

In the final analysis, nervous activity, either evoked or spontaneous, and its propagation in the neuronal network, can be explained by *atomic* properties. Should we then reinvoke the notion of “psychic atoms” advanced by Democritus? The sodium and potassium ions that cross the channels of the axon or the postsynaptic membrane are the same in the neuron as in seawater. The molecules of the neurotransmitters and their receptors are composed of carbon, hydrogen, oxygen, and nitrogen, which in themselves are in no way specific to living organisms. The nervous system is made up of, and uses in its functional activity, the same “matter” as the inanimate world. Matter organizes itself into molecular building blocks, which contribute to communication between nerves in the same way that other molecules may regulate cell metabolism or chromosome replication. The proteins have a critical role to play, for enzyme pumps, ion channels, enzymes for neurotransmitter synthesis, and receptors are all proteins. Instead of readopting the term “psychic atoms,” perhaps we should speak of “psychic molecules.”

The most striking feature highlighted by present-day research on brain electricity and chemistry is that the mechanisms responsible for activity or, if one prefers, communication in the cerebral machine resemble those found in the peripheral nervous system and even in other organs. They are found equally in nervous systems of very simple organisms. What is true for the electric organ of the torpedo fish is also true for the brain of *Homo sapiens*. At the level of the elementary mechanisms of communication between nerves nothing distinguishes man from animals. No transmitter, no receptor or ion channel has yet been found to be specific to humans. We should therefore use the term “macromolecules responsible for communication between nerves” rather than psychic atoms. Gall secularized the anatomy of the human brain; let us secularize its activity.

Into Action

Disturb the origin of the bundle and you change the animal.

—Denis Diderot, *Le Rêve de d'Alembert*

We interact with our environment and communicate with our fellow human beings by moving our lips, eyes, and hands; by a set of motor activities that we call behavior. The study of these activities took shape in 1913, through a dynamic scientific movement initiated by John B. Watson—*behaviorism*. Concerned with eliminating the subjective from scientific observation, behaviorism restricted itself to considering the relationship between variations in the environment (the stimulus conditions) and the motor response that was provoked. It was enough to know the rules governing these relationships to explain behavior. Why should one be concerned about the contents of the “black box” inserted between the stimulus and the response? As one might have expected, the narrowness of this approach led the behavioral sciences, and with them many other human sciences, to an impasse.

The development of the neurosciences has brought another way of looking at behavior, in the tradition of Franz Joseph Gall and Paul Broca. The neuronal content of the black box can no longer be ignored. On the contrary, all forms of behavior mobilize distinct sets of nerve cells, and it is at their level that the final explanation of behavior must be sought. The comparison of the brain to a cybernetic machine or a computer may be useful in defining basic rules of behavior and specifying the relevant components of the machine. Because of the way it is constructed, the cybernetic machinery of the brain performs only a limited number of operations. Not everything is possible. As J. Z. Young commented in 1964, what it can do is determined by the extent to which it contains, or is itself, a “representation” of its environment. In other words, our interpretation of the external world and our re-

sponses to it depend on the internal organization of this "machine." The very simple nervous system of a mollusc does not analyze signals from the environment as profoundly as the nervous system of a monkey or a man, nor does it produce such a wide range of responses. The critical mechanisms lie in the central nervous system, where information is transmitted through a *code*, analyzed, and then processed. As a result of these computations, motor neurons go into action and command the contraction of muscles. Let us examine in detail the different forms of *internal coding* involved in going into action.

TO SING AND TO FLEE

Who does not remember a warm summer evening with the musky scent of flowers and the first songs of the cricket? Only the male crickets take part in this concert to attract and guide the receptive females to them. This call song is part of a very complex communication network that exists between partners of the opposite sex but also between the males. For the neurobiologist, the call song—because of its simple, repetitive character, stereotyped in nature but peculiar to a given species—constitutes a "schematic" behavior that is particularly useful for the analysis of "internal" mechanisms.¹

The first pair of wings, or elytra, serve as a musical instrument. Their inner edge is the bow and the sawlike outer edge, the vibrating cord. When the male closes his wings, the bow rubs on the cord. The wing vibrates at about 5,000 cycles per second and produces the characteristic pure, flutelike sound. Powerful thoracic muscles control this closing movement. There is a close relationship between the contraction of these muscles and the production of a note. If one records the electrical impulses in the motor nerves with a microelectrode, they are also related: each impulse in the nerve corresponds to a note. One can hardly imagine a simpler form of coding (Figure 33).

The call song of the Polynesian cricket (*Teleogryllus oceanicus*) is composed of identical, repetitive phrases. They begin with a "chirp" of five notes, followed by ten "trills" of two notes. The rhythm of the impulses recorded in the motor nerves coincides exactly with that of the notes. The same rhythm is also found in the motor neurons of the thoracic nerve ganglia. It persists after section of sensory and motor

