perception and integration, the underlying mechanisms of preference and liking, and the influence of nutrients on brain development and performance. And whereas more traditional food research relies on long-term nutritional intervention and large groups of respondents, neuro-imaging may speed up research on the effect of nutrients on the brain.

*Neuro-centered design of interfaces*

The most appealing application of neuroscientific knowledge in the field of MMI is brain-machine interfaces. There is an invasive BMI approach (inserting electrodes directly into the brain) and a non-invasive (attaching sensors to a cap or headband worn on the scalp). Both are able to read brain activity — for example by measuring electrical signals, blood supply or oxygen level — and translate it into a digital form that computers can convert into an action of some kind. The brain activity measured by BMIs is sometimes related to a particular cognitive activity. Many companies hope to use an electroencephalogram (EEG) to recognise the brain activity patterns of cognitive workload, task engagement, surprise, satisfaction and frustration. Such information, derived directly from the brain, could lead to adjustments to the system to be operated. For example, in case of cognitive overload the amount of information offered to the user could be adjusted. Sometimes brain activity does not contain information at cognitive level, but is used as an output measure that can be detected by a computer system in order to recognise the user's need.

Neuroscientific research can also be of use outside the field of BMI, however. Areas that might benefit from our growing knowledge of the brain in MMI are neuro-ergonomics and neuro-mimicry. Neuro-ergonomics is an emerging field combining neuroscience with man-machine interaction studies in order to evaluate and optimise the match between a particular technology or interface and the capabilities and limitations of the human brain. Neuro-mimicry is about using our growing knowledge of how the brain works to imitate neural mechanisms in novel interfaces, machines or robots.

Last but not least, a different perspective on the symbiosis of the neurosciences and MMI is that the neurosciences can also benefit from MMI research and development. MMI can offer the cognitive neurosciences interesting research tools such as Virtual Reality (VR). Combining functional magnetic resonance imaging (fMRI) and a well-designed VR environment that gives participants a strong sense of reality could lead to a better understanding of the relationship between what people are thinking and experiencing and the associated patterns of brain activity. MMI can also support the neurosciences in designing applied research projects proposing to investigate the neural and cognitive processes underlying the interaction of humans with technology. The various ways in which MMI can exploit neuroscientific knowledge and vice versa will lead to a new field: the neuro-centred design of interfaces.

*Personalised learning*
Neural plasticity is the main principle behind learning and currently the subject of exhaustive neuroscientific research. It will therefore come as no surprise that there are many international and national initiatives uniting the neurosciences, the cognitive sciences and educational sciences in the search for evidence-based learning methods. The prevailing opinion is that the brain sciences can make a valuable contribution to education by investigating what type of training at which intensity and for what length of time is most effective and for whom, based on differences in the way the brain is organised. One future line of research in — as some call it — the educational neurosciences is personalised learning. Both educational practice and science appear to be particularly interested in how the neurosciences and cognitive sciences can contribute to personalised or customised learning. The biggest challenge in educational practice is how to gear instruction towards individual needs, largely because we lack insight into the various strategies and procedures of learning that people apply during a learning task. Our lack of knowledge means that instructional materials and traditional teaching methods do not take these differences into account. Many of the instruction methods used in schools do not invite all children to participate, stimulate them enough, or fit in with the way they learn. The neurosciences are expected to give the educational sciences a more solid basis for developing theories about these individual differences in learning abilities and strategies and motivational aspects. Such research may provide clues on how to adapt instruction to individual differences.

There are only a few examples of neuroscientific findings that can be used unconditionally to justify specific recommendations for educational policy and practice. For instance, we only have a limited understanding of human brain development, since most basic neuroscientific research so far has been conducted on animals. More quantitative and histological research on human brain development is required, including investigations of possible sensitive periods (or 'windows of opportunity') during which specific brain areas or functions related to formal education (reading, arithmetic, writing, etc.) develop optimally. The use of neuro-imaging in schools or other educational settings is promising but still a long way off, mainly because the current techniques are either too expensive or too complex to use. But there are some instances of neuroscientific research that may, already in the short term, have an impact on educational practice. Examples are the research on gender differences in brain structure and functioning, mirror neurons and the development of memory-enhancing drugs.

