

Figure 66. Hypothesis of epigenesis by selective stabilization. Spontaneous or evoked activity in the developing neuronal network controls the elimination of excess synapses formed during the stage of transient redundancy.

2. The evolution of the connective state of each synaptic contact is governed by the overall message of signals received by the cell on which it terminates. In other words, the activity of the *postsynaptic* cell regulates the stability of the synapse in a *retrograde* manner.

3. Epigenetic development of neuronal singularities is controlled by the activity of the developing network. It commands the selective stabilization of a particular set of synaptic contacts from within the total set present during the stage of maximum diversity.

These concepts have been brought together in the form of a mathematical model, which is, of necessity, simplified and schematic, but autonomous with regard to biological reality. It then becomes possible to reconcile this formal representation with experimental data.

The theory that has just been formulated has two important applications on biological grounds. The first is to give a plausible explanation for the recording of a temporal sequence of nerve impulses as a stable pattern of connections described in terms of a specific synaptic geometry. Adult structure depends on the effects of activity on a preexisting anatomical organization. Certain preexisting connections are selected by activity or "experience" without inducing any synthesis of new molecular species or structures. The second consequence, which has been the object of a rigorous mathematical proof, is that the same afferent message may stabilize different arrangements of connections, which nevertheless result in the same input-output relationship. This variability in patterns of connection may account for the phenotypic variability seen between isogenic individuals. It also takes into account the diversity of neuronal singularities within a single category of neurons, without necessitating some genetic "combining" mechanism.

THE EXPERIMENTAL TESTING OF EPIGENESIS

Mathematical theories can stand on their own, but this feature is also their weakness. In the natural sciences, particularly in biology, theories are limited by many more constraints than in mathematics. Obviously, a theory must be internally coherent and satisfy mathematical logic, but it must also accurately reflect external realities. A biological theory is useful only if it is representative of natural objects or phenomena and can thus be directly tested by experimentation. Numerous biological

theories have collapsed and disappeared from the scientific literature; many others will suffer the same fate because, in spite of infallible reasoning and convincing mathematics, they fail the test of reality.

How does our theory of the epigenesis of neuronal networks by selective stabilization fare? Experimental data are still limited. Rigorous testing first demands a description of the graphs of developing neurons. It also requires knowledge of the nervous activity in the embryo or newborn. Very few neural systems are suited to such analyses. The few data we possess concern the neuromuscular junction of the chicken and the rat and the mammalian cerebral cortex.²¹

As we have seen, the chick embryo is capable of considerable spontaneous movement. What happens if the movements are blocked—for instance, by injecting curare or the snake's alpha-bungarotoxin in the embryo? These poisons act selectively on the acetylcholine receptor at the neuromuscular junction. They do not interfere with the heartbeat or other vital processes, so the embryo will survive. The initial accumulation of receptors under the growth cone still takes place. Thus, the activity of the neuromuscular junction does not govern the formation of the first patch of receptors on the muscle. On the other hand, this activity has an effect on the storage of acetylcholinesterase, the enzyme for the breakdown of acetylcholine, at the synaptic site. The muscle must be active for this enzyme to accumulate. The same is true for the disappearance of receptors outside the neuromuscular junction, which does not occur in paralyzed embryos.²² Muscular activity is necessary to eliminate them. It does not accelerate the breakdown of the receptor; it simply blocks its synthesis. Thus, the labile receptor disappears. Embryonic nervous activity controls the expression of the genes that determine the synthesis of acetylcholine receptor at the muscle fibers. It also controls several, but not all, critical stages in the molecular organization of the postsynaptic side of the neuromuscular junction.

Does nervous activity also act on the other side of the junction, on the motor neuron and its axon? Ron Oppenheim took up Viktor Hamburger's observations on the death of motor neurons in the spinal cord, but using embryos paralyzed by snake toxin.²³ There were two surprising results. First, although the toxin acted on the postsynaptic side of the synapse, on the acetylcholine receptors, an effect was observed on the presynaptic side, on the motor neuron and its axon. There was a transfer of some sort of signal backward across the synapse, in the opposite direction to the propagation of nerve impulses. The sec-

ond surprise was that if, under standard conditions, the paralysis took place between the fourth and the sixth day of embryonic life, the embryo possessed an *increased* number of motor neurons compared with normal embryos (Figure 67). Paralysis led to more motor neurons! Did it affect their replication? No, the paralysis interfered with the process of neuron death, which is known to take place around the fifth day. It allowed the neurons that would have disappeared without the paralyzing agent to survive. This initially paradoxical finding is in agreement with the hypothesis of selective stabilization, as is the already-mentioned fact that an excess of receptors persists in paralyzed embryos. The artificial situation created by the paralysis shows that in normal conditions spontaneous activity leads to the death of a large number of neurons as well as to the disappearance of receptors outside the synapse.

