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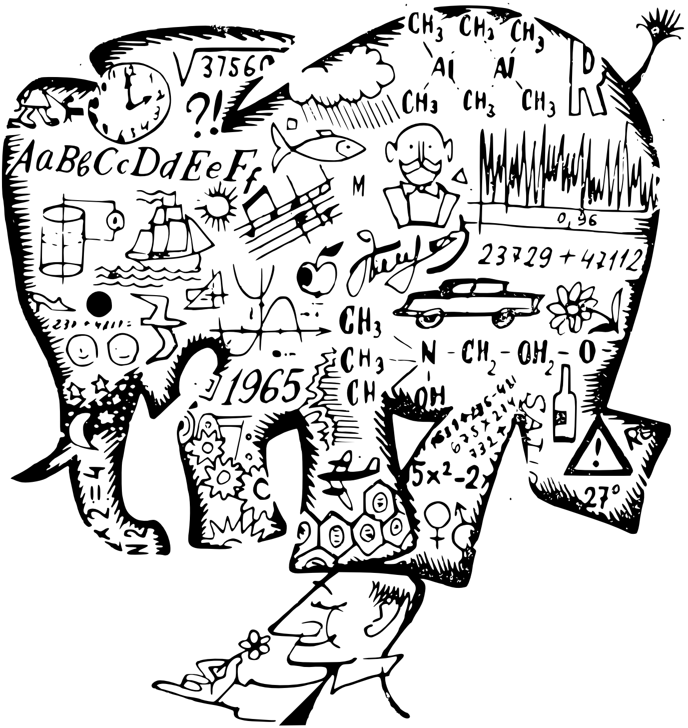

HOW RELIABLE IS THE BRAIN?

MIR PUBLISHERS

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HOW RELIABLE IS THE BRAIN?

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The book deals with topical problems of contemporary neurophysiology related to the restoration of impaired functions of the central nervous system.

The fundamental principles underlying the work of the brain, which enable it to function for many years without interruption, today command the interest of experts not only in medicine and biology, but in automation as well. This is because these principles can be utilized to make computing systems more reliable.

Translated from the Russian by
Boris Belitsky

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1 THE No. 1 PROBLEM

Day and night the mighty turbines of a giant electric station generate power. High-voltage lines transmit the power to consumers: to industrial plants, railways, and communities. The final distributors of the power are substations, and their main installations are power transformers, sometimes the height of a two- or three-storey building.

Unexpected faults may develop in a power system. To assure uninterrupted operation in the event of such an accident, substations have protective relaying systems. Dozens of pick-off elements continuously register apparatus temperature, air and oil pressure, voltage, resistance, power, and current intensity. The signals from these pick-off elements are fed to specially programmed instruments. Any departure from reference inputs at once produces an automatic reaction: part of the consumers are cut off, the reserve is switched in, the transmission is cut out, and audible and light signals make known the breakdown.

The automatic relays are not part of the main power equipment and do not participate in the actual process of power transmission. Yet a

slight fault in a relay or in a measuring circuit can cause a general power failure, despite the fact that the fault in no way affects the fundamental power process. This did, in fact, happen once at a big substation. Late one night its emergency siren started wailing, and factories, mills, and homes were left without power. An examination of the instruments by the staff disclosed that the power failure was due to a faulty relay adjustment.

. . .The middle of the twentieth century witnessed the birth of the high-speed electronic computer, which opened up truly fantastic vistas in automatic control. The reactions of the new self-regulative devices proved to be swifter and more accurate than those of the unaided human brain. These devices too, however, were found to have their "tendon of Achilles": insufficient reliability. Gerda Evans, a specialist in the computer field, recalls: "Never in my life have I been obliged to sleep and breakfast at such impossible hours as during those months when we sat at our computers for twenty-four hours a day, relieving one another at intervals. The 'ENIAC' on which we worked, though faster than any other previous mathematical apparatus, was temperamental and delicate. Some tube or other or some circuit was for ever going wrong. On those occasions we simply had to wait. Once a storm put the mechanism right off balance. We all sat glued to the telephones in our rooms, waiting for the repair crew to report that we could carry on. Several times they called us up to say that we could come over, as everything would be all right in ten minutes. But when we rushed to the spot, it

would turn out to be another false alarm. So it went on for a whole week."

In the ten years or so since then electronic computers have become larger, more complex, and more advanced. To a certain extent their reliability too has improved, although it still does not satisfy engineers. "In an electronic machine," the Soviet scientist A. A. Lyapunov writes, "a fault in even one of the hundreds of thousands of elements or a break in even one of the hundreds of thousands of contacts can put the whole installation out of order." It will be recalled that at the Brussels World Fair the distribution of hotel accommodations was entrusted to a computer. When the machine developed a fault, 50,000 newly-arrived tourists were left without accommodation for the night. . . .

