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# Developments in neuroscience

## Where have we been; where are we going?

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### INTRODUCTION

My introduction to this book on neuroethics, a volume with a large diversity of topics, is based upon a very personal selection of some of the numerous highlights that form the contributory history of the field of neuroscience. This volume shows how the way in which we look upon the brain has changed – in a relatively short period of time – from being just one of the organs that housed a soul to being the focus of a huge multidisciplinary endeavor to study the source of the mind. The focus of brain research has moved through that endeavor from the study of macroscopically visible pathologies of the brain to the subtle structural and functional differences that form the basis of psychiatric disorders and of our character. The sexual differentiation of our brain in utero – the programming of our gender identity and sexual orientation for the rest of our life – is discussed as an example of one of the many aspects of our character that become hardwired in our brain during early development. The concept of a critical window during which a developmental process can take place in order to structure brain systems and their function for the rest of our life is also why it is so difficult to repair lesions in the adult brain. In spite of this difficulty, it is now possible to sketch a series of new technical developments in neuroscience that bear the promise of leading to new, effective therapeutic strategies to tackle brain disorders in the near future.

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## WE ARE OUR BRAINS

Everything we think, believe, and do is determined and carried out by our brains. The unprecedented evolutionary success of humankind – as well as the many limitations of individual people – are determined by this fabulous organ, our brain, which determines our possibilities, our limitations, and our character, as was already recognized by Hippocrates and Descartes[1]; *we are our brains*. The rest of our body only serves to feed our brain, to move it around, and to make new brains through procreation. Brain research therefore not only deals with disorders, but is increasingly becoming a search for the answer to the question why we are the way we are, a search for the self.

Nerve cells, also called neurons, are the building blocks of our brains. These cells are specialized in (1) gathering information from the rest of our body via other nerve cells and from hormones and, through our senses, from the environment; (2) the integration and processing of information and the decision-making on the basis of this information; and (3) the carrying out of these decisions in the form of movements, changes in hormone levels, the regulation of physical processes, and the production of a never-ending stream of thoughts. Faults in this efficient, information-processing machine may be genetically based, may occur in a developmental stage or later in life, and may lead to psychiatric or neurological disorders, or

[1] It should be generally known that the source of our pleasure, merriment, laughter, and amusement, as of our grief, pain, anxiety, and tears, is none other than the brain. It is this organ in particular that enables us to think, see and hear, and to distinguish the ugly from the fair, the bad from the good, and the pleasant from the unpleasant. It is the brain, too, that is the seat of madness and insanity, of terrors and fears that crowd in upon us, usually at night, but sometimes even during the day; this is the cause of insomnia and somnambulism, of thoughts that will not come, of forgotten duties and strange phenomena.

Hippocrates, fifth century BC

I want you to look upon all the functions I attribute to this machine (the brain), such as digestion, nutrition, respiration, waking and sleeping, taking in light, sound, smell, the impression of images in the organ of observation and imagination, the retaining of these ideas in the memory, the lower movements of lusts and passions, and lastly the moving of all outer limbs, I want you to look upon all these functions as taking place naturally in this machine exclusively as a result of the nature of its organs, no less than the movements of a clock.

Descartes, 1596–1650.

to a great variety of behavioral disorders, including aggression and criminal behavior.

## The computer metaphor

When we look at the building blocks of our brains and see how they are linked, the computer metaphor appears obvious. The brain weighs 1500 g, contains 100 billion ($10 \times 10^{10}$) neurons (16 times the number of people in the world), twice as many glial cells (the cells that support the neurons in their functions) and at least 1000 times as many places where nerve cells make contact or, as Santiago Ramón y Cajal (1852–1934) put it, ``hold hands´´: the synapses. The nerve cells are connected by more than 100,000 km of nerve fibers. A possibly even better metaphor for the brain, a central control room, was proposed by Tolman in 1948. He wrote:

> We assert that the central office itself is far more like a map control room than it is like an old- fashioned telephone exchange. The stimuli which are allowed in are not connected by just simple one-to-one switches to the outgoing responses. Rather, the incoming impulses are usually worked over and elaborated in the central control room into a tentative, cognitive-like map of the environment. And it is this tentative map, indicating routes and paths and environmental relationships, which finally determines what responses, if any, the animal will finally release.
>
> Cited in Repovš & Bresjanac 2006.