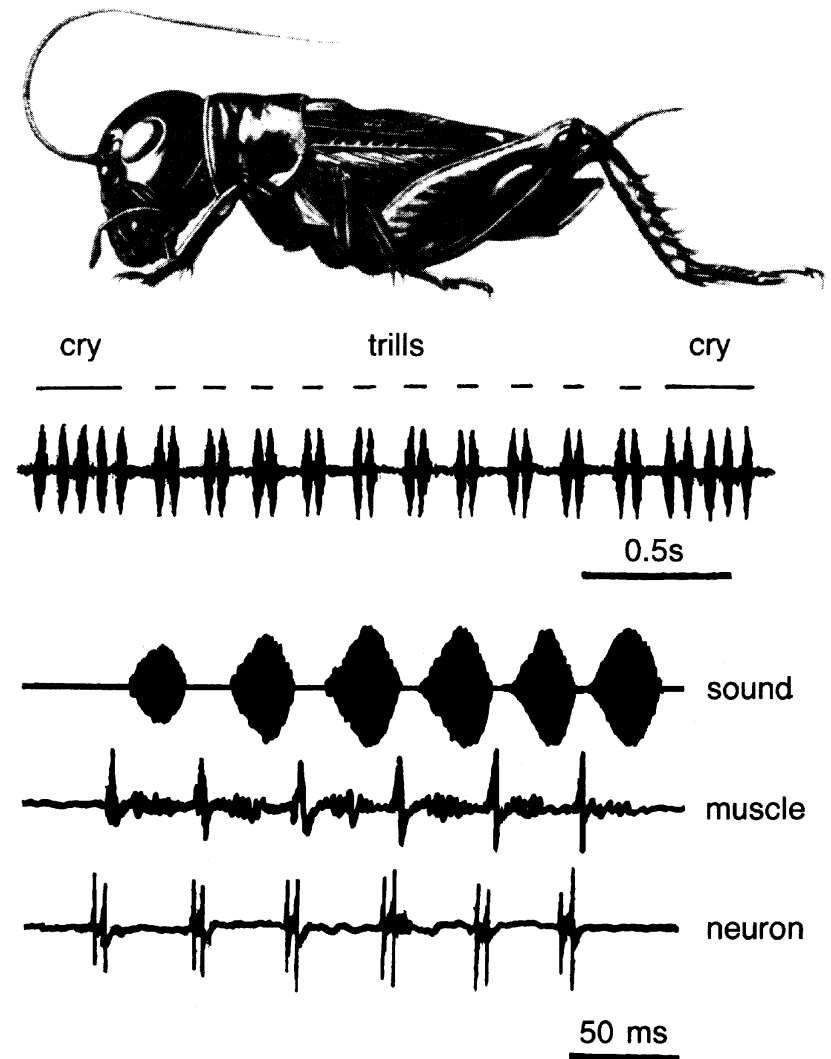


Figure 33. The song of the cricket is a simple example of a specific form of behavior directly related to the internal activity of a precise neuronal network. Above we see a drawing done by Finot in 1890 of the field cricket (*Gryllus campestris*), now in the Museum of Natural History in Paris. Below is the recording, or sonogram, of the song of the oceanic cricket (*Teleogryllus oceanicus*). The song consists of a phrase made up of a cry of five notes followed by ten trills of two notes. There is a perfect relationship between the nerve impulses propagated in the motor neurons, the contraction of the wing-closing muscles, and the emission of the sound resulting from the rubbing of the "bow" on the "string." (Redrawn from D. Bentley and R. Hoy, 1974.)

nerves, that is, after complete isolation of the ganglia. They must, then, contain spontaneous impulse generators (see Chapter 3), which produce all the characteristic features of the song in a regular, automatic fashion once they are connected to the necessary musculature.

The example of the cricket's song illustrates the two components of "going into action."

First, there are the *nerve connections*. Let us suppose that we connect the axons of the motor neurons in the wings to the muscles of the limbs. The cricket will then walk with the rhythm of the call song but will not sing. The connections between the neurons in the ganglia, and between these neurons and the muscles, define a set of cells, a stable network responsible for the production of the song—one that can be described by a mathematical structure I call a *graph*.²

Second, there are the *impulses*. Let us suppose that we artificially modify the membrane potential of one of the oscillatory neurons of the "song graph." The frequency of the impulses produced will change. The song will not have the same form. It will not have the same attractive pull on the female. The impulses spontaneously produced in this network thus determine the temporal organization of the notes according to a characteristic rhythm. They are responsible for the realization of the song.

In other words, two forms of coding are involved: the topology of the connections determines the geometry of the network, and the impulse pattern regulates the temporal expression of the associated behavior (see Figure 33).

It is possible to elaborate a mathematical model that permits the simulation or reproduction of a behavioral pattern and that therefore represents in a simplified, schematic manner its intrinsic mechanism. Such a model has been put forward for the swimming of the leech, where nearly all the neurons involved have been identified.³ With the song of the cricket, we lack some details, but it is already clear that the conclusion will be the same, that this behavior is totally determined by a particular network—a graph of neurons—and the impulses within it. The cricket's song is particularly interesting because it is relatively independent of the outside world: once begun, it continues for hours.

Progressing from insects to vertebrates, we can undertake similar studies by taking recordings from identified neurons. Yet the number of cells is now so great that in order to implant an electrode in exactly the same neuron from one animal to another seems an impossible task.

Fortunately, there are situations in which such an experiment becomes possible, as in the case of a giant cell in the medulla of fish, the *Mauthner cell*, whose cell body and dendrites are half a millimeter wide.⁴ What is more, a fish possesses only two of these cells, both of which are easily identifiable. They play a very precise role in the everyday life of the fish: they are involved in a reflex that permits it to escape from its predators. Let us observe a goldfish swimming calmly in an aquarium. If we tap on the aquarium or drop a golf ball in front of its glass wall, the fish suddenly turns around, its head moving to one side and its body changing orientation. It dodges, fleeing from the auditory or visual signal. The Mauthner cell has gone into action. It is not directly responsible for muscular contraction: hierarchically, it is above the motor neurons that command contraction; it coordinates and regulates their activity. If we make a recording of the Mauthner cell during the flight reflex, the generation of an impulse coincides exactly with the initiation of the reflex (Figure 34).

In contrast to the song neurons, the firing of the Mauthner cell is directly controlled by signals received from the outside world through the sense organs. Consider the case of the sound stimulus. The vibrations stimulate the inner ear, or lateral line, of the fish, which responds by bursts of impulses in the appropriate sensory nerve. These reach the Mauthner cell and cause a diminution of the membrane potential, as at the neuromuscular junction (see Chapter 3). If the threshold is reached, an impulse is triggered. The synapses of the auditory nerves on the Mauthner cell are *excitatory* (Figure 34D).

In other circumstances, for example, when the water is stirred up, there is no response: *inhibitory* synapses, also connected to the sense organs, block the effect of the excitatory synapses. Both types are chemical synapses,⁵ but the effect of the neurotransmitter on the receptor is radically different in the two cases. Instead of decreasing the membrane potential, the neurotransmitter in inhibitory synapses has the opposite effect. It blocks the depolarizing effect of the excitatory transmitter and sometimes even shifts the potential in the other direction: it hyperpolarizes (Figure 34D).

What causes this difference? Is it due to the chemical nature of the neurotransmitter or to the ions that pass through the channels opened by the neurotransmitter (see Chapter 2)? The charge of the transported ion is determining. If the ion is positively charged and enters the cell, a depolarization occurs, causing excitation, as we have already seen in