*Evidence based judicial practice*

The neurosciences and cognitive sciences help us understand the functioning of the brain in relation to human behaviour, including those of delinquents, witnesses, police investigators, judges, lawyers and public prosecutors. In fact, much of the current knowledge derived from the cognitive sciences could already be applied in judicial practice, but it has unfortunately not always penetrated the administration of justice yet. Our growing understanding of the workings of memory (the influence of stress, the origins of false memories, facial recognition, etc.) will be particularly important to many aspects of judicial practice, for example interrogation techniques and the status of witnesses' and victims' statements. Other, more basic neuroscientific findings— which depict the brain as an automatic device that controls our perception, attention, emotions, judgements and decisions — will have a more profound impact on judicial practice. These recent findings will fuel the philosophical discussion as to whether human beings actually possess free will. The concept of what constitutes personal responsibility for one's actions may have to be reconsidered. If a better understanding of the interactions between the neurobiological and environmental factors underlying behaviour will reinforce the belief that delinquent behaviour is the product of forces beyond the control of the offender, the legal system will have to change its assumptions about criminal responsibility. This belief can also result in a legal system that emphasises treatment more than punishment. The contribution of the neurosciences and cognitive sciences to the judicial system will obviously not be limited to investigative practice and the courtroom (i.e. lie detection, profiling, neuro-imaging evidence, determination of accountability, decision supportive systems). The brain sciences are expected to influence the punishment or treatment of delinquents, for example by improving the diagnostics of psychopathologies, facilitating better (i.e. customised) and different treatments and treatment combinations for psychopathologies, anti-social behaviour and addiction. Or by providing better insights into the effect of punishment on delinquents and how it varies from one person to the next. We should be careful though that our growing knowledge of the brain does not reinforce the trend towards preemptive criminal law resulting in preventive treatment, prosecution or incarceration of people who score high on neurobiological risk factors.

*Conditions for further successful development of the brain sciences*

Four conditions that will ensure that the brain sciences will make a significant and positive contribution to both science and society, rose to the surface during meetings and discussions in the STT Brain Visions project. We will mention them briefly here, more details can be found in chapter 1. The brain sciences, in cooperation with others (government, industry, media, educational and judicial practice and other related scientific disciplines) are encouraged to:

– Continue the trend towards interdisciplinary research (i.e. integrating concepts, methods and data from different scientific disciplines) in order to support the successful academic development of the field and work towards comprehensive theories of the brain.
– Increase transdisciplinary research (i.e. integration of scientific and non-scientific knowledge) to stimulate socially relevant applications and disseminate neuroscientific and cognitive knowledge in different relevant practices.
– Set-up a research agenda and public debate on the ethical, legal and social implications (ELSI) of the neurosciences and cognitive sciences.
– Try and maintain a proper balance between making promises and preventing hypes by avoiding or challenging oversimplification and overvaluation of their scientific findings.

Meeting these conditions will result in a good chance for the ‘brain visions’ in this book to become reality in the near and distant future.

# Appendix 1

In the course of this book we make frequent reference to various research tools used to study the brain and its functions, without explaining them in detail. It might be useful for readers to have a brief look at some of these tools. This appendix addresses the following: neuro-imaging (non-invasive and invasive), transcranial magnetic stimulation (TMS) and genomic mapping. The appendix is predominantly based on texts from the website of the Centre of Cognitive Neuro-imaging of the Donders Institute for Brain, Cognition and Behaviour, Nijmegen, and to some extent also on texts from www.wikipedia.org.

## Neuro-imaging

One important reason for the doubling of our knowledge of the brain since 1990 is the use of imaging techniques, especially functional imaging. For the first time, scientists are able to observe, in real time, not only the structure of the brain, but also its functioning, i.e. the activity in its various parts. That means that we can now study particular processes in the brain through time, e.g. blood flow (fMRI), electrical activity (EEG) and the magnetic activity of neurons (MEG). Each tool has its strengths and weaknesses, as the following subsections explain.

### Non-invasive functional neuro-imaging

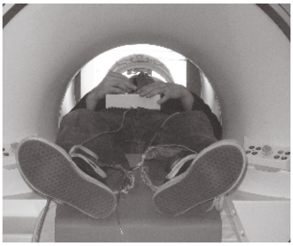

**Figure 1**
*Courtesy of the Donders Institute for Brain, Cognition and Behaviour.*

#### fMRI

fMRI is based on magnetic resonance imaging (MRI) and used to map regions of the brain that are 'activated' while performing a specific task. MRI employs radio frequency (RF) pulses to manipulate the magnetisation of nuclei in tissue, most commonly detecting the hydrogen nuclei in the water molecule. As the signal behaves differently depending on tissue type, it is possible to obtain static images providing anatomical information, e.g. with contrast depicting the grey and white matter[1] regions of the brain. The type of contrast used in fMRI is achieved by dynamically measuring the blood oxygenation level dependent (BOLD) contrast, using time series of images to assess the haemodynamic response related to neural activity in the brain.