Reliability is a constantly recurring term in present-day technical literature, the "No. 1 problem", as it has been called by A. I. Berg, Member of the U.S.S.R. Academy of Sciences. From the history of various fields of engineering we know of several "barriers" that arose from time to time to obstruct technical progress: the sound barrier, the heat barrier, the safety factor. The problem of reliability—of the probability that performance indices will be preserved over a specified period—is of paramount importance for the pervasive development of automation.

At the same time this important and formidable problem of modern automation and remote control has been solved brilliantly by nature in the brain, which at the human level is proving capable of creating more and more complicated automatic devices. The thousands of millions of

nerve cells—those tiny live "relays"—function for scores of years. Round the clock the internal organs continue their work: the heart beats, the blood circulates, and the lungs are ventilated. Except for the hours of sleep, the brain, in addition to regulating the functions of the internal organs, is also directing the "external" activities of the organism: the acquisition of individual experience, adaptation to environment, and—in man's case—the refashioning of the environment to suit his needs. Environmental conditions change continuously: darkness is followed by bright sunlight; frost, by scorching heat. Periods of relative tranquillity are followed by emergencies in which the organism strains all its resources. But the brain functions without interruption.

The organism and its "control panel", the central nervous system, are exposed to dozens of harmful, destructive influences. Mechanical, thermal, biological, and radiation effects injure eyes and limbs (receptor and effector organs) and damage nerve channels. Not infrequently the central nervous system itself is impaired: injuries, haemorrhages, and infectious processes destroy certain sections of the brain. But even in these emergency situations the brain continues to assure the vital functions of the organism and, after a certain period of time, the impaired functions are completely or partially restored.

Even the most imaginative mind cannot fail to be amazed by the compensatory capabilities of the central nervous system and, especially, its higher parts. A woman by the name of Olga Skorokhodova, blind and deaf since early childhood, has become an eminent educator. The writer Ni-

kolai Ostrovsky, confined to his bed by mortal illness, created remarkable works of literature. A pilot with both feet amputated, Alexei Maresyev, returned to his fighter plane and shot down many more Nazi planes.

Yet next door, in the world of man's mechanical helpmates, a failure in a single part of secondary importance reduces to naught the work of extremely complicated installations.

It is this striking contrast that suggests considering the specific ways and means by which nature has solved "the No. 1 problem". Quite obviously, the mechanisms that make living regulating systems reliable cannot be borrowed directly by modern engineering. The qualitative distinctions of living matter—and, foremost among them, the continuous self-renewal of its chemical composition—have placed their mark on all the manifestations of vital activity, including the laws that govern the functioning of the nerve cells. That is why our interest must be not so much in the specific elements of the structure and activities of the central nervous system as in the fundamental principles of biological protection from harmful influences, in the principles of the dynamic readjustment of damaged systems, and in the basic laws governing the compensation of impaired functions.

The problem of restoring impaired functions of the central nervous system—the supreme regulator of the living organism's activities—has for many years commanded the attention of our laboratory, now part of the Institute of Higher Nervous Activity and Neurophysiology of the Academy of Sciences of the U.S.S.R. In our ex-

position of the subject we shall, naturally, draw primarily upon the results of our own research over a period of thirty years. A popular survey of everything accomplished in the field of brain function compensation is not our object, although we shall, of course, refer to the work of many other investigators and research groups.

It is difficult to say, at the start of this survey, what exactly will prove useful to the designer, the innovator, and the engineer. Compensation phenomena will be described as they appear to the physiologist. It is for the reader to determine what can be utilized in kindred areas of science.

The writers have deliberately rejected any interpretation of biological phenomena in mathematical and engineering terms; nor will they make extensive use of terms borrowed from cybernetics or draw tempting parallels. This has been rejected for two reasons. The first is that all too often lately there have been attempts to fill in the gaps in definite knowledge about the functioning of the brain with cybernetic phraseology, which leads the reader to confuse hypothetic conjectures with what is really known to science about the central nervous system. The second reason is that as important as mathematics is to biological research and as important as it is to subject biological phenomena to mathematical analysis, mathematics is by no means the only form of theoretical thinking for the physiologist. Our science has a system of theoretical concepts of its own that can so far be translated into mathematical terms only partly.

In the belief that little will be accomplished by superficial digressions into cybernetics, the writers have confined themselves strictly to the field in which they are working, neurophysiology; it is their hope that the popular form of exposition will make their essays useful to workers in other fields of learning.