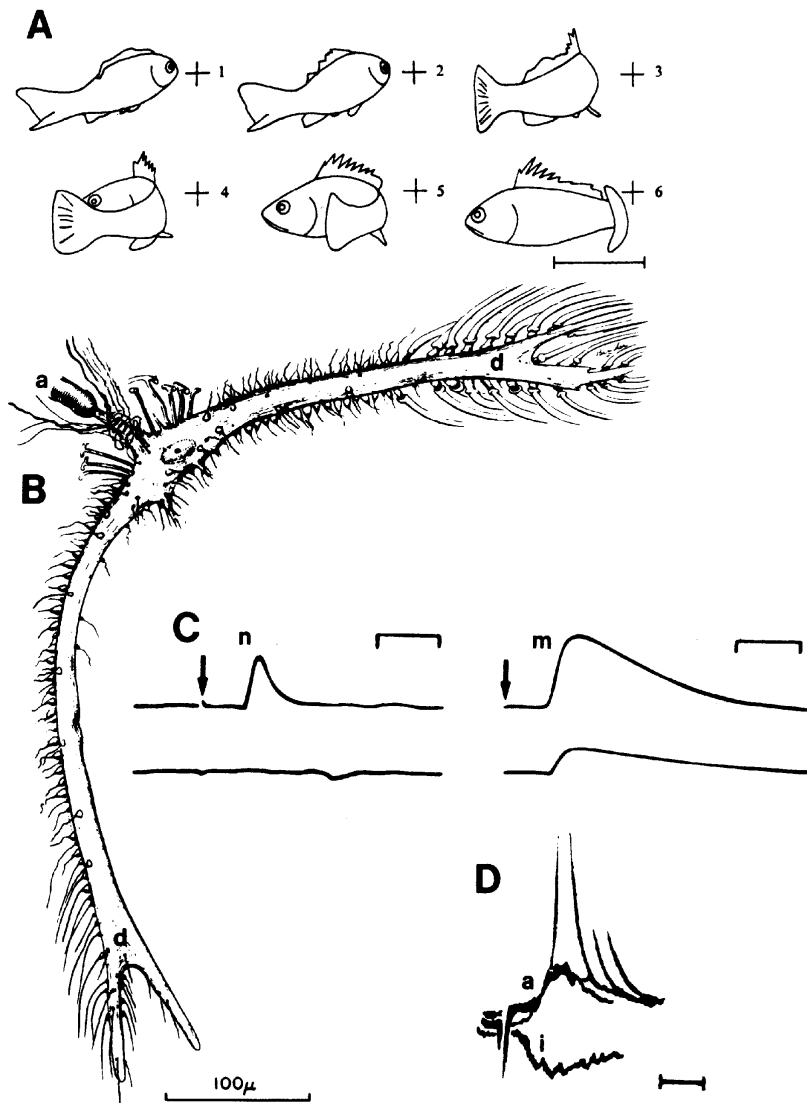


Figure 34. The firing of the Mauthner cell and the flight of the fish. **A:** These pictures show the fish every five milliseconds after a golf ball was dropped in front of the aquarium. (From R. C. Eaton et al., 1977.) **B:** This drawing of the Mauthner cell shows its giant dendrites (d) and the beginning of the axon (a). (From D. Bodian, 1952.) **C:** Here we see simultaneous recordings of the electrical impulse in the left Mauthner cell (n) and the contraction of the right trunk muscles (m). In the fish the left Mauthner cell innervates the right half of the body. (From C. Yasargil and J. Diamond, 1968.) **D:** The neuron membrane “calculates” the “activating” synaptic response (a) that triggers the nerve impulse (here cut off) and the inhibitory response (i) trying to prevent it. (From D. S. Faber and H. Korn, 1978.)

the case of the neuromuscular junction. If the ion is transported in the same direction but is negatively charged, like chloride, the electrical effect is obviously opposite in sign. There is inhibition. Cases also exist in which the receptor does not directly control the opening of a channel. It acts by the intervention of an “internal messenger,” a sort of hormone that, rather than circulating from one cell to another, remains inside the neuron. The best known of these messengers is a cyclic molecule related to ATP, called cyclic AMP (cyclic adenosine monophosphate).

The neuron membrane behaves like an arithmetical calculator. It adds positive and negative signals. If the balance is on the plus side, the threshold is reached and it fires. If negative signals predominate, the neuron membrane remains silent. In the fish, the “decision” to take escape action thus results from an elementary calculation. The calculation is itself determined by receptors and ion channels in the neuron membrane and by the local ion environment. The flight of the fish in response to a stimulus from the outside world can thus be explained entirely by the connections of the graph to which the Mauthner cell belongs, by its impulse traffic, and, most important, by the molecular properties of its membranes that determine its “decision making.”

TO DRINK AND TO SUFFER

The example of the Mauthner cell illustrates the antagonistic effects of excitatory and inhibitory synapses. Certain transmitters are specific for inhibition, others for excitation. Using the model of the Mauthner cell, and in a very schematic fashion, the excitatory transmitter becomes the escape substance in the fish. Indeed, it is tempting to give every behavioral pattern a particular chemical label. The temptation is even stronger when one considers the great variety of neurotransmitters found in the vertebrate brain, including that of man (see Chapter 3). Generally speaking, acetylcholine and glutamate are excitatory; others, like gamma-aminobutyric acid or glycine, are inhibitory. So why not a thirst substance and another for pain or for pleasure? In general terms, is there a chemical coding of behavior?

The case of thirst can serve as an example.⁶ We drink when we have lost water—for instance, after physical effort. This water loss causes a reduction in the blood volume and a change in its salt concentration.

These variations in physico-chemical properties provoke a desire to drink, through the intermediary of the nervous system. Only a few neurons are involved. They are localized in a precise region of the brain—the hypothalamus, situated, as its name suggests, below the thalamus (see Figure 13). If this group of neurons is stimulated electrically in a rat, it begins to drink continuously. If the hypothalamus is removed, the rat will no longer drink. Just as the Mauthner cell stimulates the flight behavior of the fish, these hypothalamic neurons regulate drinking behavior in the rat, and also in man. Recording their activity has helped to identify the substance that stimulates them—a hypothetical “thirst transmitter.” It is one of the numerous peptides that serve as hormones in some circumstances and as neurotransmitters in others. Called *angiotensin II*, it consists of a chain of eight amino acids. When it is injected into the blood or applied directly to the specialized neurons of the hypothalamus, bursts of impulses are released. Oscillating neurons, similar to those of the cricket or sea slug (see Figure 27), become active. Angiotensin II starts the “impulse clocks” of the hypothalamus and when its concentration passes a threshold, the animal will soon begin to drink.

Strictly speaking, angiotensin is not a neurotransmitter because it is not released by nerve terminals. Nevertheless, it informs the nervous system of the crisis provoked by the lack of water. As is well known, the kidney eliminates water in the urine, but it also has an informational role to play. What if the blood volume decreases following a loss of water? The kidney reacts by producing an enzyme that indirectly stimulates the release of angiotensin II in the blood. Its concentration in the circulation rises and becomes sufficient to excite the neurons in the thirst center. Angiotensin, therefore, acts as a chemical mediator for drinking. (It is not the only mechanism, by the way, that regulates drinking. An important role is also played by receptors sensitive to blood pressure in the great veins and the aorta.)

Pain is another example of how chemistry sheds light on the internal mechanism—in this case not of an action, but of a sensation. Pain can be relieved with an extract of the opium poppy and particularly with one of its constituents, morphine. The Sumerians in 4000 B.C. already knew of the effects of opium.

