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DEVELOPMENT AND PLASTICITY IN THE BRAIN

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This paper examines different aspects of the development of the brain before birth, and the subsequent plasticity after birth. First, rough outlines of the pre-natal formation of the neural structures are presented: cell identity, neuron migration, axon formation and initial synapse formation. Second, the paper looks at the post-natal plasticity with regard to critical periods. A short introduction to the visual system serves as a starting point for a description of Hubel and Wiesel's pioneering experiments on cats and monkeys. In addition, Harlow's experiments with sensory deprivation of monkeys are described. This leads to an attempt to link these results to a computational strategy for the analysis and representation of the connections between sensory input and motor output: feed-forward neural units that are dynamically re-grouped by reciprocal connections. The conclusion attempts to place development and plasticity in a broader context within the brain.

1. Introduction

This paper investigates different aspects of development and plasticity in the brain. It tries to sketch a picture of the current knowledge of the development of the neural structures in mammals with regard to a central concept: *critical periods*. Development can roughly be divided into two stages: pre-natal and post-natal – also called morpho- and epi-genetic respectively. Only recently have we begun to gain insight in the pre-natal development and therefore this paper only briefly outlines some of the principles governing the formation of the neural structures during that period. The main emphasis is on the post-natal. Here research has concentrated on two apparently different aspects of development: social and visual competence. Natural stimuli have been denied experimental animals, primarily cats and monkeys, at different stages during their life, and it turns out that there exist *critical periods*. For example, if an animal does not receive visual stimuli during the critical period, generally irreparable damage occurs to the visual system.

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This paper takes its inspiration from Hubel and Wiesel's pioneering work on the visual system (Hubel and Wiesel, 1962, 1977, Hubel, 1995) and Harlow's work (1958, Harlow *et al.*, 1965) on depriving monkeys social contact. The results from these and similar studies then provide the setting for an attempt to model the neural mechanisms behind development and plasticity. A distinction between neural connections of static feed-forward and dynamic reciprocal connections is suggested. The model tries to explain the apparent paradox that there exist *critical* periods during which certain invariant cognitive skills have to be learned, along with the *continuity* of the learning of other lifelong skills. This provides the background for a discussion of the classical schism between nature and nurture, and a more advanced model is described. Moreover, an effort is made to place brain development and brain plasticity in a broader context.

2. Prenatal development

2.1. Genetics and formation of the nervous system

The human genome consists of over three billion nucleotide bases. The base sequence is divided into 23 chromosomes, wherein the genes code for the 50-100.000 proteins that serve structure, metabolism, energy transduction, excitability and self-organisation. The nervous system is by far the most complex part of the body, with about 10^{12} neurons and roughly 10^{15} synapses. In the brain, there are at any instant about thirty thousands proteins at work. Since genetic sequence comprises only about 10^{9} bases, there is not nearly enough information to code for this complexity – instead the formation relies, as with other biological systems, on the principle of *self-organisation*. Large numbers of neurons are formed initially, many of them only later to become victims of the massive cell death that is part of the self-organising process.

Certain functions in the brain have to be 'hardwired', such as regulation of hunger, thirst and basic motor control, thermoregulation, growth, aspects of reproduction, respiration, and maintenance of the behavioural states – sleeping, dreaming and wakefulness. As we shall see later, there seem to be other possibilities inherent in this hardwiring, for example new born babies having preferences for face-like stimuli (Johnson and Morton, 1991) – or the fact that blind children have »normal« facial expressions – even though they have never seen other faces.

The pre-natal formation of neural structures is thought to take place as follows. First, the cell identity is formed. Then the neurons migrate to their final position, where synaptic connections with other neurons are formed. The process is genetically determined but it is primarily a manifestation of self-organisation. Together, the pre-natal neural structures form a coarse computational starting point for the post-natal fine-tuning.

2.2. Cell identity

From the study of the nematode worm *Caenorhabditis elegans*, much is now known about how the structure of its autonomous nervous system is regulated genetically (Desai *et al.* 1988). *C. elegans* has exactly 302 neurons, and among other things it is possible to describe the lineage of motor neurons from the zygote. The different mutations affecting each of the developmental stages have been isolated; from migration, through axon formation, to the final functional destination. However, it is not the case for most animals – mammals included – that cell lineage is decisive for the final positions of neurons. Instead, the neural cells are governed by local changes. This cell-to-cell interchange is the principle of self-organisation (Edelman 1987), determining the formation of many biological systems – including neural structures. In the autonomous cell formations in the nematode, some of the genes controlling development have been identified. In contrast to this, the formation of local cell interchange involves different signal molecules and membrane receptors. Signal molecules not only play a part in the development of neural cells but also of other types of tissue. Therefore, by studying the differentiation of other cells, we gain yet more knowledge about neural development.

2.3. Neuron migration and axon formation

When the cell identity has been determined, the next step in the development starts: cell migration and axon formation. It is characteristic for neurons and neural *precursors* that they migrate to their final position from the place where they start to differentiate. The epoch when a neuron is being formed is crucial to its later position and function. Experiments have shown that neurons formed at an early stage in cortical development end up in the deepest cortical layers, while neurons formed later end up in the outer layers (McConnell 1989).