A similar phenomenon occurs at the nerve terminal once the phase of neuron death is over. At the critical stage of multiple innervation of muscle fibers, the paralysis of the motor nerve, or indeed of the muscle (Figure 67), prolongs the temporary state of redundancy.²⁴ On the other hand, electrical stimulation of the spinal cord or the muscles accelerates the elimination of the excess terminals.²⁵

The biochemical mechanisms of the competition that results in the stabilization of certain nerve terminals at the expense of others are not yet completely understood. A simple hypothesis is based on the production of some kind of nerve growth factor by the muscle.²⁶ Growth factors produced by embryonic muscle fibers could act in a retrograde way, crossing the synapse from the muscle to the nerve in the opposite direction from the nerve impulse.²⁷ They would attract motor nerve endings and lead to multiple innervation of the muscle fibers. If at this stage of maximum redundancy, the synthesis of these factors stopped, the stock would become depleted and the survival of the nerve terminals would be related to the rate of utilization of the factor. If we suppose the more active the terminals are, the more they utilize, it becomes plausible that one might receive a sufficient quantity to become stabilized, while the others would "starve" and be eliminated.

Expressed mathematically, this competition model predicts the selective stabilization of one motor terminal per muscle fiber and the innervation of a fixed number of fibers by a motor neuron.²⁸ It also predicts a considerable variability in the final innervation of a muscle.

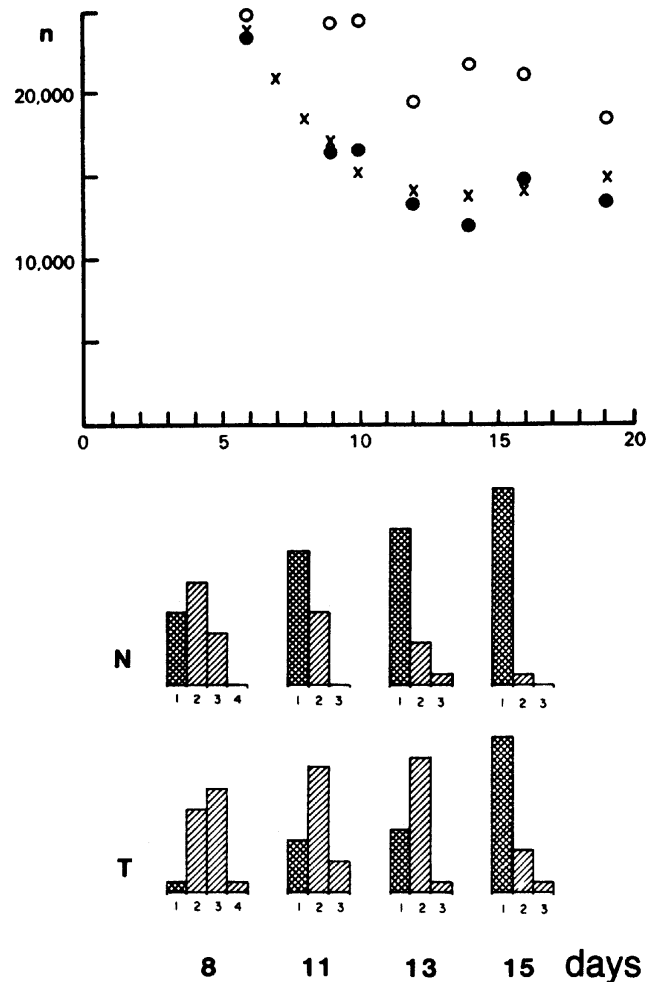


Figure 67. The effects of embryonic or neonatal activity on two regressive phenomena: cell death in the chick embryo (*top*) and the elimination of multiple innervations of muscle fibers in the rat (*bottom*). In the *upper* figure, the evolution of the total number of motor neurons (n) is shown as a function of the number of days of development. Chronic paralysis by the alpha toxin in snake venom causes a larger number of neurons to survive (open circles) than in normal controls (black dots and crosses). (From N. Laing and M. Prestige, 1978.)

In the same way, in the *lower* figure, sectioning the tendon of a leg muscle in the newborn rat paralyzes the muscle and slows the elimination of excess innervations. In these diagrams the height of the column indicates the percentage of muscle fibers with one, two, three, or four functional synapses in the normal rat (N) and the rat with the operated tendon (T). In the young rat, each muscle fiber receives three or four functional motor terminals. In the adult, there is normally only one. (From P. Benoît and J.-P. Changeux, 1975.)

For example, imagine that we can number a set of muscle fibers from 1 to 300 and that these fibers are innervated by a pool of fifteen motor neurons. At the end of their development, the neurons would share the population of muscle fibers approximately equally. There would thus be about twenty muscle fibers per neuron. However, and this is the essential point, none of the twenty fibers would show any obvious numerical order. Each neuron would participate in a "lottery" for the numbers of the fibers it is to innervate in the adult, although each neuron would "win" the same number of fibers. Thus, motor neurons would innervate a fixed number of muscle fibers, distributed without any particular geometrical regularity among the different neurons. Nor would there be any regularity in the distribution from one isogenic individual to another. The model reflects both the regularity of the innervation of a muscle and phenotypic variability.

This model also explains the "conservative" effect of the paralysis of a muscle on the evolution of multiple innervation. We need only suppose that the state of activity of a muscle controls the synthesis of the retrograde growth factor. In the embryo the muscle produces the factor. Muscle activity, especially intense during the stage of multiple innervation, stops it. Paralyzing the muscle removes this block and the factor is produced in excess. Without competition, multiple innervation persists.