2

THE CENTRAL "CONTROL PANEL" OF THE ORGANISM

In order to survive in a changing environment, a living organism must continually readjust its activities. For example, a drop in the external temperature calls for more intense heat generation and, at the same time, for less heat emission. Painful stimuli produce a reaction designed to avoid or remove such stimuli. The absence of food compels an animal to seek the nutrients it requires. Any one of these forms of activity involves various organs and systems. Some organs are known to exhibit a relatively automatic response and are able to function in complete isolation (the contraction of an isolated heart supplied with a blood substitute, alimentary canal peristalsis, etc.). Chemical substances—the hormones secreted into the blood by special glands—have a definite bearing upon the coordinated functioning of the internal organs. But the decisive and definitive role in the reactions of the organism to environmental changes is played by the central nervous system, whose supreme regulative functions are concentrated in the brain.

By the end of the nineteenth century physiology had built up quite an extensive fund of diverse information about the structure and func-

tions of the brain, as well as about its influence upon movement, thermoregulation, respiration, blood circulation, and digestion. But complete mystery continued to shroud the aspect of brain activity that forms the basis of the complex behaviour of the higher animals and man, the basis of their psychic activity. It was left to the great Russian physiologist Ivan Pavlov to reveal the mechanism of this activity by his historic experimental confirmation of Sechenov's brilliant idea concerning the reflex nature of the brain's psychic functions.

The history of science shows that the key to establishing a harmonious system of notions about certain natural or social regularities is often the discovery of the elementary "cell", the structural unit of the most complex phenomena. In this way Karl Marx began his analysis of the laws governing capitalist society by examining the simplest case of commodity-money relations. Or another appropriate example: Dmitry Mendeleyev chose the mounting atomic weights of the chemical elements as the underlying principle of his Periodic System, which covers the vast diversity of the substances that make up the Earth and neighbouring planets. Fundamental to contemporary thinking about the work of the brain is Pavlov's principle of conditioned reflex connections, of the conditioned reflex as something in the nature of a functional unit, the principal and most characteristic type of brain activity, the ultimate basis of higher nervous activity and of almost the entire behaviour of a highly-developed organism. "The central physiological phenomenon in the normal work of the cerebral hem-

ispheres," Pavlov wrote, "is that which we have termed the *conditioned reflex*. This is a temporary nervous connection between numberless agents in the animal's external environment, which are received by the receptors of the given animal, and the definite activities of the organism." [1]

In Pavlov's view, the principal fund, the physiological basis of adaptive activity in the higher animals and man consists of the inborn unconditioned reflexes. Salivation when food enters the mouth, the vigorous withdrawal of a paw in response to painful stimuli, and an increased heart rate during intense muscular activity are examples of unconditioned reflexes. In accordance with their biological significance, Pavlov divided these reflexes into several main groups, such as defensive, food, sexual, and orientating-exploratory reflexes. An inborn unconditioned component plays an important part in such instinctive animal activity as the nesting and seasonal migration of birds or the dam-building of beavers. It is unconditioned reflexes associated with the organism's vital needs that provide the initial impetus to the complex adaptive activity aimed at satisfying these needs and supporting the existence of the individual organism and the species in animals and man.

Unconditioned reflexes are produced by comparatively few stimuli, associated directly with this or that requirement of a living being (food, pain, tactile stimulation of the skin, etc.). This

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[1] I. P. Pavlov, *Psychopathology and Psychiatry*, Foreign Languages Publishing House, Moscow, p. 283.

is illustrated clearly by the case of an animal whose unconditioned reflexes are the only form of adaptation to its environment, as the dog whose cerebral cortex has been extirpated. Such a dog is capable of satisfying its hunger only if the food is put into its mouth. It recoils from an injurious influence only if there is a painful stimulation of the skin, and it does not react at all to the sight of a person threatering it with a stick. Quite understandably, an animal possessing unconditioned reflexes only can scarcely survive in natural conditions.

The conditioned reflexes acquired by animals and man in the process of their individual existence extend their powers of adaptation infinitely. Conditioned reflexes enable the brain to make use of remote signalling about effects of direct importance to the organism. In this way even the most distant signs of danger (a beast's odour, the sounds it emits, or its barely noticeable movements) produce a defensive reaction in an animal, which in response to these signs either flees or prepares for a struggle. When a stimulus registered by the sense organs coincides with the action of factors producing an unconditioned reaction (food, pain, etc.), this can turn the stimulus into a conditioned signal that may subsequently by itself produce an advance reaction of the organism.