Neurons use radial glial cell fibres to control their migration to the final location. When this location has been established – and sometimes even earlier – the formation of axons begins. The axon uses a growth cone to reach its target. We are gradually beginning to understand this exciting process that could be loosely compared to finding one's way from New York to Los Angeles without a map, and where roads are being created as one proceeds. Axon formation is governed by a series of guidance clues, using among other things molecular interchange with other cells. The process is complex and most often leads the axons to their targets. But it is not an infallible process, and therefore, in addition to distinct guidance clues, several mechanisms exist to eliminate axons that – using the above metaphor – have ended up in Canada.

2.4. Initial synapse formation

It is essential to neuronal survival that the axon establishes contact with the target cell that contributes with trophic factors, stabilising further development. Many of these essential trophic factors, which are securing the survival of distinct groups of synapses, have been identified. In contrast to this are the so-called growth factors that stimulate cell division.

A synapse can only function if receptors that fit with the pre-synaptic neurotransmitter exist on the post-synaptic membrane. Studies of the synapse formation have to a large extent concentrated on the synaptic connections in the peripheral nerve system, since synapses are more readily available there. But presumably many of the results from the study of neuro-muscular connections also apply to the central nervous system.

McMahan and Wallace (1989) cut motor axons and showed that they grow back to their old synaptic sites, and form new synapses precisely at the location of the original synapse. By elimination, it was shown that the only guidance clue for this process could come from the basal lamina at the old synaptic site. The way the new axon recognises this is presumably determined by the so-called glycoproteins associated with the basal lamina. Such a molecule, s-laminin, functions as a stopsignal, getting the new motor axon to the synaptic site and making it stop there.

Even if the synapse makes initial contact with the post-synaptic target cell, it could well happen later during development that the competition with other synapses for trophic factors leads to an elimination of the neuron (more on the post-natal competition later).

Our knowledge of the principles governing the pre-natal formation of the neural structures is still very limited. The above rough outline of the processes involved is contributing to shape a clearer picture of the development of the brain. But so far we have only a highly schematic understanding of how the actual decoding from the genetic material to the extremely complex, self-organising biological tissue takes place. Hopefully with the ever accelerating pace of the mapping of the human gene-material, »The human genome project«, we might soon have some of the tools needed to gain a more thorough understanding of the genetic base behind the pre-natal shaping of the nervous system.

Concerning the non-genetic component behind the pre-natal processes, one could inquire after the pre-natal role the uterus renders the embryo. It is by way of this symbiosis that the nutrients for the creation is being supplied. But as many of the neural structures are in place early during pregnancy, is the embryo then being supplied with sensory stimuli *in uterus*? The development that is being completed post-natally as described below, might already be starting in the uterus. Hubel (1995) thus speculates whether the patterns that can be observed in the early visual centres, already are founded in the fetal retina by wave interference in the uterus.

3. Postnatal plasticity

> *» ...The baby is certainly not born knowing the alphabet or able to play tennis or the harp. All these accomplishments take training, and by training, we surely mean the molding or modification of neural circuits by environmental influences.«*
>
> *David H. Hubel*

As described above, various structures are established pre-natally within the brain, for example centres for respiration control, temperature and other vital functions. But not all of the individual's characteristics are determined at the time of birth, among other things to allow for the individual to adapt to the enviroment. After birth, the neural structures formed pre-natally are *fine-tuned* in what is part of what one might call learning. In the following we will focus on this plasticity.

In the process of learning, well-defined critical periods exist, where specific neural structures are especially sensitive. If specific stimuli are not received within these periods, the damage can be beyond repair. In some species of birds a special kind of critical period called *imprinting* has been observed. When newborn birds open up their eyes for the first time, they attach themselves to a moving object in the immediate environment, this of course normally its mother, which also explains the natural benefit of the system. Lorenz (1937, 1965) was among the first to study this phenomenon. In some species, the period of imprinting is believed to be limited to a couple of hours.

Specifically for the visual system, critical periods exist where *vision* is trained. Because of the general risk involved in operating on small children, one used to wait before surgically correcting innate defects on the visual system such as cataracts or strabismus. When the operation establishing the *physical* framework for normal vision was carried out later in life, the vision of the patients did not improve significantly. Because of the defects, the visual system had not received the required stimulation during the critical period in early childhood. Since cataracts convert the optical lens into an opaque diffuser, and therefore make it impossible to deduce shapes, patients permanently loose the ability to distinguish shapes. Strabismus patients develop eye-dominance, that is the dominance of one eye over the other, as they would otherwise see a double image. Which means that they lack the ability for three dimensional vision (stereovision). This was not significantly improved by the operation. It shows that if the visual-system is not trained during the critical period, it will suffer permanent damage. In acknowledgement of this fact, the two defects are now being corrected earlier.

3.1. Harlow's experiments on monkeys

By chance, Harlow (1965) and his colleagues got to study change in the social pattern that appeared in infant monkeys reared in isolation. They had isolated newborn monkeys in an attempt to raise infection-free individuals for experiments. However, this isolation produced various social defects in the infants. If the monkeys, after having been isolated, were let out amongst normal monkeys, they did not behave normally. Among other things, they did not defend themselves against assaults from other monkeys in the group.