The formation of the neuromuscular junction, then, depends on epigenetic regulation, in which activity plays an important role at several critical moments. In this respect it must be stressed that the regulatory mechanisms used are similar, whatever the muscle fiber, even whatever the muscle. A small number of genetic determinants within the genetic envelope are sufficient to explain how the innervation of muscles develops. Once again, economy is effected by their being shared.

Can the findings from the neuromuscular junction be applied to other systems, such as the cerebral cortex? The available data are more fragmentary but already indicate that cortical development is at least partially regulated by activity. In Chapter 2, we discussed at length the organization of the cerebral cortex into "stripes," or slabs. In the visual cortex, neurons in alternate columns respond to stimulation of one or the other eye. This characteristic organization is due, as we saw, to the way in which the thalamic axons project to the cortex. Pasko Rakic, in

1976 and 1977, and David Hubel and Torsten Wiesel, in 1977, showed that this organization did not yet exist in the fetal monkey during the third and fourth months of gestation. The axons were distributed diffusely, with those responding to the right or left eye mixed together. Segregation into columns began around the fifth fetal month and continued for several weeks after birth. Cells that had responded to both eyes gradually came to respond to one only. Although the synaptic mechanism is not yet established, the evidence suggests that cortical neurons in layer IV initially receive axons from both eyes but later become innervated by axons from one eye only.

Is the segregation of the ocular-dominance columns controlled by visual experience just as experience controls the innervation of muscles? In a series of classical experiments, Hubel and Wiesel showed that closing one eye by suturing the eyelids during the first six weeks of postnatal life had long-lasting effects on the adult monkey.²⁹ The columns, or "stripes," corresponding to the closed eye became narrower while the stripes corresponding to the other eye widened (Figure 68). If an eye was closed at birth and opened three weeks later, the width of the stripes recovered. Similar experiments in the adult had no



Figure 68. Consequences of closing an eye on the left and right ocular-dominance columns in the visual cortex of the macaque. In the *left* figure, one eye had been surgically closed in a two-week-old monkey and the pattern examined eighteen months later by an anatomical method similar to that mentioned in Figure 20. The bands corresponding to the closed eye (in black) have narrowed, compared with those corresponding to the open eye. In the *right* figure, the same experiment was performed on an adult monkey. There is no effect on the normal organization of the bands (From S. LeVay et al., 1980.)

effect. There was a *critical period* during which abnormal activity in the visual system caused an irreversible lesion. Balanced activity in the visual pathway is necessary for the development of a normal adult network.³⁰ In humans similar effects to those produced by the experimental lid suture arise naturally from congenital cataracts, when the lens of the eye is opaque at birth. The resulting amblyopia, or loss in the sharpness of vision, can be interpreted as a disturbance of visual-cortex innervation.

How the synaptic mechanisms are affected by these changes in nervous activity is not yet completely elucidated. It seems as if the target neurons initially receive functional terminals from both eyes and that lack of activity in one eye results in the retraction of the corresponding nerve terminals, leaving in place the fibers coming from the other eye. However, experimental confirmation of this interpretation in terms of selective stabilization is still lacking.

As already mentioned, during cortical development the nerve fibers that connect the two hemispheres via the corpus callosum are also subject to regression. In 1979 G. M. Innocenti and D. O. Frost showed that the occlusion of an eye, or even experimental strabismus, could change the course of development of callosal innervation. Once again, "inactivity" causes the preservation of redundant connections. Thus cortical development is subject to significant epigenetic regulation through nervous activity, and many features of this control are compatible with the hypothesis of selective stabilization. But how far does the influence of this epigenetic regulation extend? It seems probable that it intervenes particularly in the intrinsic differentiation of a given cortical area, that it participates in the development of its synaptic "micro-organization." But does it influence the development of relationships between different cortical areas?

HEMISPHERIC SPECIALIZATION—A GENETIC OR EPIGENETIC PROCESS?

Especially in man, one finds a remarkable series of areas specialized in what Colwyn Trevarthen in 1982 called "cooperative understanding" between individuals of a social group. Among others, one can obviously point to the language areas, usually localized in the left hemisphere (see

Chapters 1, 2, and 5). Does this hemispheric specialization result from active epigenesis or, on the contrary, is it the result of strict genetic determinism?³¹

Research into this problem has often been confused with research on the preferential use of the left or right hand. Contrary to what might be expected, the same hemisphere is not necessarily responsible for both handedness and spoken language. Not all left-handed people speak with their right hemisphere. This observation was an early result of a very discriminating test developed by Juhn Wada and Theodore Rasmussen in 1960. Each cerebral hemisphere is fed by one carotid artery. When a barbiturate, such as Amytal, is injected in one carotid, the corresponding hemisphere is temporarily anesthetized. If this hemisphere is the one responsible for language, the subject temporarily loses his speech. If the other hemisphere contains the language centers, speech is preserved. It has been found that 5 percent of right-handers speak with their right hemisphere and 70 percent of left-handers with the left hemisphere! This means that handedness is not necessarily associated with the hemisphere controlling speech. The two phenomena are regulated quite differently.