Haemodynamics stands for the changes in blood flow and blood oxygenation which are closely linked to neural activity. When nerve cells are active, they consume oxygen carried by haemoglobin of the red blood cells in local capillaries. The local increase in oxygen consumption leads to a significant increase in blood flow, delayed by approximately 1-2 seconds. This haemodynamic response reaches a peak after 4-5 seconds, before falling back to baseline. Consequently, the relative concentrations of oxyhaemoglobin and deoxyhaemoglobin — as well as the regional blood flow and blood volume — change locally. Because haemoglobin is diamagnetic when oxygenated but paramagnetic when deoxygenated, the interplay of these haemodynamic processes results in a change in the magnetic susceptibility of blood, which in turn leads to a slight change in the local magnetic field and hence in the MR signal intensity. The MRI signal of blood therefore depends on the level of oxygenation that can be detected using an appropriate MR pulse sequence like the BOLD contrast. However, by using other MR pulse sequences, we can also measure changes in cerebral blood flow (CBF) or blood volume (CBV) directly.

1 The cell bodies of neurons and the glial cells supporting the neurons constitute the grey matter of the brain. White matter is composed of the axons connecting the different areas of grey matter to each other carrying the nerve impulses between neurons.

The BOLD signal is composed of signal contributions from larger arteries and veins, smaller arterioles and venules, and capillaries. Experimental results indicate that the BOLD signal can be 'biased' towards the smaller vessels, and hence closer to the active neurons, by using larger magnetic fields. It has been estimated that about 70 percent of the BOLD signal arises from larger vessels in a 1.5 Tesla scanner, but about 70 percent arises from smaller vessels at 7 Tesla. Furthermore, the size of the BOLD signal increases as the strength of the magnetic field increases. Hence there has been a push for larger magnetic field scanners to improve both localisation and sensitivity.

A major advantage of fMRI over other neuro-imaging techniques is the high spatial resolution that permits the identification of cortical areas active during a particular cognitive process. The spatial resolution can range from 1 to 2 mm. However, the temporal resolution, roughly 1 second, is relatively poor compared to the electro-physiological measurement with EEG or MEG. fMRI thus allows accurate inferences about where in the brain a particular cognitive process is instantiated; for inferences about the temporal nature of activation processes, EEG or MEG recordings are more suitable. Unlike EEG and MEG, fMRI does not provide a direct measure of neural activity because it records local blood flow and oxygenation changes that are a result of brain activity. fMRI thus allows us to look at neural activity through a vascular filter; it does not require neural activity to be synchronous, or demand a particular geometrical orientation of the neurons. Furthermore, fMRI is a sort of temporal integration of the haemodynamic response (in the range of several seconds) and does not measure the immediate activity changes of groups of neurons.

fMRI is one of many MRI techniques. Another one — which also has been mentioned in the book a couple of times — is diffusion tensor imaging (DTI). DTI detects the preferential direction of the brain's white matter tracks, its 'wiring'. This technique makes it easier to understand how the brain works, as it reveals brain areas are connected to one another and how.

### EEG

EEG detects the brain's electrical activity directly through electrodes placed on the patient's scalp. Today, the international standard has moved towards recordings taken from 128 electrodes. The technique measures general patterns of brain activity, such as the speed of the neural spikes. EEG is frequently used in research studying event related potentials (ERPs). The ERP is an electrical change in the brain that relates to an event occurring either in the external world or within the brain itself.

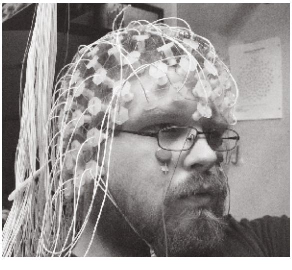

**Figure 2**
*Courtesy of Jan Ruotsala, www.flickr.com.*

EEG measures spontaneous rhythmic electrical activity occurring in multiple frequency bands. Event-related synchronisations in the alpha (8-12 Hz) and lower beta (18-30 Hz) bands are the electrophysiological correlates of resting or idling cortical areas. Measurements of transient periods of desynchronisation or synchronisation of EEG, especially in the gamma frequency range (around 40 Hz), in relation to different aspects of information processing have been used in recent years to draw inferences about the neural organisation of perception and cognition.