After living in the colony for weeks, the monkeys raised in isolation still did not show signs of normal social behaviour. Those monkeys that had been deprived of social contact from birth did not seem to develop the social patterns normally observed in monkeys within a group. Furthermore, it appeared that this defect could not easily be reversed at a later time. This suggested the existence of special critical periods in the lives of monkeys, during which social conduct to a high extent is established. As can be seen, critical periods also exist for behaviour.

Subsequently, experiments have been conducted to study critical periods and learning in more detail. In the late sixties and the beginning of the seventies, Hubel and Wiesel (1962) carried out a series of experiments, that in principle were very similar to Harlow's. Like Harlow *at al.*, Hubel and Wiesel studied the effects of depriving an animal of certain stimuli. However, in order to understand the phenomena more clearly, they chose to work on the visual system.

3.2. Brief description of the visual system

In order to describe Hubel and Wiesel's experiments and subsequent conclusions, a brief introduction to the visual system is necessary. *Figures 1* and *2* give a schematic overview of this system. Incoming light on the retina is transformed to nerve impulses by rods and cones. Furthermore, centre- and centre-surround-cells exist in the retina with synapses on the rods and cones, respectively sensitive to light areas surrounded by dark and dark areas surrounded by light.

Through the optical nerve, signals are transmitted via the optical chiasm, as is shown in *Figure 2*, where the right optic tract has been incised. At the optical chiasm, the signals are divided according to which part of the visual field they originate from: impulses from the left *and* the right eye's right visual field are directed to the left cortical hemisphere, and reversely from the left part of the visual field. The main part of the signals go to the primary visual area (Brodmann area 17 or V1) through the Lateral Geniculate Nucleus, LGN. A small fraction of the signals get processed in other parts of the visual system, such as the motion centre, MT. In V1, the signals from the centre- and centre-surround-cells co-operate to enable detection of lines of different orientation.

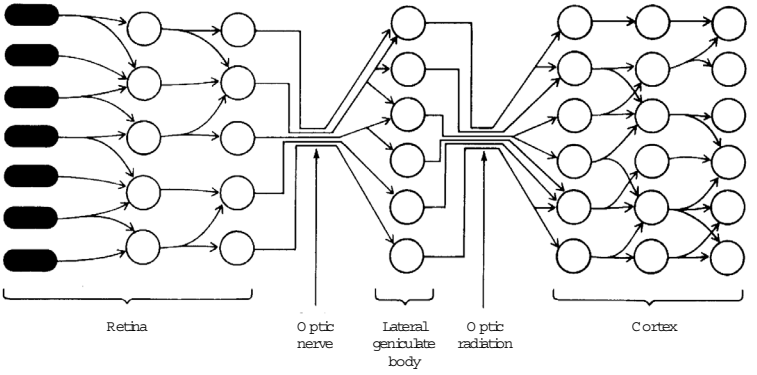


Figure 1. A schematic overview of the platelike organization of the visual system. (Adapted from Hubel, 1995, p.27)

An example of how this is believed to happen is shown in *Figure 3*. Four diagonally placed and more or less overlapping centre-cells impinge upon one cell in V1 through synapses. This cell is thereby responding to diagonal lines. It is believed that progressively sophisticated analysis is carried out in the higher levels of the visual system. In passing it should be noted that centres for motion, colour and feature selection have been experimentally detected (Zeki, 1993).

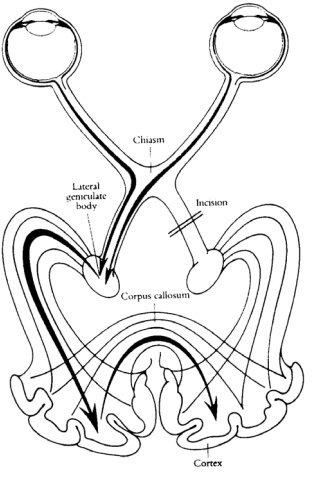


Figure 2. Schematic figure of the visual system where the right optic tract has been incised. (From Hubel, 1995 p.141)

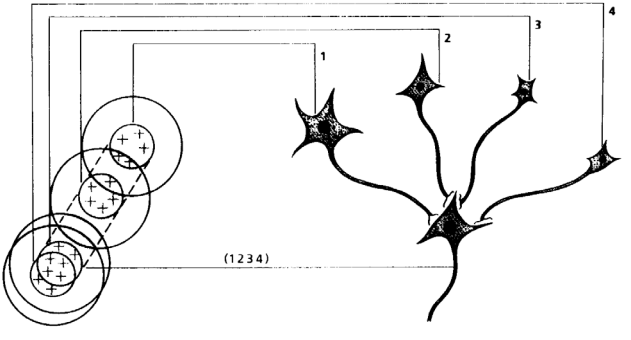


Figure 3. A simple line-orientation selective cell receiving input from several centre–surround cells (Adapted from Hubel & Wiesel, 1962)

3.3. The experiments of Hubel and Wiesel

As mentioned, both sides of the visual cortex receive visual stimuli from both eyes. In V1, cells are found that to a higher or lower degree respond either equally well to stimuli from both eyes or solely from one eye; respectively binocular and monocular cells. The eye on the same side as the observed cell is referred to as *ipsilateral* while the eye in the opposite side is called *contralateral*. Hubel and Wiesel used a grouping of the recorded cells in V1, shown in *Figure 4*.