First, let us consider handedness, before turning to the problem of speech. Irrespective of culture, about 90 percent of human beings use the right hand for writing and difficult manual tasks. This preference was already present in prehistoric man. The "negative" handprints outlined on the walls of caves formerly inhabited by Cro-Magnon man are left hands in 80 percent of the cases. Thus, the people who outlined them must have used their right hands to apply the color. They also used their right hands to attack their victims with the primitive weapons that they manufactured. Could this already have been a reflection of their cultural environment? Cro-Magnon man's symbolism remains mysterious, but a long historical tradition has given negative attributes to the left. In French, apart from its meaning as an orientation in space, *gauche* has a pejorative sense, which has even been adopted in English. According to Christian tradition, at the Last Judgment, the good will be with the lambs at the right hand of the Son of God and the evil with the goats on his left. Could it be that a strong cultural heritage was sufficient to impose a "right-handed" epigenesis, or is it that tradition has simply accentuated an innate feature?

Let us look at the heredity of handedness. Its familial incidence does not obey simple laws. Families of left-handers do exist, but there are

right-handers in left-handed families and left-handers in right-handed families. Statistics derived from a large sample of families show the following proportions for right-handed children: 92 percent when both parents are right-handed, 80 percent when one parent is right-handed and the other left-handed, 45 percent when both parents are left-handed.³²

Can these observations be interpreted on the basis of a genetic model? The simplest model imaginable would be based on the hypothesis that handedness is determined by a single gene present in two forms: a dominant one (R) for right-handedness and a recessive one (L) for left-handedness. This model would predict that all children of left-handed parents (LL) should be themselves left-handed, but this is not the case. Such children are often right-handed. We must therefore look for another mechanism.

In 1972 Marian Annett proposed a more satisfactory genetic model, which also involves a single gene but invokes a very simple additional hypothesis. Individuals possessing at least one active form of the gene would all be right-handed; those who did not would have an equal chance of being right- or left-handed. This model would explain the fact that half the children of left-handers are right-handed. But it would remain in the realm of theory if there did not exist a very illustrative natural example found in the mouse and even in man.

This is the *situs inversus* mutation (iv).³³ This mutation, which affects only one individual in 10,000, does not involve handedness or hemispheric specialization, but the arrangement of the viscera. Affected individuals have their heart on the right, the liver on the left, and the intestines the wrong way around. In other words, their viscera present a mirror image of those of a normal individual. There is a noteworthy analogy with the heredity of handedness: the descendants of "inverted" mice are half normal and half inverted. It would seem as if mice that have two copies of the mutant gene (iv/iv) have one chance in two of being inverted. Mathematically the results agree with Annett's model. Normally, the embryo is curled up in the uterus in a "left-handed" spiral. But in the uterus of an iv/iv mother fertilized by an iv/iv father, half the embryos are curled toward the left and the other half to the right (Figure 69). The number of embryos forming "right-handed" spirals coincides exactly with that of inverted adults. The experimental data thus confirm the theoretical model.

What is the mysterious mechanism by which a single mutation of

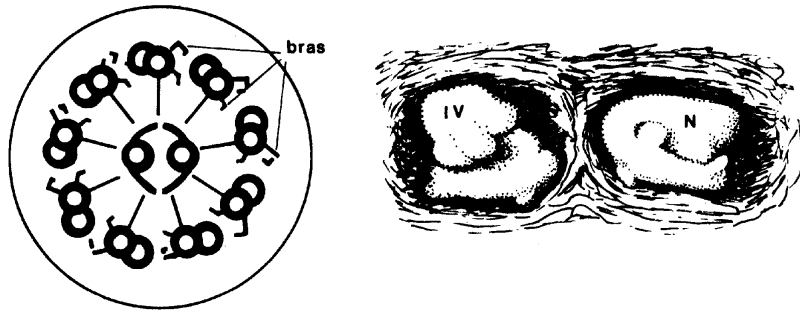


Figure 69. The inverted viscera mutation suggests a genetic model for the determination of the asymmetry of the cerebral hemispheres. Individuals with this mutation have the heart on the right and the liver on the left. The right figure shows that in the mouse with this mutation (IV) the embryo is curled in the uterus in the opposite direction from the normal embryo (N). (From Layton, 1976.) This mutation causes a paralysis of the flagella, shown schematically in a section viewed under an electron microscope in the left figure. We see that there is a loss of the "arms" that hold together the tubular elements (black circles), essential for their movement. (From B. A. Afzelius, 1976.)

a chromosomal gene can invert the arrangement of a whole set of organs? In 1976 B. A. Afzelius made a remarkable observation. Examining three patients with a total inversion of their viscera, he noticed that they showed curious symptoms of chronic sinusitis and bronchitis, apparently unrelated to the inversion of their organs. Moreover, their sperm were straight, stiff, and motionless. In the cells of these patients, cilia and flagella were completely paralyzed, and consequently the mucus was not eliminated from the respiratory pathways by the ciliated epithelium of the bronchi. When examined under the microscope, the flagella had an unusual structure. Normally, a flagellum contains nine pairs of very fine microtubules held together by hooklike "arms," but in these patients the hooks were missing (Figure 69). The microtubules could no longer move in a coordinated fashion; cilia and flagella were paralyzed.

What could be the relationship between changes in flagella movements and the arrangement of body organs? A probable hypothesis is that when the embryo consists of only a few cells, the movement of groups of these cells determines the left or right orientation of the organs that will be derived from them. Movements of cilia or flagella permit the cells to reach their definitive position. In the absence of these movements, the cells are arranged haphazardly on the right or the left. Thus, an apparently insignificant event, the paralysis of cilia and

flagella, can provoke a complete change in the symmetry of the viscera, if it interferes with an early stage of development.