One of the great strengths of electrical and magnetic recordings is their high temporal resolution, which is in the order of tenths of milliseconds. In order to understand the neural dynamics of human cognition, we need to know not only where in the brain certain cognitive operations take place, but also when they occur. EEG/ERP and MEG recordings are far better at this than the haemodynamic measures provided by PET and fMRI.

A disadvantage of EEG/ERP on the other hand is the poor spatial resolution. EEG is most sensitive to a particular set of post-synaptic potentials[2]: those which are generated in superficial layers of the cortex, directly abutting the skull. Currents from dendrites (i.e. certain nerve fiber) which are deeper in the cortex, in midline or deep structures (such as the cingulate gyrus or hippocampus) have far less contribution to the EEG signal. Furthermore, the meninges[3], cerebrospinal fluid[4] and skull 'smear' the EEG signal, obscuring its source. It is mathematically impossible to reconstruct a unique current source for a given EEG signal, as some currents produce potentials that cancel each other out (i.e. the inverse problem). However, the development of new mathematical tools for inverse modelling has opened up new ways to deblur the scalp EEG or to determine the location of the neural sources that generate the surface potentials. In addition, combining fMRI with EEG in research experiments makes the inverse problem more tractable. There are some (technical) problems in combining both research tools though. For example, since the data derived from each occurs over a different time course, the data sets do not necessarily represent the exact same brain activity.

EEG/ERP has a few advantages over the other brain imaging techniques. From a technical point of view, EEG/ERP recordings are the least complicated and the least expensive among brain imaging methods. Also, it is the only technique that does not require head immobilisation. This means that EEG has considerable advantages in studies involving subjects less tolerant of head restraint (e.g. children and elderly). The EEG/ERP method therefore provides an excellent tool for pilot research and as the standard co-registration technique in combination with other scanning facilities.

2 Post-synaptic potentials are changes in the membrane potential caused by the presynaptic neuron releasing neurotransmitters from the terminal button at the end of an axon (i.e. certain nerve fiber) into the synaptic cleft.

3 The system of membranes which envelops the central nervous system.

4 The fluid inside and around the brain.

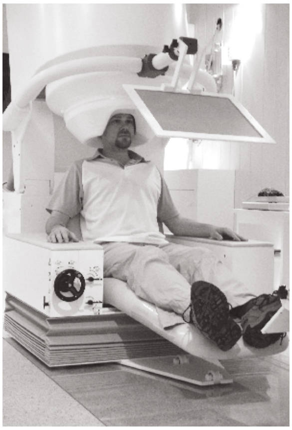

**Figure 3**
*Courtesy of the Donders Institute for Brain, Cognition and Behaviour.*

## MEG

When a neuron receives a synaptic input, a small dendritic current flows that produces a magnetic field. When a sufficiently large population of neurons receives synaptic inputs within a short time-window, the dendritic currents accumulate, producing a field large enough to be detected outside the head. Magnetoencephalography (MEG) is a technique that allows us to measure these magnetic fields.

MEG is based on SQUID technology. The superconducting quantum interference device (SQUID), which was introduced in the late 1960s, is a sensitive detector of magnetic flux. Today's whole-head MEG systems contain a large number of SQUIDs (between 100 to 300) connected to sensor coils in a configuration roughly following the curvature of the head. Since the environmental magnetic noise level produced by traffic, elevators, etc. is several orders of magnitude higher than the neuro-magnetic signals, the MEG system needs to be placed in a magnetically shielded room.

As the magnetic field measured by MEG is produced directly by electrical neuronal activity, it is possible to detect signals from the brain on a sub-millisecond timescale. This makes MEG fundamentally different from such imaging technologies as fMRI, which measures blood flow changes occurring on a much slower timescale. The activity measured by MEG may be the result of an evoked response, such as visual stimulation, or spontaneous activity such as alpha waves.[5]

When analyzing the data measured by a whole-head MEG system, it is often possible to estimate the brain sources producing the signals. The major advantage of MEG is that the neuro-magnetic fields are largely unaffected by inhomogeneities in the skull and the scalp. Electrical potentials on the scalp, as measured by EEG, are usually strongly influenced by these inhomogeneities. In practice, this means that source estimation based on MEG signals involves less guesswork and is more accurate than when based on EEG signals. Another important difference between MEG and EEG is that MEG is insensitive to current flows oriented perpendicularly to the scalp. Only the tangential component of a current flow will produce a measurable field. This in fact makes EEG and MEG complementary techniques, and MEG and EEG signals are often recorded simultaneously.