Like all sensations, pain arises from the stimulation of sensory terminals. They are found throughout most organs, but particularly in the skin and the viscera. These terminals are quite special: they consist of

the end branches of dendrites, naked and highly forked, and they respond to various physical signals such as heat, cold, and pressure. But they also respond to certain internal chemical substances produced by the organism following irritation or a lesion. One of them, called *prostaglandin E2*, became famous because aspirin, one of the most widely used of all medicinal substances, blocks its synthesis and in this way attenuates certain painful sensations. These polyvalent nerve terminals “sound the alarm” by producing bursts of impulses that travel along the nerves to cell bodies situated in dorsal root ganglia connected to the spinal cord. In the spinal cord these “pain neurons” form synapses with relay neurons, which send their axons upward toward the brainstem and the rest of the brain.

The transmitter released in the spinal cord by these pain neurons is known. As in the case of thirst, it is a peptide, eleven amino acids long—*substance P*, one of the first peptides isolated from nerve tissue.⁷ Substance P is present in the pain nerves, which extend from their peripheral sensory endings to the spinal cord.⁸ Electrical stimulation of these nerves brings about its release. When it is applied locally to relay neurons in the spinal cord, it produces impulses that travel to the brain. Substance P may then well serve as the pain transmitter in the spinal cord.

So where does morphine act? On the periphery like aspirin or in the spinal cord at the substance P synapses? The isolation of its receptor has provided an answer to this question. As with the acetylcholine receptor (see Chapter 3), success came with the use of tracers—in this case, not snake venom, but a radioactive derivative of morphine, which exists in two mirror-symmetrical molecular forms (Figure 35).⁹ Al-

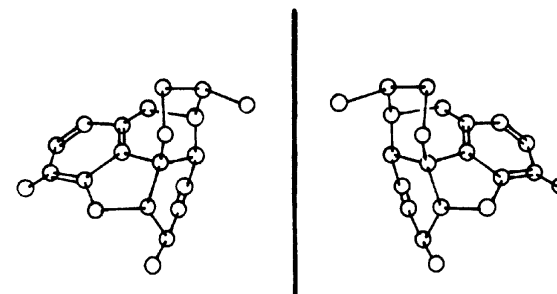


Figure 35. Formulas of levorphanol (on the left) and dextrorphan (on the right). The one is the mirror image of the other. Of these two optical isomers, only levorphanol binds to morphine receptors and stops pain.

though they are chemically composed of the same atoms, only the "levo" form (levorphanol) stops pain because it is a suitable key, fitting the physiological receptor lock, as opposed to the "dextro" form, which binds indiscriminately. The correct receptor is present in nerve tissue where we would expect it: in the spinal cord and, of course, the brain.

What is the use of this receptor? Morphine is prepared from a poppy, which, as far as we know, does not possess a nervous system and cannot suffer pain. Does morphine take the place of a natural substance present in the nervous system, a sort of "endogenous morphine"? Indeed, such substances have been isolated. Once again, they are peptides: very small ones, consisting of five amino acids, called *enkephalins*,¹⁰ or longer ones, the *endorphins* (abbreviated from "endogenous morphine"). Enkephalins or endorphins bind with high affinity to the same receptor that recognizes the levo derivative of morphine. This may seem surprising because morphine belongs to a group of chemicals, the alkaloids, that differ radically from peptides. Yet if we look closer—using, for example, a physical method that reveals the shape of molecules—remarkable structural analogies appear (Figure 36). Their geometrical configurations in space are so similar that the enkephalin key and the morphine key fit and turn in the same receptor lock.¹¹

How does the opening of the lock stop pain? The current hypothesis is that both endogenous and exogenous morphine block the pain message at the substance P synapses in the spinal cord. We know that a synapse can be blocked in several different ways: at the nerve terminal by suppressing the release of a transmitter or, on the other side of the

synaptic cleft, by inhibiting the receptor. In 1977 Thomas Jessel and Leslie Iversen showed that morphine uses the former mechanism; in effect, the opiates inhibit the release of substance P by the pain nerves. In the spinal cord the endogenous morphines, the enkephalins, play this role. A dual chemical "mediation" occurs: pain transmission by substance P, pain relief by enkephalins.¹²

Angiotensin II informs the hypothalamus about water loss in the organism and controls drinking. It sends signals from the *milieu intérieur* to the nervous system. Substance P transmits pain messages received from the skin or other organs toward the central nervous system, and the enkephalins control this transmission. Both examples demonstrate the intervention of chemical messengers specific to a particular activity or sensation. The hypothesis of a chemical coding is confirmed, but this in no way eliminates the two forms of coding already mentioned: one based on the geometry of connections, the other on the temporal succession of nerve impulses. Chemical coding complements the others. First, it permits a type of additional signaling, one that involves not the propagation of impulses along cables, but the diffusion of chemical signals over long distances using, for instance, the bloodstream. Above all, it creates a diversity in connections that otherwise have a similar geometry. Indeed, only a small fraction of sensory fibers that enter the spinal cord, those specialized for pain, utilize substance P as a neurotransmitter. The others are engaged in the perception of heat and cold or tactile sensation and use different transmitters. Chemical labeling creates diversity. It allows finer and more precise relations between neurons and therefore between a particular behavior or sensation and a specific network of nerve cells.

TO ENJOY AND TO BE ANGRY

The capacity for enjoyment, like that for suffering, is inscribed in our neurons and synapses. Once again the hypothalamus plays an important role. Removing a particular area of the hypothalamus, as we have seen, stops drinking in a rat. The same operation in other parts of this essential brain center upsets the heartbeat or the body temperature; in yet other parts, it changes eating habits or copulation. As might be expected, electrical stimulation of the same areas has the opposite

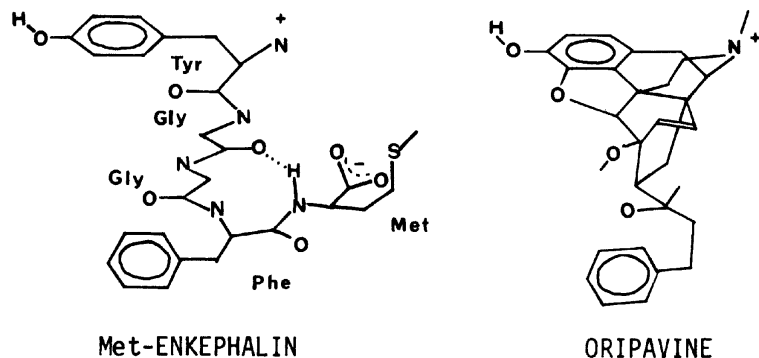


Figure 36. The structural analogy between an "endogenous morphine" synthesized by certain categories of neurons (met-enkephalin) and an opiate (oripavine). (From B. P. Roques et al., 1976.)

effect. On this hypothalamic map, each distinct “geographical” area is colored differently by its chemical signals. Most frequently these signals are peptides: drinking involves angiotensin II; eating, cholecystokinin; lovemaking, the hormone LHRH.