The staggering numbers of cells and synapses work so efficiently that our brains do not consume the energy of more than a mere 15 W bulb. Michel Hofman has calculated that this means that the total energy costs of the brain of one individual are only 1200 euro per life time at the current price level. You cannot even buy a decent computer with that kind of money. But what this means is that one can make one billion neurons work for 80 years at a cost of 1200 euro! A fantastically efficient machine, then, with parallel circuits, better equipped for image processing and association than any computer. The volume of the biological clock of the brain, the suprachiasmatic nucleus (see Figure 1.1A), is only 0.5 $mm^3$, and this is sufficient to regulate all our day/night rhythms (waking, sleeping, eating, drinking, procreation, hormone levels, etc.). Try imagining what 1500 $cm^3$ (3 million times more) can do!

The product of the functions and interactions of all those billions of nerve cells is our ``mind´´. ``The brain secretes thoughts, as the kidney secretes urine´´ (Jakob Moleschott, 1822–93). One can actually see a human being think during a functional scanning session: which

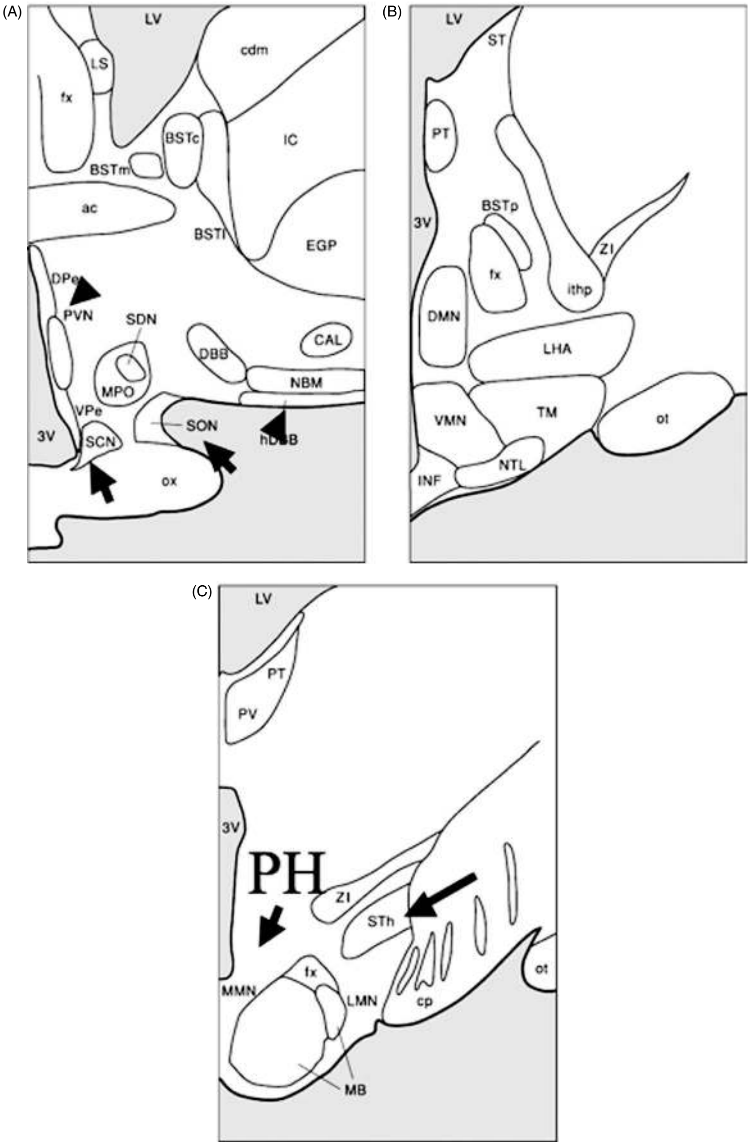


**Figure 1.1** Scheme of the hypothalamic area. Arrows indicate the structures mentioned in the text. NBM, nucleus basalis of Meynert; PH, posterior hypothalamus; PVN, paraventricular nucleus; SCN, suprachiasmatic nucleus; SON, supraoptic nucleus; STh, subthalamic nucleus.

brain areas are activated when we read, calculate, listen to music, hallucinate, are in love, or are sexually aroused. Using real-time functional MRI as a biofeedback system, it is even possible to train brain areas to function in a different way. Patients thus trained to control the frontal part of the anterior cingulate gyrus (see Figures 1.2, 1.3) were able to diminish their chronic pain (DeCharms *et al*. 2005).