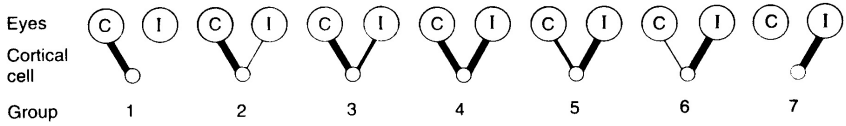


Figure 4. Groups of Cortical cells receiving input from contra- and ipsilateral eyes (From Kandel et al., 1993 p.948)

Group 1 and 7 were used for cells that responded exclusively to stimulation from respectively the contralateral and the ipsilateral eye. Cells that respond equally well to impulses from both eyes belong to Group 4. In determining the category of cells in their experiments, Hubel and Wiesel used microelectrodes implanted close to the cell in V1. If the cell was stimulated, the electrode would register the electric impulse, which could then be seen on, for example, an oscilloscope. By stimulating the retina in each eye, they could determine to which group the cell belonged. The normal distribution of ipsilateral and contralateral cells in the primary visual cortex for cats and monkeys is shown in *Figure 6*.

Another method used by Hubel and Wiesel (1962) in determining the ocular dominance of cells was to inject radioactively labelled deoxyglucose, which sufficiently resembles normal glucose for cells to absorb it, but which cannot be digested, hence it accumulates in the cells. Following injection, the test animal was subjected to specific stimuli, for example in the form of induced light stimuli in one eye. Subsequently, by observing the occurrence of radioactivity in the brain, it can be determined which cells were stimulated during the experiment. An example of such a recording is shown on *Figure 5*. The right eye in an adult monkey has been injected with radioactively labelled deoxyglucose and when the film is developed the radioactivity show up white.

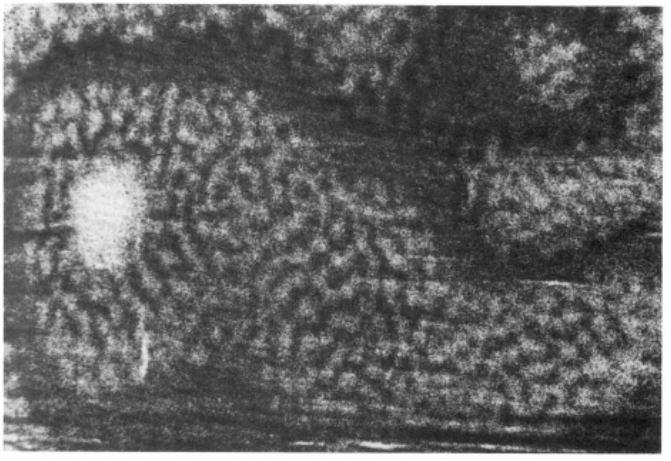


Figure 5. After injection of deoxyglose, the visual fields of the anesthetized monkey were stimulated with slowly moving vertical black and white stripes. The resulting autoradiograph shows dense periodic labeling, eg. in layers 5 and 6. Layer 4Cβ (the dark gray narrow outside) is uniformly labeled as expected because the cells are not orientation selective. (From Hubel, Wiesel & Stryker, 1978)

Hubel and Wiesel's original experiment was to close *one* eye of a one-week old kitten, just at the time where it would otherwise have opened its eyes for the first time. When the eye was reopened ten weeks later, Hubel and Wiesel could establish that the eye itself did not seem to have been damaged. But as recordings were made from the cat's cortex later on, an abnormality appeared. In normal cats the monocular cells are equally distributed between the left and the right eye. With the experimental animal it was found that from a total of 25 observed cells, none could be stimulated by the eye previously closed, and that five of the cells could not be stimulated at all. This result is shown together with the normal situation in *Figure 6*.

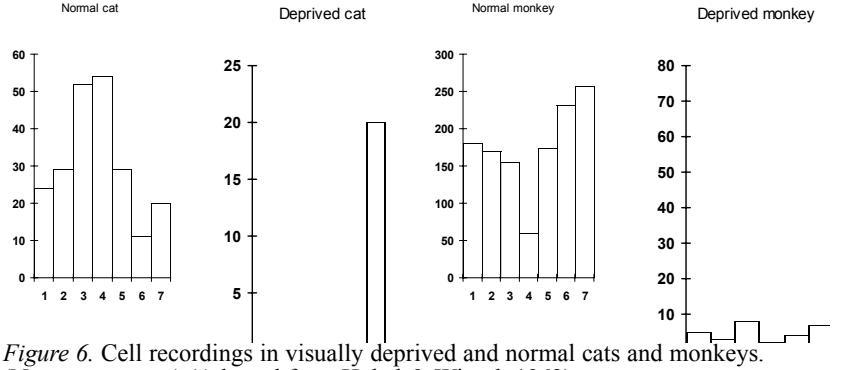


Figure 6. Cell recordings in visually deprived and normal cats and monkeys. (N = no response) (Adapted from Hubel & Wiesel, 1962)

To determine whether the abnormality was due to damage to other parts of the visual system, Hubel and Wiesel examined the pathways from the retina. They found that both the actual eye and the retina functioned satisfactorily. They concluded that the observed damage was caused by the lack of stimuli in V1. Hubel and Wiesel replicated the experiment on both cats and monkeys and the results were consistent.