Left-handers are not particularly more susceptible to bronchitis than right-handers. Handedness does not depend on the structure of flagella! But it might very well be explained by a mechanism similar in principle to that determining the arrangement of the organs. What, in this case, might the early effect of the gene be? In 1968 Norman Geschwind and Walter Levitsky reexamined some of the very detailed research of nineteenth-century anatomists and made an important discovery. Using simply a camera and a ruler, they showed that, in humans, there were characteristic anatomical differences between the hemispheres. On the upper surface of the posterior temporal lobe is an area called the *planum temporale*. It had a larger surface area on the left in sixty-five out of a hundred brains they examined and on the right in eleven (Figure 70). The slope of the Sylvian sulcus was also steeper and the frontal lobe more rounded on the right than on the left. As was established later, these differences exist in the human fetus before birth.³⁴ The planum temporale was larger on the left in most fetuses and neonates examined at ten to forty-eight weeks after conception (54 to 77 percent). Anatomical asymmetry between the hemispheres thus

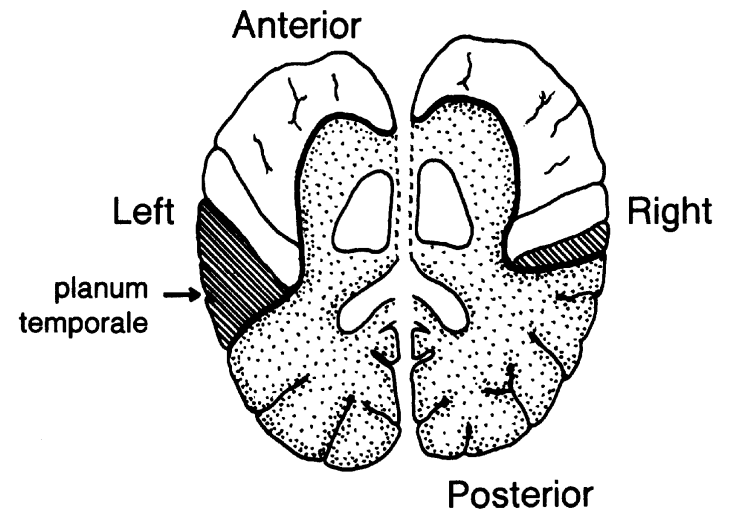


Figure 70. Anatomical differences between the right and left hemispheres in man. The planum temporale of the temporal lobe is larger on the left than on the right in the majority of brains examined. (From M. LeMay, 1982.)

precedes any form of "education." It is determined by genetic factors, perhaps influencing the tangential proliferation of the neurons in the planum temporale so that they divide for a longer time on the left than on the right.

In reality, however, it is not so simple. Any strictly genetic model predicts, as we have seen, a much greater concordance between identical twins, whose chromosomes are identical, than between twins developed from different eggs. Yet, as far as handedness is concerned, no major difference can be observed between identical and nonidentical twins. Even more surprising is the fact that twice as many left-handers are found among twins, identical or not, than among nontwins.³⁵ Could intrauterine experience reverse the effect of the genes? That is not yet known, but we do know that neurological disorders are more frequent in twins of either sort than in the general population. Perhaps crowding in the uterus provokes minor trauma, which cancels out the initial interhemispheric differences and forces the balance in the other direction!

Clinical observations on the development of language areas in children can be useful in studying hemispheric dominance. Before discussing this problem, we should remember that language areas are different from those concerned with handedness and that they do not necessarily develop in the same hemisphere.

Circumscribed lesions of the cerebral cortex in children provoke language difficulties, similar to those observed by Paul Broca in the adult. But are these lesions mainly in the left hemisphere, as in the adult?

In the 1960s a study of about sixty cases led to the suggestion that in children aphasia could result from damage to the right hemisphere as well as to the left. In addition, it was believed that the aphasia was entirely reversible. In other words, there was an *equipotentiality* of the cerebral hemispheres at birth, with their specialization appearing only when language was acquired.³⁶ Later proposals evolved in the opposite direction, and today a subtler view is held.³⁷ In 1983 A. Roch-Lecours focused on a group of very special aphasias, those that affect right-handers after a lesion of the *right* hemisphere. They are very rare in the adult, appearing in only 0.4 percent of cases, but in children, although still rare, they are ten times more frequent. In the early stages of development, the right hemisphere thus has a certain potential that is lost in adult life. Other clinical data support this interpretation.

In a fortunately small number of newborns, serious epileptic crises or invasive tumors make it necessary to remove one hemisphere totally. In most known cases, this operation does not interfere with the acquisition of language,³⁸ but it is very clear that nine or ten years later these children do not possess all the linguistic abilities of a normal child. Removal of the left hemisphere causes problems with the understanding and production of sentences with complex syntax. After surgical removal of the right hemisphere, deficits in the performance of visual and spatial tasks are observed. Well-studied cases are still sparse, but probably, as Roch-Lecours indicated in 1983, we are born with *two* language areas, but the left area, because of its innate properties, is ready to dominate and will do so immediately or within a year after birth.