## Invasive neuro-imaging

Alongside the non-invasive techniques mentioned in the section above, there are also imaging techniques that require the insertion of a specific particle (PET, molecular imaging) or electrodes (electrophysiological recording) into the brain.

5 Alpha waves or rhythms are one type of brainwaves originating from the occipital lobe during periods of waking relaxation. See www.wikipedia.org.

**Figure 4**
*Source: www.philips.com.*

## PET

PET is based on the principle that local blood saturation increases when the neurons fire. A short-lived radioactive tracer isotope — incorporated in a metabolically active molecule (such as glucose, water or ammonia) — is injected into the circulatory system of the respondent or patient; this is why PET is called an invasive technology. When an isotope decays — in about two minutes in the case of oxygen (O15) — it emits a positron. After travelling up to a few millimetres, this positron encounters and annihilates with an electron, producing a pair of gamma photons moving in opposite directions. These gamma rays released during isotope decay are measured by a detector in the PET scanner. More highly activated areas in the brain will contain more radioactive blood, since the oxygen isotope is attracted to these areas.

The spatial resolution of PET is fairly good (although not as good as fMRI or MEG), but the temporal resolution is on the low side. Only a single PET scan can be made per minute. The use of radio-active material means that a respondent can only take part in a PET study once a year, for just a few hours. That is why PET is not used much as a research tool in experiments involving human subjects, for example in cognitive neuroscience. It can, however, be used in repeated investigations of the same subject in pre-clinical studies involving animals. The major challenge for PET — although mainly significant in clinical settings — is the search for new tracers that are ligands for specific receptor subtypes or enzyme substrates. These tracers permit the visualisation of receptor pools that play a role in neurological disorders or psychiatric diseases, for example dopamine receptors in Parkinson's disease.

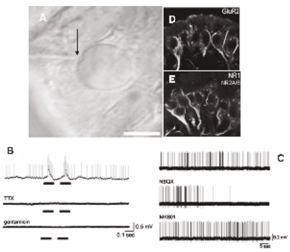

**Figure 5**
*Direct recording of synaptic activity.*
*Source: www.inmfrance.com.*

## Electrophysiological recording

There are two kinds of recordings. Intracellular recordings are made from neurons in vitro, e.g. slices of rat brain tissue. This method involves measuring the voltage or current across the membrane of a neuron by means of a microelectrode inserted into the cell.

Extracellular recordings are made from neurons in vivo, in other words recordings of brain activity in living animals made by inserting micro-electrodes into the living brain (which is why it is considered an invasive technique). An electrode will usually detect the electrical activity generated by the neurons adjacent to its tip. With a 1-micrometre tip, the electrode will detect the activity of one neuron at most, known as the single-unit recording. The signals during the single-unit recording are much smaller than during intracellular recordings. If the electrode is slightly larger than 1 mm, it will record the activity of a group of neurons, referred to as multi-unit recording. This method is often used with living animals to record changes in brain activity in a particular area during normal activity. Some of the problems encountered by scientists when using electrophysiological research tools are: identifying optimal brain regions for electrode implantation; identifying coding strategies of neurons in particular brain regions; understanding the limitations of brain plasticity; and the biocompatibility and durability of electrodes.

One important trend in neural electrophysiology recording is the use of multielectrode arrays (MEA) to both register and stimulate neural activity. The MEAs are used to culture neurons — usually dissociated neurons from rat embryos — for some weeks or sometimes months. The array consists of about sixty electrodes on a glass substrate, which keeps the MEA transparent so that neuronal morphology can be observed with a microscope. The MEA is connected to amplifiers and a computer that allows both stimulation of and recording from neurons lying on or near to the electrodes. MEA recordings help us to learn the language that neurons speak. Stimulating the cultured neural network by means of MEA will increase our understanding of the emergent properties of ensembles of living neurons, e.g. how neurons in living brains change during learning. These insights will lead to new and better computer models of neural networks, which we can then use to create artificial cognitive systems.