There are still people who credit the heart with special, mystical properties, in relation to our feelings, our emotions, our character, our love, and even our soul. Of course, our heart rate increases when we experience emotions, but only because the autonomic nervous system commands it. Yet there are anecdotes about heart transplant recipients who underwent a change of character reminiscent of the donor. The *Telegraaf*, a big Dutch newspaper, printed the headline: ``Is the soul localized in the heart? Claire Sylvia (47) got the heart transplant from a boy. She now whistles to girls and is drinking beer´´. Sylvia, in 1997, wrote in her book that she was convinced that the character of her donor, a young motor cyclist, was transplanted along with his heart and lungs. There are also anecdotes of heart transplant patients whose taste in music, favorite color, or preference for art, food, recreation, or career changed into that of the donor. Someone who had received a

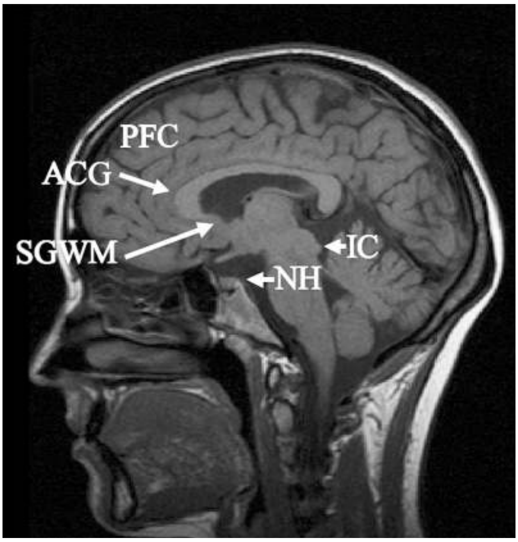


**Figure 1.2** Frontal MRI scan. ACG, anterior cingulate gyrus; IC, inferior colliculus; NH, neurohypophysis; PFC, prefrontal cortex; SGWM, subgenual cingulate white matter.

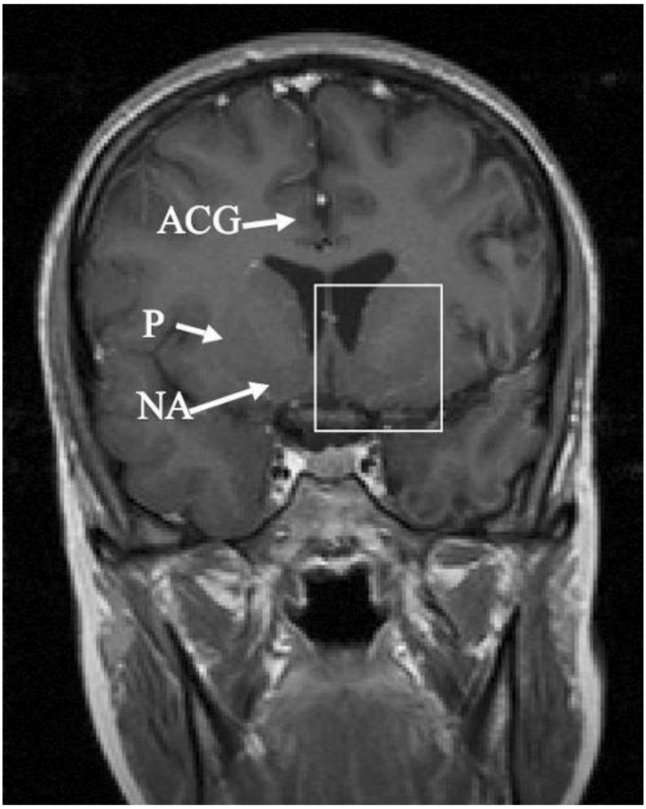


**Figure 1.3** Frontal MRI scan. The white square indicates the hypothalamic area that is shown in more detail in Figure 1.1. ACG, anterior cingulate gyrus; NA, nucleus accumbens; P, putamen.

donor heart reported to have seen the face of the murderer of his donor in a dream (Pearsall *et al.* 2002). A woman reported that she could suddenly play chess after receiving the heart of a professional chess player. One may wonder how the presumed information from the heart is transported to the brain after a transplantation during which all nerve connections are cut, so before we can take these reports seriously we need a well-controlled study that completely excludes any possibility that the recipient receives information about the donor, that makes unwanted manipulations of the interviews impossible, and that takes into consideration the effects of the immunosuppressive medication that is taken after a transplant and that might affect behavior.