Subsequently, Hubel and Wiesel wished to determine whether the observed abnormality in the closed eye derived from the lack of light stimuli or from the lack of shape stimuli. Experimental animals were fitted with an opaque lens for a period of time, which made it possible for light to pass through but made it impossible to determine contours. The result was similar to the experiment where one eye had been closed completely. Therefore, it was concluded that it was the lack of contours and not the lack of light that caused the observed abnormality in the animals.

3.4. Critical periods

By varying the timing and duration of the eye-closure, Hubel and Wiesel wished to confirm the existence of critical periods for the formation of the visual system and to determine their duration. The experiments showed, analogous to Harlow's discoveries, that there *are* such well-defined periods in which deprivation of visual stimuli causes severe and irreparable damage to the visual system. Specifically for monkeys, it was found that if the eye-closure was done after the fourth month, even prolonged closures would have less effect than a short closure during the first weeks. In adult cats it was shown that even closures for several years did not have any effect on the cortex. On the basis of their experiments Hubel and Wiesel found that the critical period for the visual system of a cat is from about four weeks until about four months. The critical period for monkeys starts immediately after birth, and does not end until the age of about one year.

The necessity of stimuli during the critical periods was emphasised by experiments where alternately one eye and then the other was closed – this is called *eye reversal*. Not too surprisingly, it showed that the cortex develops a clear majority of cells in favour of the eye that was open during the critical period.

3.5. Synaptic competition

From the experiments with closing one eye, it would be natural to take the formation of the neural structures as being analogous to the formation of muscles in the body. Those muscles that are not being used will shrink with time, as was observed in experiments with neurons from the closed eye. Following this interpretation, it would be expected that if *both* eyes in an experimental animal remain closed during the critical period, very few neurons would be found that respond to stimuli. When Hubel and Wiesel (1962) performed such experiments, it turned out *not* to be the

case. Half of the neurons were functioning normally. One fourth responded abnormally, and the rest did not respond at all. From the relatively high portion of normal neurons, it became clear that the formation of neural structures *is* different from the formation of muscles. It is more appropriate to view the formation as being the result of mutual competition in the brain. The merits of this competition hypothesis can be judged by looking at experiments in which one eye is closed. Certainly, the open eye enjoys an advantage as it still receives stimuli. Confirmation of the competition hypothesis came from the experiments by Sherman (1973).

Sherman's idea was that according to the competition hypothesis, those centres in the brain that did not receive any stimuli during the critical period would shrink only if they were in competition with others. Since visual fields overlap, Sherman recorded from neurons belonging to the non-overlapping part of the visual field – i.e the visual field near the nose. The results ultimately confirmed the hypothesis.

3.6. Hebbian learning

The competition hypothesis can be explained at the cellular level by the model of Hebb (1949) on synapse strengthening. Hebb suggested that the synapses between two cells will be strengthened if the cells fire together. The essence was summed up by Shatz (1992): »Cells that fire together wire together«. The model gives a plausible explanation of the ocular dominance observed when one eye is closed during the critical period. In *Figure 7*, C is taken to be a genetically determined binocular cell that responds equally well to impulses from the neurons in the left and the right eye (A and B, respectively in *Figure 7a*). If the left eye is closed, A is not stimulated. As a result, C and A cannot fire together, which means that the synapse from A to C will weaken over time, as is shown in *Figure 7b*, C will eventually become monocular and only respond to signals from the right eye. Thus critical periods could be interpreted as stages in development where the synapses are especially plastic.

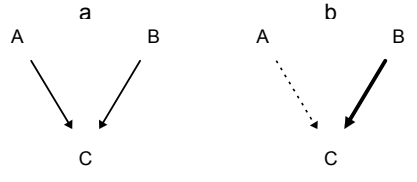


Figure 7. Hebbian learning. Strengthening of synapse B over A (see text)

3.7. How the cat changed its stripes

The original experiments by Hubel and Wiesel were followed by many others. Here we shall only briefly mention the classic experiment by Blakemore and Cooper (1970). For a couple of hours every day, newborn kittens were confined to a room consisting of only vertical black and white lines. The rest of their day was spent in darkness. After a certain period, the neurons in the early visual centres were probed, and it turned out that the great majority responded only to vertical lines. Subsequent trials showed that the kittens were unable to navigate in rooms with only horizontal objects. The kittens clearly did not see them. By stimulating only certain types of neurons during the critical period, Blakemore and Cooper had demonstrated an expansion of these at the expense of neurons responding to horizontal lines.