These small groups of neurons with their specific chemical labels regulate a variety of functions and behaviors that are so critical that we often call them “vital.” Humans, like rats, devote a large part of their time, when they are not asleep, to drinking, eating, and copulating. A single cell, the Mauthner cell, allows the fish to escape from its predators. In man several thousands of neurons, in a precise part of the hypothalamus, make final decisions about the balance of energy and the survival of the species. The most fundamental behavioral patterns in our lives depend on no more than 1 percent of the total volume of the brain, and the triple coding—electrical, chemical, and by nerve connections—is involved in their determination.

But these behavioral patterns do not appear anytime or anyhow. The sensations of thirst or hunger or sexual desire do not immediately lead to drinking, eating, or copulating. Instead, a state of motivation is created that incites one to drink, eat, or make love; it disappears after these desires have been fulfilled. In 1855 Alexander Bain wrote in *The Senses and the Intellect* that “every state of pleasure replies to an increase, every state of pain to a decrease of part of or all the vital functions.” Of course, Bain did not have our knowledge of the hypothalamus. In today’s context, his remark takes on a new significance. Thirst corresponds to a desire to drink, which can become “painful,” and drinking calms this thirst. Frustrated sexual desire is agonizing; its harmonious satisfaction appeases the anguish. Could “pleasure” regulate these vital behavioral patterns? Might there be in the hypothalamus a “pleasure center,” which would concretize this link? How could it be identified?

Laboratory animals cannot use words to answer the experimenter’s questions about sensations of pleasure or displeasure that they may experience. In 1954, in a very ingenious way, James Olds and Peter Milner succeeded in obtaining a reply from a laboratory rat. Suppose that we implant a stimulating electrode in a hypothetical pleasure center. An electrical current discharged from the electrode will create a sensation of pleasure. Let us now give the rat a device for stimulation so that by pressing a pedal it can induce a current. While exploring its

cage, the rat may accidentally tread on the pedal. If the electrode is in the right place, the rat will enjoy this sensation and repeat the operation. It will stimulate itself.

Several self-stimulation points have been identified in the rat. They are found particularly in the hypothalamus, close to the various vital centers that play a key role in drinking, eating, and copulating. But the rat, even after satisfying its appetite for sexual activity, continues to self-stimulate. The self-stimulation points are therefore distinct from the vital centers. Other points of self-stimulation have been identified outside the hypothalamus, for example in the brainstem. Careful analysis of their geography reveals a remarkable coincidence. The self-stimulation points correspond to areas where cell bodies and processes contain a specific neurotransmitter—*dopamine*. Another remarkable finding: blocking the dopamine receptors by an antagonist such as pimozide or haloperidol stops the self-stimulation. Further, certain drugs that give humans a subjective sensation of pleasure or euphoria, such as cocaine or amphetamines, seem to act in a similar way to dopamine. In the hypothalamus and the brainstem, dopamine synapses can thus be regarded as “pleasure” or “hedonic” synapses, where “the cold information regarding the physical dimensions of a stimulus is translated into the warm experience of pleasure.”¹³

The functional significance of these pleasure synapses is still not completely understood. Situated at the crossroads between sensory pathways and the vital centers of the hypothalamus, they regulate the expression of “vital” behaviors, sometimes by inhibiting them, sometimes by deciding to carry them out. Thus they participate in the development of motivational states that enable us to “go into action.”

Do emotions, or what we care to call emotions, belong to these motivational states? Donald O. Hebb, in 1949, distinguished among the emotions “those in which the tendency is to maintain or increase the original stimulating conditions (pleasurable or integrating emotions)” and “those in which the tendency is to abolish or decrease the stimulus (rage, fear, disgust).” This distinction is based on the postulate of a close relationship between emotion and pleasure. Does the hypothalamus intervene once again? In the 1930s Walter Hess noted that the stimulation of discrete regions of the hypothalamus elicited not pleasure but “anger” in the cat, causing it to arch its back, make its

fur stand on end, raise its tail in the air, and spit at and attack anything that moved. As soon as the stimulation stopped, the cat's rage stopped. Obviously, this attack of "rage" was very artificial. It represented only an external and partial manifestation of an affective state that can take on very diverse forms, particularly in man. Nevertheless, the hypothalamus once again plays a decisive role, as do other higher brain centers.

James Papez brought them to light in 1937 when examining patients suffering from rabies. They presented major emotional disturbances with anguish, rage, and terror, which he attributed to the lesions provoked by the spread of the virus. The virus attacks principally the hippocampus. This "old" cortex, as we saw in Chapter 2, corresponds to the cerebral hemispheres of reptiles and primitive mammals, which have moved to the interior with the expansion of the neocortex (see Figure 14). It is part of a group of structures called the "limbic lobe" by Broca, structures that are closely connected to the hypothalamus and contain the amygdaloid body and the septum. Continuing the tradition of Gall, or Fritsch and Hitzig, Papez proposed that the group of neurons that made up the anatomical substrate of the emotions was localized in this limbic system (Figure 37).

Almost at the same time, in 1939, Heinrich Klüver and Paul Bucy performed a striking experiment with a monkey. Removing a large part of the limbic system, as well as part of the nonlimbic cortex, provoked startling changes in behavior. The animal, normally wild and frightened, became placid and calm; it was tame. At the same time it developed curious oral behavior. It put anything it found in its mouth, even food it ordinarily did not like. It also showed exaggerated sexual activity, masturbating incessantly and copulating indiscriminately, even with individuals of the same sex or those of different species. Similar symptoms can be observed in humans, usually associated with a lesion of the amygdala, which, as we have said, is part of the limbic system.

Clearly, the genesis and expression of emotions do not depend on such simple mechanisms as do vital behaviors. The hypothalamus participates, but in conjunction with higher nervous centers like the limbic system. One cannot speak of an emotion center. A whole constellation of groups of neurons, a set of "integration foci," contributes. But each of these neuron groups is connected with the others in a specific way, with a precision comparable to that of the song neurons of the cricket