### Optical and other molecular imaging

In molecular imaging brain scientists try to detect a carrier, for example a monoclonal antibody with a contrasting agent, with a scanning technique like MRI, PET or optical methods. The complex is injected into the body to detect very specific molecular structures in the brain that can be picked up by the antibody. The challenge here is threefold: producing different antibodies to detect different molecular structures; producing antibodies at nano scale capable of passing the blood-brain-barrier; and combining the antibodies with the right contrasting agents.

Optical molecular imaging, or more precisely two-photon excitation microscopy in combination with fluorescent agents, is a particularly fast-emerging technique. This research tool is used in living animals. Optical imaging provides information on the source of the neural activity at the level of synaptic connections and beyond, as well as its time course, which is important for studying the functionality of the activity. The identification and cloning of the gene for green fluorescent protein (GFP) has been crucial for the development of optical imaging. Different GPF variants make cell tissue light up when viewed with light microscopy. This has enabled a better understanding not only of the structural biology of the brain at the level of the synaptic circuits, but also of the function of populations of neurons in the intact brain.

## Transcranial Magnetic Stimulation (TMS)

**Figure 6**
*Courtesy of Clinical Neurophysiology, UMC St. Radboud, Nijmegen.*

TMS is a non-invasive technique that influences the electrical activity of the brain. TMS uses a coil placed on the outside of the skull. The coil produces powerful, rapidly changing magnetic fields to stimulate an electric field in the brain by electromagnetic induction. rTMS is repetitive transcranial magnetic stimulation, which can differ in frequencies (from one to twenty Hz) and intensity (i.e. number of stimuli per second, the duration of the train of stimulation, interval between the stimuli and the total number of trains and stimuli). The magnetic field reaches brain areas located at a maximum of three and half centimetres below the skull. TMS can stimulate brain activity areas but can also disrupt brain activity. The exact details of how TMS functions are still being explored.

The advantages of TMS (or rTMS) as a clinical tool have yet to be proven, but its use as a research tool in cognitive science and neuroscience is less open to debate. There are two related applications of TMS in research. In the first place, TMS can be used to simulate neuropsychological disorders in healthy people — an interesting application, also referred to as 'virtual neuropsychology', since it is always hard to find respondents for neuroscientific or cognitive scientific research with a particular mental disorder. TMS is also important as a neuroscience tool in combination with fMRI because it can demonstrate the functional causality between a stimulus or certain behaviour and a certain brain area. fMRI only shows the activity in brain regions associated with a task or stimulus; by themselves, imaging studies do not prove that a particular area is the source of a given mental process. Using TMS, researchers can make causal inferences. If activity in an associated area is suppressed with TMS and the subject then has more trouble performing the task at hand, it proves that the area is involved in performing the task.

TMS will need to be improved in quite a few ways as a research tool, but two important shortcomings have already been overcome. First, the problem of neuronavigation, which enables researchers to target a particular brain area with TMS as accurately as possible, has now been solved by combining specific software with fMRI software. Secondly, it is now possible to maintain higher frequencies, e.g. 20 Hz, for a longer period of time. Two further problems remain. The first is the depth to which TMS can be used. This is now 3.5 cm, but 7 cm would be preferable (although TMS will still influence the brain regions in between) for stimulating or knocking out deeper brain areas. Secondly, the physiological effect of TMS is still not clear. We do not know precisely what happens on the neural level during TMS.

## Genomic mapping

Fifty percent of the human genome is involved in the evolution, structure and functioning of the nervous system. In this section we describe two different approaches to genetic research of importance to the molecular or genetic analysis of the brain: functional genomics and comparative genomics.

Functional genomics involves developing and applying experimental approaches to assessing gene function based on information obtained in genome-sequencing projects. This field of molecular biology is characterised by high-throughput techniques such as DNA micro-arrays, proteomics, metabolomics and mutation analysis. Bio-informatics is indispensable in this field, given the enormous datasets and the target of finding patterns and predicting gene functions. One important advantage of functional genomics is that it enables scientists to ask new types of questions requiring the analysis of large numbers of a system's components simultaneously, for example to enhance our understanding of complex physiological functions. Micro-arrays are another interesting possibility; they allow geneticists to discover the full range of genes being expressed in single neurons. If this technique can be made minimally invasive, it could also tell us something about the physiological processes taking place in the brain of humans or animals while they are in the act of thinking.