## BRAIN DEVELOPMENT

### During development we make our own brains into a unique machine

The computer metaphor only partially applies to the brain. The ``hardware´´ of our brain is soft, and some systems are very malleable. Our brain is a living machine that changes continuously with use, especially during development. Everything we do or observe during development may result in lasting changes in the numbers of cells, circuits, and cell contacts. Our environment and the use of our brain strongly and permanently influence its structure, and therefore its function, which makes it unique. Each of the brains of identical twins has already become unique in this way at the moment of birth (Steinmetz *et al.* 1994). The brain thus only partly develops on the basis of hereditary information. A child´s brain development is influenced in the womb, by hormones and its mother´s stress, and by the random silencing of genes, and it is threatened there, too, by any medication, alcohol, and nicotine taken by the mother during pregnancy. If the mother smokes during pregnancy the chances of the child´s later showing Attention Deficit Hyperactivity Disorder (ADHD), becoming aggressive, or displaying criminal behavior, increase (Brennan *et al.* 1999; Neuman *et al.* 2007).

During development the brain makes an excess of cells and connections. The brain systems´ functioning determines which of these cells and connections are effective and will ultimately survive. This competition among brain cells to survive is called ``neuronal Darwinism´´. It is thus not just a child´s practicing its movements that determines the construction of its brain and any ensuing functions; the child´s learning, experiencing, seeing, and thinking also organize the structure, and therefore the function, of its brain. A multitude of factors that influence the structure of the brain during early development determine our character. Whether we will feel like a man or like a woman (gender identity) and our sexual orientation are determined in utero. Although it has often been postulated that postnatal development is also important for the direction of our sexual differentiation, any solid proof of this possibility is lacking (Swaab 2007).

During our first couple of years our environment also determines the structure of the brain systems that are involved in language, and this gives us our mother tongue. This system is not plastic, as is apparent from our accent when we learn another language later on.

Moreover, we are exposed to the religious convictions of our environment at an age when whatever our parents say is considered to be the truth, and our religious convictions are thus imprinted in our brains and not easily changed. However, the synapses are a brain system that does remain plastic throughout life. They undergo small alterations in brain areas where, for example, memories are stored.

The brain is thus only partly created on the basis of genetic information and for a major part built under the influence of its functioning during early development. As no one´s experiences and thoughts are exactly the same, every brain becomes unique in the process of development. This is how our character is determined. The environment is also involved, especially in early development, through such influences as language and religion. Our brain makes our culture and our culture shapes our brain development.

In the course of our development we make our own brain into a unique feature, a person, and sometimes a personality.

## Development causes restrictions

During our development our options become ever more limited by the growing organization of our brain. This process has already started in the womb. We are not born a *tabula rasa*, as Locke and Rousseau thought. At the moment the ovum is fertilized the risk of many of our future deviations (e.g. dementia) are already genetically determined. The choice of mother tongue, sexual orientation and gender identity, and level of aggression is made for us during our development. It is impossible to dissuade transsexuals from their idea that they are living in a body of the wrong sex and that the body should be changed. There is no other option; once the brain is organized it is virtually impossible to change anything. Our last bit of elbow room is taken from us once we are born, by the only efficient manipulation of the brain in existence: a thorough upbringing. Commercials and television finish the job. That is why all over the world teenagers are listening to exactly the same music in exactly the same designer clothes. Neuronal Darwinism seems to underlie the neurobiological processes for these continuous limitations, which cause our brains to function more and more efficiently, but at the same time to lose increasingly more degrees of freedom, leaving us with the paradox that the only person with any real freedom is the fetus, who is unable to enjoy this freedom owing to its immature nervous system. Once we have reached adulthood, our ability to modify our brains, and therefore our behavior, has met with too many structural restrictions of our brain. We have then acquired our ``character´´.