3.8. Critical periods for higher cognitive functions in man

There is abundant evidence of critical periods for higher cognitive functions in man. Here, we briefly sketch the current picture of the critical formation of the unique human skill: a primary language with grammatical structure. From the study of children brought up deprived of contact with other humans (so-called *wolfmen*), we know that if a primary language is not learned during early childhood it is almost impossible to learn at all. In France in 1797, an 11-12 year old wolfchild was found. By the time of his death at the age of 40, he had only learned a few words. From 31 known cases of wolfmen, only one learned to speak fluently (Zeki, 1993). This very clearly supports the idea that the concept of critical periods also applies to the learning of language. It should be noted that wolfmen do not display normal social behaviour which could be seen as being analogous to Harlow's work on monkeys. The lack of physical contact in childhood results in abnormal social patterns. This suggests the existence of critical periods even for such complex traits as social behaviour of man.

4. Theory of analysis and representation

One of the most fundamental tasks of the cerebral cortex is the analysis and representation of the relation between the spatiotemporal patterns of sensory input and motor output. Combinatorially, there is an astronomical number of possible relations between those patterns and therefore it puts special computational requirements on the neural structures that have to handle this almost overwhelming complexity.

The experiments by Hubel and Wiesel (and others) mentioned above have shown that there are critical periods in the formation of neural structures. It has been demonstrated that critical time windows exist in the

development during which formation *has* to take place in order for cognitive categories, such as sight or language, to function properly. However, it is still possible for the fully-grown adult to learn new skills, as combinations of already established critical cognitive categories. For example, it is possible to develop writing abilities by combining other more basic motor and sensory categories. This apparent paradox shows that there must be essentially different ways to form cortical structures.

How does the brain manage to be plastic both on short and long timescales? It is possible to think of many ways that such a cortical representation could come about, but it is of the essence that it is reflected by the biological structure of the brain. One horrendously inflexible possibility would be to represent the world in such a way that one feature of the world was captured by a single one neuron. Since the system would then have to include as many neurons as features, if the system components were one hundred percent reliable, this possibility is not biologically sound.

Another far more plausible option is the concept of »component reuse« known from other biological systems. The representation is the result of the evaluation of groups of broadly-tuned feature-specific neurons, which is called *coarse coding*. It might seem uneconomical, as several neurons are used to describe one feature. But every neuron can participate at different instances in the representation and analysis of different features, and thereby substantially reduce the required overall number of neurons. This characteristic makes the system computationally robust, since neurons can be spared locally without affecting the system globally.

The problem with this strategy of representation is that those sub-sets of the world that are subsequently being represented contain many components which are overlapping, both in the real world and in the internal feature representation. In order not to mix neurons from different parts of the analysis, it is important to identify at an early stage what belongs where. Such a strategy demands a dynamic selection process that can regroup the distributed neuron groups in ever changing new connections. At one level the signals are chosen, and at the next level they are being re-associated through the feed-forward connections: dynamical re-grouping within a fixed hardwired structure. One way to avoid the combinatorial explosion stemming from trying to code all possible features or combinations of those is, as mentioned, to use the combination of feed-forward connections with broadly-tuned neurons, together with a dynamical selection process that can reiterate the representation and analysis of the complex relations in the experienced world, with arbitrary precision.

The system would, then, use two types of connections: feed-forward and reciprocal associative connections. The former using neurons with feature-selective receptive fields (RF), while the latter is not contributing to the synaptic structure of the RF neurons but rather needs the greatest

possible freedom to form dynamical assemblies of those neurons. Hereby, it is clear that the conditions for the structure, development, and activity-dependent formation of these two types of connections have to be different. As described above, feed-forward connections are created primarily in the pre-natal period while the reciprocal connections might be formed in the pre-natal period but only find their final form post-natally and are as such *plastic* during life.

Similar ideas have been suggested by Changeux (1983) and Edelman (1987). Singer (1995) also speculates along the same lines and suggests the two complementary strategies:

- *Feed-forward connections*. Frequently occurring relevant relations in input are analysed and represented using nets of neurons with fixed but broadly tuned response features – so-called feature specific neurons.
- *Reciprocal associative connections* or feedback connections. Dynamical association of feature-specific neurons in functionally coherent assemblies. This are called *reentrant* connections by Edelman (1987).

In the following, we will use the visual system to show the biological foundation of the system in the brain.

4.1. Activity-dependent plasticity of feed-forward connections

As mentioned above, many neurons in the visual system acquire their characteristic feature selectivity already during the pre-natal period, and could thus be said to be evolutionary and genetically determined. It was also shown that a great part of the neurons in V1 only develop in a normal way if given stimuli during the critical period. This activity-dependent adjustment by the connections is based on the principle of Hebbian strengthening of the synapses (Hebb, 1949). It was also described how neurons in V1 can be made to prefer certain directions but they *cannot* develop preferences for patterns upon which they would not normally react. It suggests that neurons only can develop preferences within what is predetermined genetically.

Very little is known of the extent to which preferences for more complex compounds of features are activity-dependent. Rodman *et al.* (1993) have found neurons in the inferotemporal cortex of infant monkeys that respond to faces, which could lead to the interpretation that even such complex relations in input are represented by genetically predetermined feed-forward connections. It is not known whether this applies to other patterns, such as part of the social competence in Harlow's monkeys.