In conclusion, an innate predisposition, based on a genetic model such as that proposed by Marian Annett, weights the balance in favor of one of the hemispheres, usually the left. For a certain time during the first stages of development, the other hemispheres can take over at least some of its functions, as, for instance, after minor trauma or, more dramatically, after the total ablation of one hemisphere. Epigenetic regulation thus intervenes in the differentiation of language areas. It seems as if at a certain critical moment similar, if not strictly identical, neural structures exist in both hemispheres, but are lost selectively on the right or on the left during the long period of apprenticeship leading to adulthood. We are still a long way from a cellular or molecular analysis of hemispheric specialization in humans, but the data we possess are obviously compatible with the hypothesis of selective stabilization. We have already seen that in animals there is a significant loss of fibers in the corpus callosum linking the two hemispheres during postnatal development. Could this process participate in hemispheric specialization? Could this be an important piece of evidence in favor of the hypothesis of selective stabilization?

THE CULTURAL IMPRINT

The brain's capacity to produce and combine mental objects, to remember them, and to communicate them is seen most vividly in humans. Mental representations are propagated in different coded forms from one individual to another and perpetuate themselves

through generations, without requiring any sort of genetic mutation. A new form of memory is born outside the individual and his brain. Signs and symbols that evoke mental objects are recorded on substrates containing neither neurons nor synapses—on stone or wood, paper or magnetic disks. A *cultural tradition* is formed.

A remarkable feature of the development of the human brain, already pointed out, is that it continues long after birth (see Figure 56). As we have seen, brain weight increases by a factor of 4.3 up to adulthood. Most of the synapses of the cerebral cortex are formed *after* birth. The fact that synapses continue to proliferate postnatally permits a progressive “impregnation” of the cerebral tissue by the physical and social environment. How is this cultural imprint acquired? Does the environment “instruct” the brain by leaving its imprint, as a bronze seal does in a piece of wax? Or, on the contrary, does it simply selectively stabilize successive combinations of neurons and synapses as they appear spontaneously during development?

In 1968 the eminent linguist Roman Jakobson studied the way in which the babbling of children is transformed into spoken language. According to him, the child “can accumulate sounds that are never found in a single language or even a group of languages.” The child produces an abundance of “wild sounds,” of which only a few are found in adult language.³⁹ This phenomenon does not seem restricted to humans. In 1982 P. Marler and S. Peters found the same thing in the learning of song by the swamp sparrow (*Melospiza gregaria*). Like the song of the cricket (see Chapter 4), that of the sparrow can be analyzed quantitatively from two-dimensional graphic recordings, or *sonograms*, with frequency on the *y* axis and time on the *x* axis. The song of the adult male in captivity is very simple: it never consists of more than two types of syllable. In contrast, before the “crystallization” of the adult song at about 335 days of age, the number of different syllables produced is always greater. Forty to fifty days earlier there are four to five times more! Marler was even able to record nineteen different syllables in one fledgling. As the twittering of the young bird changes into the song of the adult, there is a marked decline in the number of types of syllables produced (Figure 71). What is more, the two types that persist in the adult may differ from one individual to another. There is both elimination of syllables (“syllabic attrition”) and variability in the definitive song of the adult. The crystallization of the song looks as if it might represent the selective stabilization of syllables!

Sparrow fledglings produce a great variety of syllables spontaneously, but they are also capable of imitating “model” songs synthesized by a computer. They invent and improvise but also imitate. Are such imitations incorporated in the adult song during the attrition process? Yes, imitated syllables can be used in the two syllables of the male’s song. Marler and Peters found about fifty types of different syllables in the songs of all their “educated” sparrows; among these nineteen, or 42 percent, were imitations. Thus education can lead to a considerable artificial diversification of the song.

The young sparrow does not imitate just any model song. If exposed, for example, to the song of a related species of sparrow—the song