We are indeed limited in our choices not only by the conventions of society but also by the way our brain has developed. Child abusers were abused when they themselves were children. How ``free´´ is the abuser not to go down the road of abuse himself? How ``free´´ is an adolescent, whose brain must learn to deal, in a very short time, with sex hormones, which change the function of nearly every brain structure during puberty? In adulthood brain disorders can change a person completely. The brain of RAF terrorist Ulrike Meinhof turned out to be damaged when it was examined after her suicide in prison in 1976. She had had an aneurysm, a widening of a blood vessel, that was pressing on the amygdala (Figures 1.4 and 1.5) earlier and her prefrontal cortex was damaged during surgery. The pressure on the amygdala can give aggression while the damage done to the prefrontal cortex during surgery may cause impulsive behavior. So both lesions could explain the change in behavior from discerning journalist to terrorist. How free was her will?

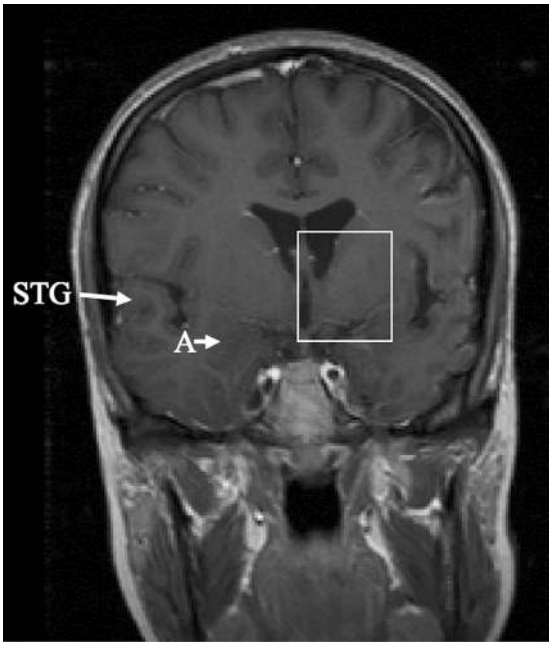


**Figure 1.4** Frontal MRI scan. The white square indicates the hypothalamic area that is shown in more detail in Figure 1.1. A, amygdala; STG, superior temporal gyrus.

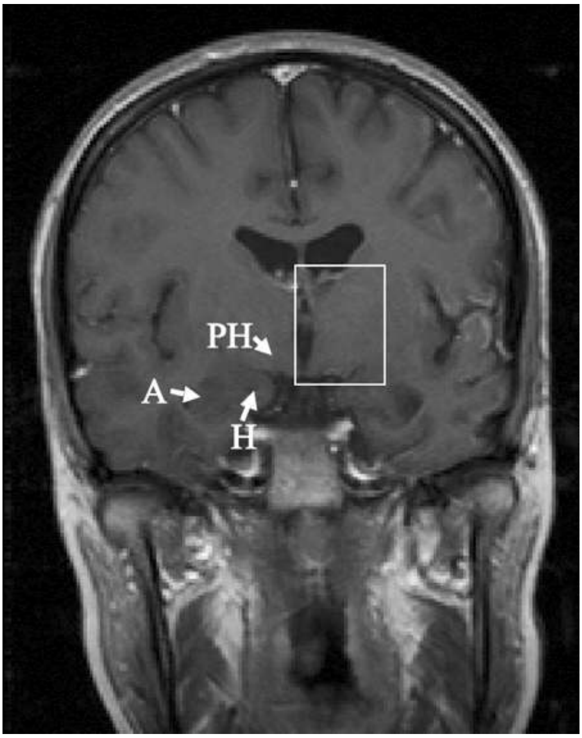


**Figure 1.5** Frontal MRI scan. The white square indicates the hypothalamic area that is shown in more detail in Figure 1.1. A, amygdala; H, hippocampus; PH, posterior hypothalamus.

## Sexual differentiation of the brain as an example of early imprinting

Sexual differentiation of our brain starts in the womb and brings about permanent changes in brain structures and functions, mainly through the interaction of the developing neurons with the sex hormones of the child.

The testicles and ovaries develop in the sixth week of pregnancy. This happens under the influence of a cascade of genes, for which the sex-determining gene on the Y chromosome of boys, SRY, is a trigger. The production of testosterone by a boy´s testes is necessary for the sexual differentiation of his sexual organs between the sixth and twelfth week of pregnancy. The development of the female sexual organs in the womb is primarily based on the absence of testosterone. The brain of a boy is permanently organized by two peaks in