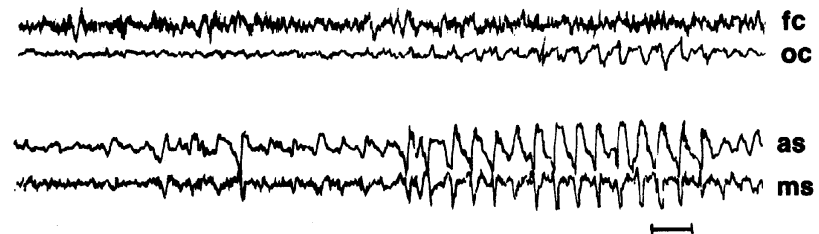
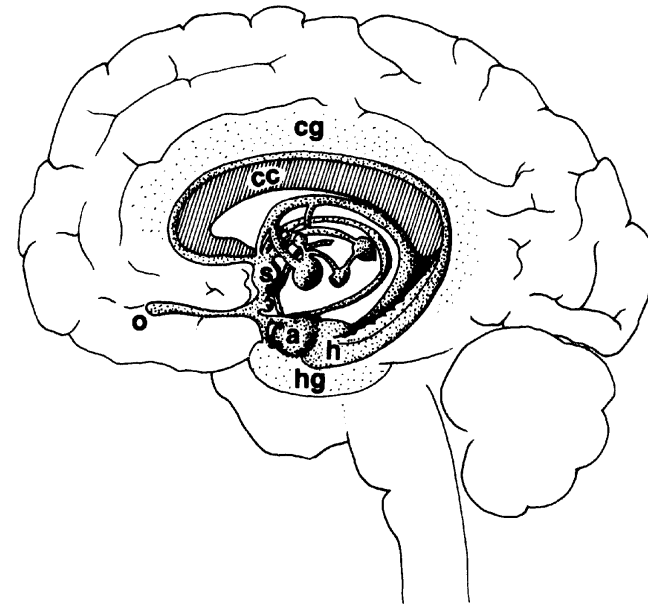


Figure 37. The limbic system. Inherited from primitive mammals, this complex ensemble of nuclei and nerve pathways is closely connected to the hypothalamus, the brainstem, and obviously the neocortex. It is involved in the genesis of emotions and related behavior. This explains the importance given to it by such authors as Paul MacLean and Arthur Koestler. Above, one sees the septum (s), amygdala (a), hippocampus (h), cingulate gyrus (cg), and hippocampal gyrus (hg). Below are EEG recordings from various parts of the brain during orgasm—the fronto-temporal cortex (fc), occipital cortex (oc), left anterior septal area (as), and right median septal area (ms). Slow, high-amplitude waves similar to those recorded during epilepsy appear, principally in the septum. Bar length: 1 second. (From R. G. Heath, 1972.)

or the Mauthner cell of the fish. To take up the comment of Denis Diderot in 1769, the connections of this graph form "a sort of skein of wool where the slightest thread cannot be broken, ruptured, displaced, or missing without serious consequences for the whole."

TO REACH ORGASM

Orgasm is for man, and perhaps even more for woman, the supreme ecstasy. From Saint Theresa of Avila to Simone de Beauvoir, whole libraries have been written about the quest for this intense wave of pleasure and emotion. Nevertheless, we lack precise descriptions of this "ineffable" state and our knowledge of its mechanisms is sketchy. The physiological manifestations such as local muscular contractions, changes in cardiac rhythm and blood flow, tell us little about the sensation of orgasm. They do, however, demonstrate that in woman the sensation precedes the purely physiological response by two to four seconds. In man, orgasm can take place even without ejaculation. Orgasm is then, above all, a cerebral experience and it is at the level of the brain that we must look for it.¹⁴

The few data available on its material nature stem from electrophysiological recordings and stimulation performed, as in many studies related to brain function, on subjects with serious neurological problems that only surgery can relieve. In sixty patients studied by Robert Heath in 1972, electrical stimulation of specific regions of the brainstem, lateral hypothalamus, and septum provoked a sensation of pleasure. Hedonic synapses do exist in humans! Do they intervene at the moment of orgasm? For the moment we have only a few recordings, taken during orgasm in two subjects. Contrary to what we might expect, they show no major change in electrical activity of the cerebral cortex. In one of the subjects, a man, spikes and slow waves of high amplitude, mixed with rapid oscillations in potential, appeared in the limbic system, in the septum, at the moment that he experienced orgasm. In form, these waves resembled those found during an epileptic seizure. They corresponded to the synchronous activity of a large population of neurons (see Chapter 3), and each slow wave was the result of thousands, if not millions, of elementary electrical impulses. Thus a mini-epileptic attack develops temporarily and locally in the septum. In the other subject, a woman, the same rhythmic phenomenon was recorded in the septum, but it spread to the amygdala and thalamic nuclei. But this discharge never invaded the neocortex. It remained limited to the limbic system and adjacent areas.

Our understanding of the chemistry of orgasm has not yet advanced

as spectacularly as that of pain. Nevertheless, an important observation deserves to be reported. In 1972 Heath noted that the injection of acetylcholine in the septum of a female subject provoked an intense sensation of sexual pleasure, culminating in repeated orgasm. Acetylcholine induces orgasm in the septum. Could dopamine, and the pleasure synapses that contain it, be involved? Perhaps, but we have no data. The few additional observations available do not deal with the production of orgasm or its sensations, but with its consequences.

The Hottentots knew that stretching the vagina of a cow brought about the flow of milk. Oxytocin, a hormone released into the blood by the pituitary gland, acts on the mammary gland; once again, the hypothalamus controls this reflex.¹⁵ Curiously, in woman, and also in man, a similar phenomenon takes place during the sexual act. Orgasm brings about a massive discharge of oxytocin. Why? We do not know, but at the same time other peptides are released into the blood and their importance is clearer.

In 1563 the Portuguese physician Garcia d'Orta noted that the use of opium diminished sexual activity and could even cause impotence. The administration of synthetic opiates (such as methadone) or natural peptides diminishes the number of copulations and the percentage of successful mountings in the male hamster. Drugs that block the effects of the opiates, such as naloxone and naltrexone, have the opposite effect. For instance, they provoke "irrelevant" erections in man as well as in the monkey. In addition, after orgasm the blood level of endorphin-type peptides increases markedly—in the hamster by at least four times after five ejaculations.¹⁶ A similar release in the central nervous system probably accounts for the abolition of pain and the contented feeling that follows orgasm and also, quite conceivably, for the usually agreeable changes in one's mood that accompany it.

The release of endogenous morphines may also explain the diminishing of sexual appetite that usually follows orgasm. Could it be that the endorphins set up a feedback with the pleasure synapses of the hypothalamus or the brainstem? The hypothesis is seductive! We know that the hormone LHRH acts on a hypothalamic nucleus to induce copulation in both the male and the female. It has recently been discovered that the opiates block the release of LHRH and therefore inhibit copulation. The endogenous opiates then may serve as regulators of libido. A lack of opiates in the hypothalamus would engender a sensa-

tion of frustration and thus an increase in libido. On the other hand, their release at orgasm would temporarily extinguish sexual desire. Could the level of free endogenous opiates be a measure of what Sigmund Freud called, rather clumsily, "psychic energy"?