4.2. Mechanisms for synaptic selection of feed-forward connections

Hebbian learning as sketched above was for long nothing but a theoretical concept until the *N*-methyl-D-aspartate (NMDA) receptor was discovered. *Figure 8* is a figure of this receptor's mode of operation. In (a), both the synapses A and B release glutamate. B uses NMDA receptors, shown in white, while A uses conventional Kainate/Quisqualate (KQ) receptors, shown in black. Before learning, B is ineffective because of the lack of KQ receptors, and the post-synaptic cell cannot fire. In (b), the NMDA receptor opens because A is now active, causing post-synaptic depolarisation. Which, in turn, makes Ca^{2+} flow in, helping B partly by increasing the number of KQ receptors and partly through other post-synaptic processes. In (c), this leads to B now being usable alone.

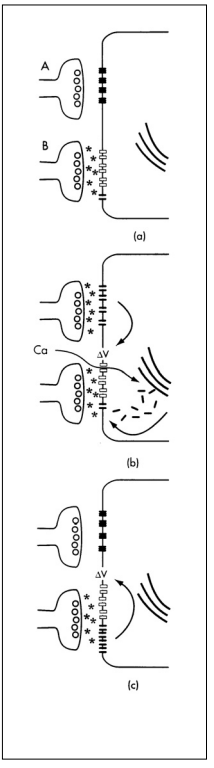


Figure 8. NMDA. See text for explanation (From Carpenter, 1996 p.264)

NMDA receptors and Ca^{2+} flow are major contributors to the process discovered by Bliss and Lømo (1973) called long term potentiation (LTP). A similar process called long term depression (LTD) was discovered by Ito (1989). This paper will not touch on this interesting field of research but it should be mentioned in passing that LTP and LTD are potential candidates for explaining the molecular processes underlying learning and memory. Even though some researchers (Rose 1993, for example) have pointed out that it might be a process only observed in heavily deprived experimental animals.

4.3. Plasticity in the mature brain

Both feed-forward and reciprocal connections are modifiable within their respective genetic potential during development. The feed-forward connections lose much of their functional plasticity after the critical periods, while synapses from the reciprocal associative connections retain the possibility of changing throughout the entire lifespan of an organism. The reduced plasticity of the feed-forward connections is probably responsible for the invariance of the cognitive categories given early in development, whereas the repeated adaptation of the reciprocal connections could be taken as an expression of the ability for analysis and representation of new motor patterns and perceptual objects. Learning could pro-

bably then be seen as the activity-dependent changes of the reciprocal connections using LTD and LTP. Studies of the somatosensory system have shown dramatic changes after increased stimulation and denervation. Since these changes took place over great distances they cannot be explained as changes in the feed-forward connections, but have to be ascribed to a re-grouping of the reciprocal associative connections.

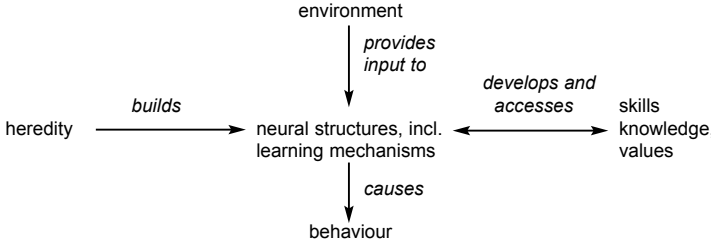
5. Conclusion

> *»...To move things is all mankind can do;... for such the sole executant is muscle, whether in whispering a syllable or in felling a forest.«*
>
> *C. Sherrington (1924)*

In the study of human development, from conception through to the fully-grown and to ultimate demise, we come across many seeming paradoxes. Why do humans for example develop teeth twice? Or why does the sucking reflex disappear in infants? In the study of the development of the brain, the paradoxes become even more noticeable: why, for example, are children better at learning than adults? The discovery of critical periods, during which certain abilities have to be learned if they are not to be lost forever, can seem paradoxical at first glance. Why do we not retain the ability to learn throughout life, just as we keep touch and vision for example? But this way of thinking is based on a misunderstanding of the evolutionary biological principles governing the development of organisms. We are not ready-made from birth but are controlled by a symbiosis of genes and stimuli governing the formation of our differents parts, »components«, following the principle of minimisation: parts are formed when the *need* arises – neither before, nor after. This principle stems from the fact that all processes – and in particular neural structures – need energy. The brain uses a fifth of the body's oxygen and similar proportions of energy, which means that there is fierce competition for resources. Therefore the question in connection with critical periods is not »why does the ability to learn disappear?« but rather »when is this type of learning needed?«. Because of the competition for resources, different types of learning have critical periods at different stages of development.

One of the reasons why humans are not fully-grown at birth is that otherwise we would not be able to pass through our mother's pelvis. But obviously another reason is that we to a large extent need to adapt to a changing world. And thus, development continues throughout life. The realisation that we need to *adapt* to the world typically leads to the conclusion that behaviour is controlled by both heredity and environment. Thereafter, the discussion tries to establish their more exact relation.