Comparative genomics is a branch of molecular biology that studies the genomes of different species or strains. The underlying assumption is that comparison helps to identify aspects of gene function and to find genes based on the evolutionary conservation of DNA sequences. The more genomes of different species are unravelled, the more comparative genomics becomes an important analytic method. Understanding genetic differences between humans and other primates will help us learn about different cognitive functions such as language acquisition, vision or hearing.

In addition to the study of interspecies variation, there is also the study of intraspecies variation, i.e. polymorphism. What is particularly interesting here is the study of genetic polymorphism that underlies critical differences in phenotype, for example individual differences in cognition. The ultimate goal here is to connect intraspecies variation in genes and gene expression with cognitive differences (with the help of neuro-imaging techniques). At the moment, DNA technology enables simultaneous detection of polymorphisms in many genes. It is feasible that researchers will produce a DNA chip within the next decade that provides an individual profile of polymorphisms in the genes relevant for cognition.

# Survey Organisation

## Acknowledgements

This publication is a result of the STT foresight (i.e. future study) Brain Visions and reflects the cooperation of a transdisciplinary group of experts from academia, industry, consultancies, government and educational and judicial practice who took part in this project. STT owes many thanks to all those who have unselfishly put much time, enthusiasm and energy into this project. Special thanks goes out to Reinout van Koten and Jacqueline Broerse of the department of Science Communication at the VU University who helped to set up, organize and analyse the fifteen expert group meetings in 2007.

## Method

The STT foresight study 'Brain Visions' is based on the STT method of 'knowledge fusion'. This method aims the transfer of knowledge by bringing actors from different backgrounds together in expert groups. These groups consist of researchers and developers from academia and industry, policymakers and other end-users with the aim to integrate scientific knowledge as well as non-scientific knowledge from different sources. By bringing these actors together, STT facilitates the formation of transdisciplinary networks and transdisciplinary thinking. Both are important in order to gear knowledge generation towards ideas on application possibilities. Scientists are not always aware of what they have to offer end-users in industries or public organisations and the latter are usually not well-informed about recent scientific findings. In the STT expert groups the different actors share their knowledge and creatively and constructively think on (socially) relevant future applications in five meetings. The STT project is directed by a steering group that – together with the project-manager – decides on the design and realisation of the project. They also play an important role in reading through the drafts of the final report.

The shared views of the three different expert groups on future applications of the brain sciences in the areas of food, MMI and education are expressed in the final report 'Brain Visions'. The views can be quite broad, like personalised learning, or more specific, like autonomous learning robots. The different views are written by the individual experts based on their own background and expertise. The views on the application possibilities of the neurosciences and cognitive sciences in judicial practice are not based on the method of knowledge fusion. These particular views are individual views of different stakeholders from science and judicial practice who gave a lecture at a one day conference entitled Justice and Cognition on November 22$^{nd}$ 2007, in Zeist, the Netherlands.

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| Ing R. Mente | Senior Innovation Advisor, Ministry of the Interior and Kingdom Relations and Senior Researcher Research en Innovatie CIP, Dutch Police Force |
| R.M.M. Mulder | Director, Study Centre Kerckebosch |
| Drs C. Steegers | Researcher Technology Assessment, Rathenau Institute |

## Conference Speakers

| | |
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| Mr F. Bauduin | Vice President, Amsterdam District Court |
| T. Bethlem | Investigative Specialist, Amsterdam-Amstelland Police Force |
| Prof Mr Y. Buruma | Professor of Criminal Law and Criminal Procedure, Radboud University |
| Mr H.J. Donker | Investigative Public Prosecutor, Breda Public Prosecutor's Office |
| Prof M. Gazzaniga | Professor of Psychology, Director of the SAGE Center for the Study of the Mind, University of California, Santa Barbara |
| Prof Dr R. Kahn | Professor of Biological and Clinical Psychiatry, Utrecht University |
| Drs E. Meijer | Researcher, Experimental Psychology Capacity Group, Maastricht University |
| Prof Mr Dr H. Nijboer | Judge, Amsterdam Court of Appeal, Director of the Seminary for Evidence Law, Leiden University |
| Mr Drs J. Staman (moderator) | Director, Rathenau Instituut |
| Prof Dr W.A. Wagenaar | Emeritus Professor of Experimental Psychology, Leiden and Utrecht University |
| Mr I.N. Weski | Criminal Lawyer, Weski Heinrici Advocaten |
| W.H. Woelders | Deputy Chief of Police, Utrecht Regional Police Force |

## Project Management

This study was organised by Ira van Keulen (project manager), Reinout van Koten (project assistent) and Annette Potting (project secretary).