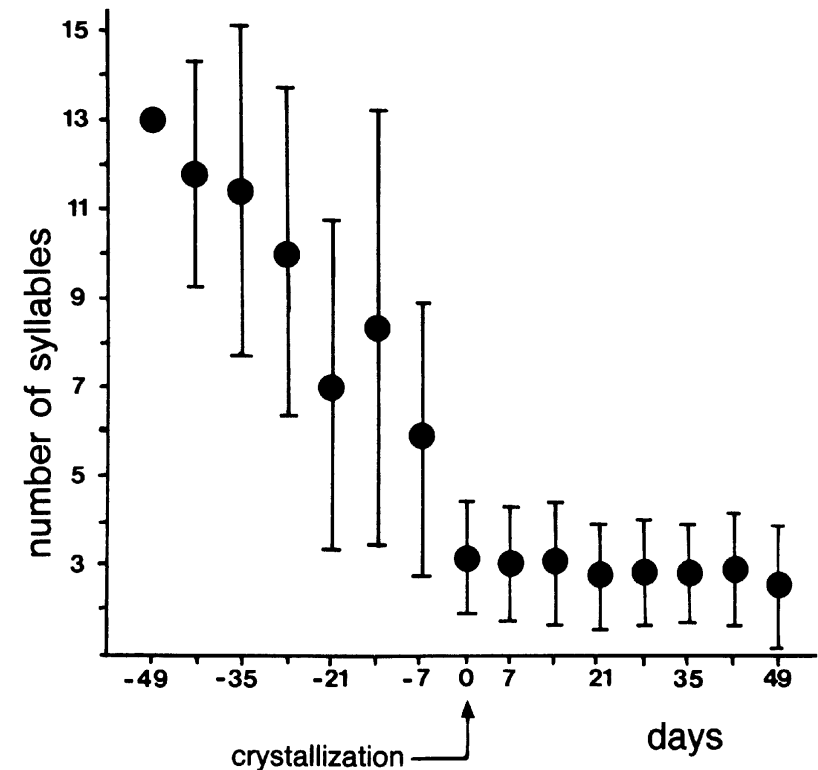


Figure 71. The song of the young swamp sparrow (*Melospiza melodia*) consists of a repertoire of about fifteen syllables and sometimes more. The “crystallization” of the adult song is accompanied by the loss of more than three-quarters of the syllables produced by the young. There is “syllabic attrition.” (From P. Marler and S. Peters, 1982.)

sparrow (*Melospiza melodia*)—young swamp sparrows will imitate only a few of the syllables of the song sparrow. As adults, they incorporate even fewer of them in their definitive song. There is thus an elimination of foreign syllables both during imitation and attrition. The capacity to learn is limited by the genetic envelope peculiar to a given species.

For humans, the process of learning speech is certainly more complex than the learning of song by the sparrow, but there are several common features.⁴⁰ As infant babbling becomes real language, it is quite probable that there is an “attrition” of spontaneous or imitated syllables. Obviously, the nervous centers involved in the production of the bird’s song are different from language areas, but common rules at the cellular and synaptic levels could have similar effects.

The phenomenon of attrition can also be seen in man in language perception. In Japanese, for example, the phonemes “ra” and “la” do not exist, in contrast to Western languages like English or French. Japanese adults have great difficulties in distinguishing between them. On the other hand, Japanese babies of two or three months can do it easily, just like their Western counterparts.⁴¹ The acquisition of language, then, is accompanied by a loss of perceptual capacity. These few, very limited data can again be easily explained by the concept of selective stabilization.

The invention of a *written* representation for mental objects is incontestably a cultural phenomenon. But the identification of written signs and their combination requires that they be committed to memory beforehand. The percepts evoked by these signs must be linked to concepts. Obviously, the human brain was capable of all this *before* the invention of writing. The use of writing necessitates a long apprenticeship, which is much easier for the child than the adult. Writing leaves an impression on the brain, but where? Our lack of knowledge here does not allow us much room for speculation. We might expect that many areas are involved. First, obviously, the visual areas—the primary and particularly the secondary (see Chapter 6)—must be used. We are also aware of the importance of the right hemisphere in visual and spatial tasks. But neurological data are often hard to interpret; moreover, experimentation is difficult, if not impossible. Nevertheless, the diversity of human culture provides fantastically rich material, and there are a few rare situations where nature has carried out its own experiments, even providing controls!

Figure 72. “Neuronal man,” written in Kanji (on the left) and in Kana (on the right). Different parts of the brain are used to interpret the ideograms of Kanji and the phonetic signs of Kana. (Calligraphy by Shigeru Tsuji.)

Japanese writing uses two systems of signs. *Kana*, rather like an alphabet without being one, is made up of sixty-nine symbols, each corresponding to a distinct sound. *Kana* is phonetic and combinative. *Kanji*, on the other hand, is not phonetic but ideographic. As in Chinese, each sign has a specific meaning, but the relationship between the sign and its sound is quite arbitrary. The number of *Kanji* signs is, of course, much greater than that of *Kana* characters, (3,000 are necessary to read a newspaper); their form is also more varied and complex. In school, *Kana* is taught first, with *Kanji* being introduced only at the end of the first grade (Figure 72).

Do these two forms of writing use different regions of the brain? Since the beginning of the century Japanese neurologists have realized that localized vascular lesions in the cortex can cause difficulties with spoken

and written language in Japanese, just as in Western, patients.⁴² Certain lesions in the left hemisphere, in Broca's or Wernicke's areas, may have a greater impact on the use of Kana than Kanji. Other lesions of the same hemisphere cause selective difficulties in writing and reading Kanji, whereas the use of Kana seems normal. When Kana or Kanji characters are presented to the right or left hemisphere through one or the other visual field, the results also suggest that the left hemisphere is more specialized for Kana and the right for Kanji, particularly in the case of nouns.⁴³ This difference between the hemispheres in the use of Kana and Kanji agrees well with what we already know about their respective roles from Chapter 5. The formal, abstract, combinative nature of Kana suits the left hemisphere well. In contrast, recognition of Kanji characters appeals more to the particular capabilities of the right hemisphere in processing and storing images.

The precise geography of the cerebral territories receiving the imprint of the two systems used in Japanese writing, or even alphabetic writing in general, is still a *terra incognita* whose exploration must await the future. Nevertheless, present observations indicate that a significant variability in the organization of the cortex is related to the cultural environment.

Certain authors even go as far as to think that the differentiation of language areas varies between illiterate and educated people. It has been noted that aphasia following left-hemisphere lesions is less frequent in illiterate patients than in patients who can read and write. Other authors, however, have been unable to confirm these results.⁴⁴ Tests of differential listening through each ear suggest that the right ear is more efficient than the left in illiterate subjects, while in literate subjects the efficiency of the two ears is about equal.⁴⁵ Is this enough to conclude that the epigenesis of cortical organization can be influenced by reading and writing? It is possible, but a convincing demonstration remains to be seen.