The example of orgasm was chosen for several reasons. Certainly this experience occupies an important place in the everyday life of human beings. But that is not our concern. In contrast to the other forms of behavior discussed so far, orgasm is not primarily manifested by an action clearly visible to the outside world; it is essentially a subjective sensation, experienced internally. We have no data to allow a precise, cell-by-cell and synapse-by-synapse description of the diverse electrical impulses and synaptic potentials responsible for it. Recordings from the septum and data on the effects of acetylcholine there nevertheless allow us to conclude that internal experiences like orgasm are similar in nature to behavioral patterns visible to the outside world. The little we do know of the electrical and chemical processes involved supports this conclusion.

Once again, we must not underestimate the importance of the diversity of the neurons involved, even if they constitute only a tiny fraction of all the neurons in the brain. The multiplicity of the chemical mediators strikingly illustrates this point. Acetylcholine, endogenous morphine, and dopamine distinguish some of these neuron groups. The chemical makeup of the cells that participate in a sensation as well defined as that of orgasm is closer to a canvas by Georges Seurat than a composition by Piet Mondrian.

A few years ago the discovery of chemical transmitters led us to believe for a moment that it would be possible to assign a specific chemical label to all forms of behavior or sensation. The example of the chemistry of orgasm shows that things are not so simple. One cannot say that there is one transmitter for singing, pain, or depression. One can simply state that the graph of neurons used in a particular behavior or sensation contains one or several critical links that use a specific neurotransmitter. A chemical "cut" in this link will certainly interfere with the expression of the behavior. But if the same transmitter exists in neurons of another network, there is a good chance that the chemical scalpel will also attack there. Morphine blocks pain messages from the spinal cord but causes impotence through its action on the hypothalamus. Hughlings Jackson's and Head's criticisms of a too narrow view of a "center" also apply to chemical coding. There is no trans-

mitter for anger or pleasure, any more than there is an isolated center for them. So "organization is sufficient for everything? Yes, once again," as La Mettrie wrote—on the condition, of course, that one includes chemistry.

TO ANALYZE

As we saw in Chapter 2, the human brain is characterized by the privileged development of the neocortex. In the course of mammalian evolution, its area and the number of its neurons and synapses increased. On the other hand, lower structures—in particular the limbic system, the hypothalamus, and the brainstem—changed little. A cat deprived of its cerebral cortex at birth can walk, climb, feed itself, and even attack moving objects. In the same way, a baby born with no cortex wakes and sleeps regularly, feeds, sucks its thumb, sits up, yawns, stretches, and cries. It can follow a visual stimulus with its eyes and react to a sound. It pushes away unpleasant objects and is capable of voluntary movements. Thus, automatic behavior and some voluntary actions depend more on structures surrounded by the neocortex than on the cortex itself.

To hope to describe the functions of the cortex in terms similar to those used for the cricket's song or the rat's drinking behavior seems overly optimistic. However, a concrete way of going about it is to follow to the letter J. Z. Young's proposition that the organism is a "representation" of its environment. If this proposition applies to the neocortex, one should be able to discover these anatomical representations by exploring its surface; "reading these signs," if they exist, should help us define its role.

Since the end of the nineteenth century, through David Ferrier and Korbinian Brodmann, and more recently through David Hubel and Torsten Wiesel, we know that the sense organs project to distinct cortical areas after relay in the thalamus (see Figure 6). These areas are situated in the occipital lobe for vision, the temporal lobe for hearing, and the parietal lobe for touch. Each area thus "represents" a physical parameter to which the sense organ is sensitive. A first level of representation of the world in the cortex thus consists of territories distributed like continents, each corresponding to a major category of physical signal, reaching the organism through impulses in the sensory nerves.

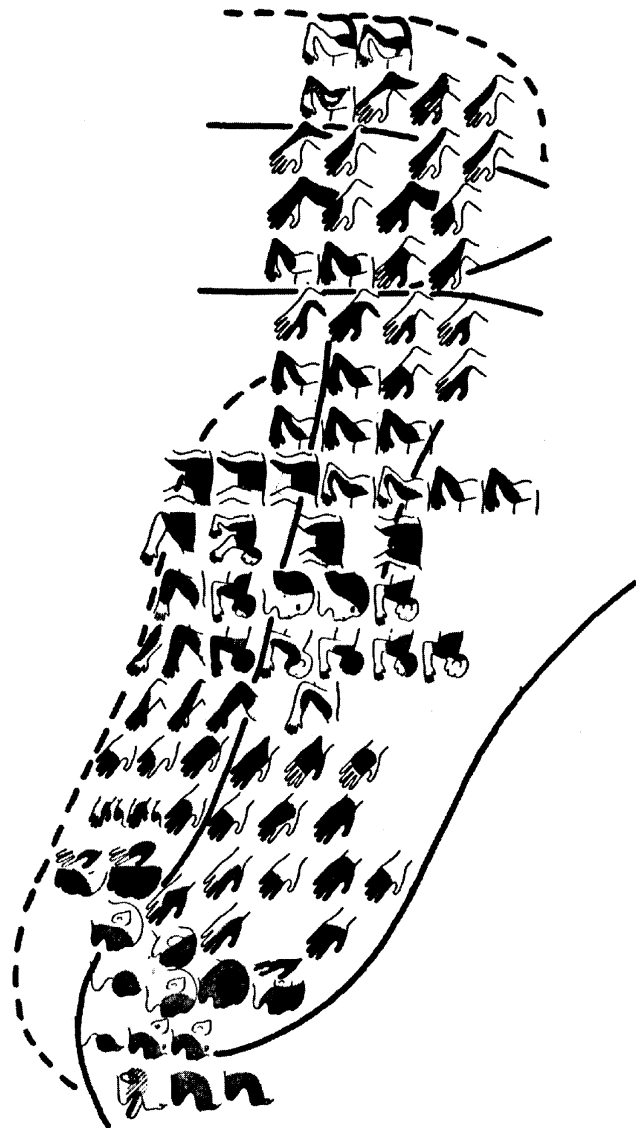


Figure 38. Map of the area involving touch in the macaque. Each little figure indicates a recording point on the surface of the cortex; the body part represented shows where the stimulation caused a response. Thus tactile stimulation of the tail causes a response in the dorsal region (at the top of the map); stimulation of the tongue, a response in the ventral region (at the bottom). (From C. N. Woolsey, 1958.)