Usually, the contrast between the behaviour of animals and that of humans – between nature and culture – is emphasized. This leads to the view that man is above the unfree »biological determinism« of animals and the sole creator of autonomous cultural symbols and values. By birth, we are supposed only to have been given a few reflexes and the unique ability for general-purpose learning. Stated in such an extreme manner, this is of course an absurd belief that gives man a privileged status among animals, and it cannot be upheld. In recent decades, a much more sophisticated picture of the formation of the neural structures has begun to emerge. The following diagram (Pinker, 1994) is also greatly simplified but is a better approximation of the numerous connexions between the different factors contributing to the formation of the brain:



All cognitive abilities, »skills«, such as perception, learning and behaviour are dependent on a fundamental neural structure. In this article, we have tried to outline the current knowledge of the pre-natal and post-natal processes which ultimately control the formation of the brain. It shows a complex, self-organising pattern of interactions between processes. As Crick (1994) writes: »...consciousness is a product of neural structures«. But this does not necessarily mean that man (or other animals) is subjugate to the much feared »biological determinism«. The brain seems to be massively parallel with distributed units and such systems are not necessarily deterministic. The distributed units influence each other over time, which means that *timing* plays a fundamental role in the brain. Time is, incidentally, crucial to all analogous computation.

A fundamental question in connection with the shaping of cognitive abilities is how we can *consciously* use those? Of late, one has finally been able to glimpse some of the answers to this fascinating question. In the following, we shall finish up by briefly touching on the role that the associative reciprocal connections might have in the development of the conscious control of invariant cognitive abilities.

Recently, a revolutionary new theory of consciousness was put forward by Cotterill (1995). Within the currently accepted paradigm, consciousness is primarily associated with perception and stimuli, but challenging this view, Cotterill suggests that we should rather think of consciousness

as being associated with muscular movement and the resulting response from the environment. This new paradigm forces us to see the *environment* rather than the *individual* as the black box being investigated.

The current paradigm has focused on the fact that humans are visual animals since half of the cortex is dedicated to the processing of visual sensory information. Thus, perception has been seen as a key player in the shaping of consciousness. It has been noted that memory appears to be closely related to the visual system, which can be seen from the experiments of Standing (1973). Apparently there exists no upper limit to the number of pictures that can be remembered and later recognised. The new paradigm needs to explain these findings, which in this case amounts to explaining how vision could be a muscular activity. Cotterill points out that in Noton and Stark (1971), it was found that the perception and recall of an image has to do with recognition of the eye-movements made during scanning, rather than recognition of the image as a whole. Amongst other things, this would explain why we recognise caricature drawings. Computationally, this could also explain why our visual memory seems inexhaustible.

More speculations on the muscular nature of sensory input would unfortunately take us too far from the scope of the article but it should be clear that the new paradigm looks quite promising. Here we shall only briefly discuss one of the implications for the above mentioned model. It states that feed-forward and the associative reciprocal connections are used for the analysis and representation of the relations between sensory input and motor output. The new paradigm suggests that we look upon sensory input as essentially being spatiotemporal sequences of *motor* input. In connection with the idea of the brain being a machine, it certainly makes sense, as input is now essentially the same as output. The prediction and internal feed-back in the neural structures then supply the brain with the information needed in order to *interact* with the environment. Both prediction and internal feed-back are heavily dependent on the reciprocal connections, and it could well be that the very process of thought arises from them. The continuous dynamic re-grouping of feed-forward connections by reciprocal connections would certainly provide the necessary feed-back mechanisms, as was already pointed out by Cotterill and Nielsen (1991). Ultimately, these feed-back mechanisms would seem to play a very important role in the determination of the intelligence of the organism.

5.1. Summary

This paper has described two important components in the formation of the brain: development and plasticity. How and when are the neural structures formed? Before birth the neural structures are roughly formed, then fine-tuned after birth in critical periods, and re-associated through

dynamic re-grouping throughout life. The visual system is used as a model for the other distributed systems in the brain, as it is accessible and above all testable. It seems reasonable from the study of other sub-systems (language or motor activity, for example) to extend the conclusions to the whole brain. We point to some fundamental strategies in the analysis and representation of the relation between sensory input and motor output. Static feed-forward connections with broadly tuned neurons are formed early in development, and can later be re-grouped by reciprocal associative connections. In this perspective, the idea of critical periods is very important. Critical periods can be seen as windows in the development, in which specific learning *has* to take place if at all. When we learn a »new« skill as fully-grown, this skill is based on the reuse of other skills. How we *consciously* use these skills and how reciprocal connections seem to play a very important part in this, is briefly touched upon in relation to the exciting new conjecture by Cotterill on the subject of consciousness.

In sum, then, we believe that the following points have been established:

- Feed-forward connections seem to a larger extent than reciprocal connections to be genetically determined.
- In contrast to the reciprocal connections, the feed-forward connections loose the ability for activity based change at the post-natal stage. The reciprocal connections have the ability to form new representations of sensory input.
- It is not clear how those reciprocal connections formed during the learning process become permanent. One suggestion could be that LTP and LTD are part of the process. The formation of *permanent* reciprocal connections could be synapses being exposed to these molecular processes until the point where changes are irreversible.
- The plasticity post-natally and later in life could be seen as a further step in the pre-natal development, with the important difference being that the basic neural structure has been laid out and is no longer subject to change. Instead, plasticity can be seen as the dynamic re-grouping of static feed-forward connections.
- The continuous dynamic re-grouping of feed-forward connections by reciprocal connections would certainly provide the necessary feedback mechanism that is likely to play an important role in the shaping of consciousness.

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