“TO LEARN IS TO ELIMINATE”

The “complexity” of the human brain needs no emphasis; S. Atlan is right to insist that the use of this term usually reveals our ignorance. The development of new techniques for anatomical and functional exploration should allow rapid progress in this field and help to fill some

of the more obvious gaps in our knowledge. Such methods will, however, encounter fundamental difficulties. An organization can be described only to the extent that it is reproducible from one individual to another. As we saw in Chapter 6, the power of the genes perpetuates the major organizational features, such as the shape of the brain and its convolutions, the organization of its areas, and the general architecture of the brain tissue. But considerable variability, as seen in identical twins, remains, despite the genes' power. It becomes obvious as soon as our analysis reaches the cellular or synaptic level. In the water flea, or daphnid, this variability is limited to the geometry and number of synapses, but in mammals it affects the number and distribution of neurons. In humans it even influences our hereditary tendency to use the right hand. This phenotypic variability is intrinsic. It is the result of the precise “history”⁴⁶ of cell division and migration, of the wandering of the growth cone and its fission, or regressive processes and selective stabilization, which cannot be exactly the same from one individual to another even if they are genetically identical. The way in which the brain of the higher vertebrates, especially humans, is constructed introduces a basic variability. The human brain cannot be compared to a compilation of a million sea slugs' abdominal ganglia, in which most of the neurons can be numbered and labeled.

The theory of epigenesis by selective stabilization of neurons and synapses during development takes variability into account. Indeed, this is one of its major advantages. The formal mathematical approach used in this context is intended as a rigorous demonstration that “different learning inputs may produce *different* connective organizations and neuronal functioning abilities but the *same* behavioral capacity . . . in spite of the totally deterministic character of the model.”⁴⁷ In other words, according to this scheme, experience—which is never the same from one individual to another—leads to a similar behavioral performance, although based on different neuronal and synaptic topology. Individuals who speak with their right hemisphere do not use a different language from those speaking with the left hemisphere. The behavioral code is, to use Gerald Edelman's expression, “degenerate.” Epigenesis ensures the *reproducibility of function* despite anatomical variations resulting from the way in which the machine is built.

Several observations converge in support of this theory. The number, topology, and connections of neurons are all affected by regression, as are the types of syllables learned by sparrows, and probably also by man!

Regression affects the peripheral as well as the central nervous system, suggesting that it is a generalized phenomenon, related to the development of neuronal networks. The very early activity of the nervous system in the embryo, together with the role of its spontaneous or evoked activity in regulating various formative stages of a synapse and its evolution up to adulthood, also supports the theory. The facilitating effect of nervous activity on certain cellular or synaptic regressive processes lends additional support. Nevertheless, it still remains to be shown that this theory can be applied strictly to the development of neuronal graphs in the central nervous system.

The laying down of "redundant" and "variable" neuronal or synaptic topologies—the substrates of epigenesis—costs much less in genetic information than would a point-by-point coding of the diverse neuronal singularities found in the adult. The genes that make up the genetic envelope, in particular those that determine the rules of growth and stabilization of synapses, can be shared by all neurons in the same category, perhaps by several categories of neurons. The number of genes necessary for epigenesis through selective stabilization is also relatively low.

Another advantage of the theory of selective stabilization is that it takes into consideration a unique and characteristic property of the nerve cell—that of establishing thousands of discrete, individual contacts with other cells through its synapses. Convergence at the dendrites and divergence through axonal branching create a possibility of "combining" connections, not only for the cell but also for the neuronal "system." Selective stabilization involves populations of nerve cells. As we saw in Chapter 5, the properties of convergence and divergence permit combinations of nervous activity. In this way mental objects can participate in the epigenesis of the brain, with percepts becoming associated with concepts. Future developments in neurobiology will, it is hoped, permit us to discover to what extent mental exercise, either spontaneous or evoked, contributes to the fine tuning of cerebral-cortex connections, including those of the language areas.

According to this scheme, culture makes its impression progressively. The 10,000 or so synapses per cortical neuron are not established immediately. On the contrary, they proliferate in successive waves from birth to puberty in man. With each wave, there is transient redundancy⁴⁸ and selective stabilization. This causes a series of critical periods when activity exercises a regulatory effect. If we consider that the

growth of axonal and dendritic trees is innate and that selective stabilization defines acquired characteristics, the innate can be differentiated from the acquired only by detailed study at the synaptic level. This study is made difficult by the intimate association of growth and epigenesis, and their alternation over time. One has the impression that the system becomes more and more ordered as it receives "instructions" from the environment. If the theory proposed here is correct, spontaneous or evoked activity is effective only if neurons and their connections already exist before interaction with the outside world takes place. Epigenetic selection acts on preformed synaptic substrates. To learn is to stabilize preestablished synaptic combinations, and to eliminate the surplus.

Finally, the theory takes into account the paradox dealt with in the preceding chapter: the nonlinearity, noticeable during evolution, between the complexity of the genome and that of cerebral organization. Let us consider this in the light of the still intriguing problem of the evolutionary origins of the human brain.