# Project Cooperation

The Dutch Advisory Council on Health Research (Raad voor Gezondheidsonderzoek, RGO) has cooperated with this project. This cooperation has been formalised in the context of the Dutch Consultative Committee of Sector Councils for research and development (Commissie van Overleg Sectorraden COS), of which both RGO and STT are members.

## RGO

The Dutch Advisory Council on Health Research (Raad voor Gezondheidsonderzoek, RGO), established in 1987, advises the government, especially the ministry of Health, the ministry of Education and Science, and the ministry of Economic Affairs, on matters relating to health research, health services research and the infrastructure of such research. Since February 2008 the RGO is part of the Health Council of the Netherlands.

Health research is defined as research on epidemiologic and etiologic aspects of disease, diagnosis, prevention, cure and care, and the development of relevant technology. Health services research concerns aspects of health services such as structure and organisation, its function, and the demand for health services. The RGO's main task is to set priorities for research aimed at the solution of problems in health and health services and to give recommendations on financial and infrastructural matters.

The recommendations by the RGO are given after a comprehensive investigation of the field of interest. Each report is based on a careful balance of the scientific requirements and the social needs for health (care) research.

For more information on the RGO please visit: www.rgo.nl

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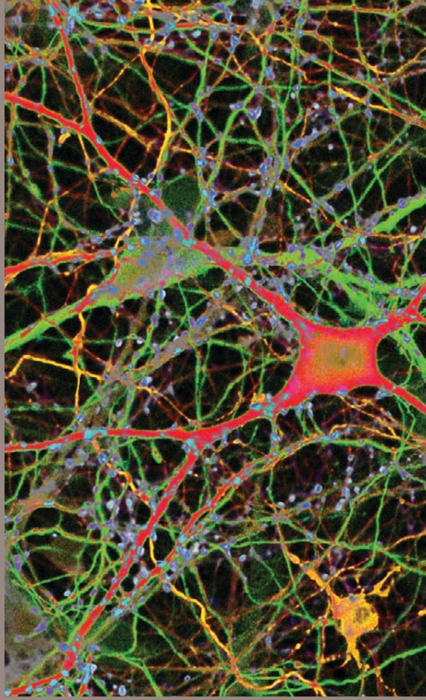

*Neuroscientific research aims to understand the workings of the human brain and mind. Like genetics, it tries to unravel the biological basis of human nature. Following the explosion of knowledge in the genetic sciences over the past twenty years, the same revolution is expected in the neurosciences and cognitive sciences in the decades ahead. The biology of the mind will be to the 21st century what the biology of the gene was to the 20th.*

*Never before has scientific research got so personal, not even in genetics. Research on the brain and mind deals with our very selves, the conscious and unconscious behaviour that defines our identities and personalities. If we come to fully understand the workings of the brain and mind, we will understand how we ourselves think and behave, with potential relevance in every domain of life.*

*So far the brain sciences have been largely technologically driven. Every new technology, for example the various neuro-imaging techniques and patch-clamp technology, has pushed the field forward in ever-larger steps. The new advances have expanded our knowledge of the anatomy of the brain, the way individual neurons process information and communicate with one another, how the major sensory input systems collect and represent information, and how output systems such as muscles are addressed. Nevertheless, we still face major challenges in understanding the brain and mind. After all, the brain is the most complex system known to mankind.*

*We do not need to understand everything about the brain and its mechanisms to be able to think about how to use our rapidly growing knowledge, however. The STT project Brain Visions offers conclusive proof of this. In three expert groups and one large-scale conference, STT has explored how society can profit from the mounting scientific insights into the mechanisms of the brain and the mind in four important areas of application: food, man-machine interfaces (MMI), education and judicial practice. This STT publication reflects the ideas of and discussions between the more than seventy experts from academia, industry, government and other relevant professions participating in the Brain Visions project.*

*The publication is intended for everyone with an interest in the imminent revolution in the brain sciences and how it could change the way we eat, communicate, learn and judge. In addition, the publication offers some clues about the conditions that will allow the brain sciences to develop for the benefit of society.*

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