Careful mapping of these cortical territories has revealed surprising details. Take the case of touch. The sensory receptors involved are found over the entire body surface and some are situated in deeper tissues. If we stimulate a monkey's thumb, for example, and try to record an evoked electrical response (see Chapter 3) in the cortical territory devoted to touch (areas 1, 2, and 3 of the parietal lobe), the first recordings are likely to be disappointing. When the electrode is randomly placed in this area, the chances are that no evoked response will be seen, however intense the stimulation. Let us, then, move the electrode systematically from one point to another over the cortical territory. Suddenly, an electrical potential appears. A few millimeters further on, the wave disappears. At this new position there is no longer a response from the thumb but from the index finger. Little by little, the map of a hand can be made out. If we pursue our exploration, the whole half of the body opposite the hemisphere being explored will appear. The figurine we are tracing on the surface of the cortex begins to look like a monkey (Figures 38 and 39). Working from the lower part of the hemisphere toward the top, we can recognize, in succession, the tongue, the head, the arm and the hand, the trunk, the leg and foot, and the tail.¹⁷ Obviously, the resemblance is not perfect. First of all, the body occupies three dimensions but the figurine only two. The loss of one dimension distorts the projection. There are also discontinuities between contiguous regions of the body. The face, for example, is separate from the rest of the head. A striking feature is that the relative areas occupied by different body regions seem out of proportion. The hand, for instance, appears gigantic; its surface is almost equal to that of the rest of the body. If we move from the monkey to the rat or mouse, the map is no longer dominated by the hand, but by the snout and particularly the whiskers (see Figures 39A and 57). In man similar maps were drawn in 1950 by Wilder Penfield and Theodore Rasmussen from a large number of observations of patients suffering from epilepsy or discrete cortical lesions. The figurine, or sensory *homunculus*, possesses enormous lips, an immense hand, much smaller feet, and a ridiculously small trunk and sex organs. As in the monkey and the rat, the cortex occupied by the projection of different parts of the human body has little relation to the actual body surface area, but represents the importance of the organs to the sensory life of the individual: the whiskers in the rat, the hand in the monkey, the hand and the mouth in man. It is, in fact, directly proportional to the density

of sensory endpoints on the body surface. It represents an image of the points of contact of the individual with the outside world (see Figures 38 and 39).

The ear and the retina also project on the cortex, but in a way that does not at all resemble the homunculus. In the case of touch receptors, the entire body serves in a way as a sense organ. With vision, the situation is different. One does not see with one's hands or one's lips.

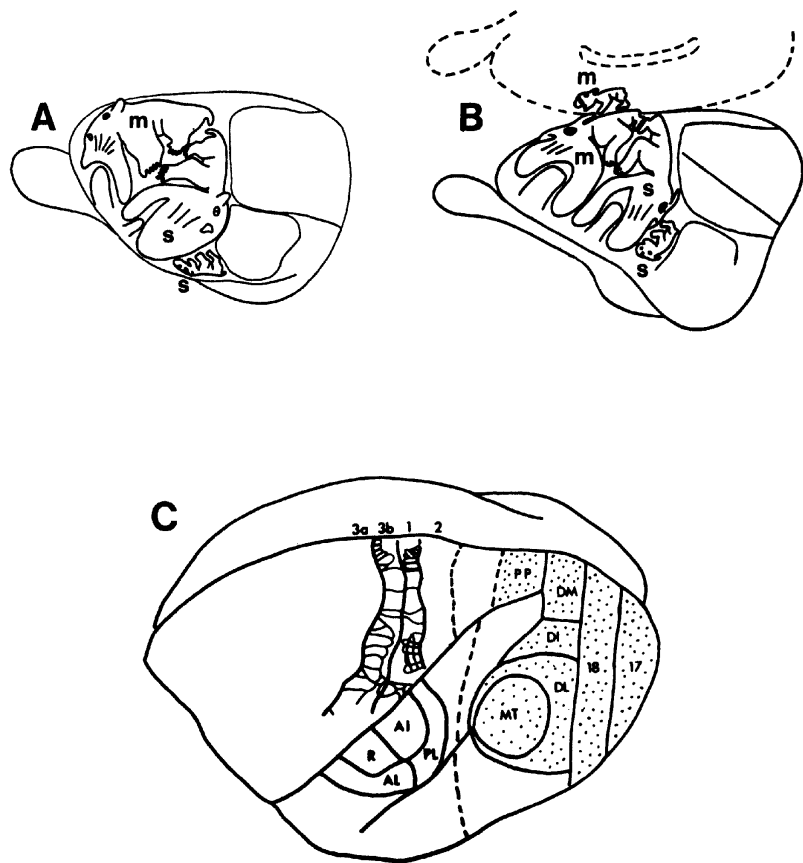


Figure 39. At the top, we see representations of the body in the motor (m) and somatosensory (s) areas of the cortex of the rat (A) and rabbit (B). In the rat the area occupied by the snout, particularly the whiskers, is large, reflecting the importance in its life of sensation from this area. (From C. Woolsey, 1958.) Below (C), we find that in the owl monkey (*Aotus*), the number of sensory representations increases markedly. In the occipital region (dotted), the areas marked 17, 18, DL, DI, DM, PP, and MT each correspond to a map of the retina. (From J. H. Kaas et al., 1979.)

The cortical map reflects the distribution of the retinal neurons that line the fundus of the eye and receive the inverted image of the outside world as transmitted by the lens. The representation of the retina on the primary visual area (area 17) is nevertheless very distorted. It is divided into two so that the relationships between neighboring points are preserved only for each half-retina. The cortical map becomes difficult to read, but the relative simplicity of the division and the almost mathematical regularity of the projection of the retina on the cortex allow us to find our way.

Pursuing similar studies on different mammalian species, Jon Kaas and C. S. Merzenich and their collaborators drew more and more precise maps; they also made some fascinating observations.¹⁸ In the territory concerned with the sense of touch in the monkey, they found that instead of a single figurine there were several, lined up side by side. Each figurine played a distinct role. One responded to certain skin receptors, a second responded to the skin but not to the same receptors, a third received the projection of sensory receptors in muscles, and a fourth responded to deep receptors of another sort. A similar situation is found in the visual system. In the monkey one can find up to eight representations of the retina, all placed closely together in the neighborhood of the primary area (area 17) and occupying the association areas of the cortex. Here again, it is not exactly the same aspects of the visual world that are analyzed in each representation. Certain projection areas are more specialized in recognizing orientation; others are concerned with direction; still others, with the identification of color (see Figure 39).

Is the same multiplicity of cortical representations found in all mammalian species? At least eight visual areas exist in the macaque, whereas in the hedgehog, a primitive insectivore, only two representations of the retina are known. In the same way the ear projects to two distinct areas in the squirrel but to three in the tree shrew (a primitive primate), four in the owl monkey, and six in the rhesus monkey. The number of representations increases as the neocortex increases its surface area. They have not yet been counted in man, but one would expect them to be even more numerous than in the monkey. The increase in number of these representations may coincide with the extraction of more and more varied and complex features from the environment. It is the basis, to recall Pavlov's remarks, of a more and more detailed analysis of the environment.