The specific manifestations of conditioned reflex activity are extremely diverse. We draw particular attention to this fact because some investigators still tend to treat the conditioned reflex as a relatively elementary form of brain activity. In the opinion of N. A. Bernstein, for

instance, the volitional movements of the higher animals and man are not conditioned reflexes because there may be no external signal for them. And I. S. Beritov takes the view that, besides acts of behaviour of the type of conditioned and unconditioned reflexes, animal behaviour may also follow another pattern, governed by images of objects in the world around them.

In connection with statements of this kind, it seems appropriate to recall that mechanistic notions about the organism as an absolutely passive object of environmental influences were always alien to Pavlov. Indeed, he pointed out repeatedly that a living organism was a complex system, which in the process of evolution had acquired the ability to maintain its physico-chemical composition and survive individually and as a species. By virtue of its very origin, a living organism is always active, for it responds to environmental influences according to their biological effect (beneficial or baneful). In man this activity acquires a new quality, since collective work and articulate speech create the conditions for transforming the environment instead of mere adaptation to it, as is observed in the case of animals.

The term "conditioned reflex" implies nerve connections that did not exist in the brain from birth, but arose under the influence of the environment and persist in the central nervous system. At the same time the specific forms of conditioned connections can be quite different. There can be a direct connection of the signal and the reaction, or else a connection of those indifferent stimuli (association) that are only

later used by the organism in its adaptive activity, or else most complicated chain reflexes, or else the formation of systematized groups of reactions (dynamic stereotype), or else the switching of conditioned signals that have different meanings in different situations, and so on to special generalized speech signals in the case of human beings. The conditioned reflex in the Pavlovian sense is not a particular case, not one of the many faculties of the brain, but a universal principle, a functional "building brick" in the giant edifice of the higher nervous activity of animals and man.

For half a century the Pavlovian school have used the phenomenon of the conditioned reflex for the establishment and comprehensive study of the laws of higher nervous activity, moreover not only of normal activity, but also of some pathological forms. This has made it possible to establish and subject to a very detailed study the laws, or rules, governing the formation of a conditioned reflex, the irradiation and concentration of the processes of excitation and inhibition in the cortex, cortical analytical and synthesizing activity, mutually inductive relationships, etc. This trend, it should be noted, was the principal one in Pavlov's classic studies of the physiology of the cerebrum. It remains the principal trend to this day in the work of his followers, who for this purpose use as a test not only the classic salivation reflex, but a wide range of other simple and complex responses, produced in experiments with or without restriction of the freedom of the experimental animals to move.

But the experimental usefulness of the con-

ditioned reflex in its natural ultimate expression, i.e., in the form of the activity of certain effector organs, is by no means confined to establishing and studying the regularities of higher nervous activity, as is believed by some researchers abroad and in the Soviet Union. Pavlov and his pupils obtained extensive evidence that by means of the conditioned reflex as a functional indicator it is possible to carry out highly delicate investigations of structural and functional principles underlying individual forms of this activity and their mechanism. Indeed, it is sufficient to cite as an example the establishment of the facts providing the basis for the theoretical principles concerning the dynamic localization of functions in the cortex, the cortical representation of unconditioned reflexes, the functional mosaic of cortical structures, or the cortical irradiation and concentration of nervous processes. Needless to say, the possibilities of using conditioned reflexes for these purposes have in no way been exhausted, and, in fact, some Soviet scientists are employing them successfully today to establish and study the structural and functional principles of various forms of cortical inhibition, induction relationships, the summation of nervous processes, etc.

It should not be concluded from this that the above aspects of brain functions can be studied only by using as an indicator the conditioned reflex in its classic form. This is by no means so. A trail-blazer in science, Pavlov believed that other, novel, and more refined techniques would yield even more in studying the mechanism of various phenomena in the activities of the brain

and other organs, as well as in establishing the delicate structural, functional, and physico-chemical principles of these phenomena. Such techniques, he felt, would in due course either be developed by the physiologists themselves or would be borrowed by them from the physicists, chemists, mathematicians, etc. For one thing he prophetically predicted that the day was close at hand when it would be possible to extend the mighty power of the physiological experiment to the living cell, including the living nerve cell. That day has indeed come. Present-day powerful electron microscopes have revealed structural details in nerve cells that nothing was known about before. Major advances in biochemistry and physical chemistry have helped to throw light on many aspects of the functional biochemistry of the nerve cell and on the dynamics of the intimate fermentation and physico-chemical processes that take place in it. All this is now being probed with success.

What is more, for over ten years now the nerve cell has been a direct object of physiological experiments. This is true not only of the nerve cell of the spinal cord and the medulla oblongata, the cerebellum and the midbrain, but also of the nerve cell of the cerebral cortex.

The advances in neurophysiology in the past few years are intimately connected with the extensive application of electronic instruments, which have made it possible to register the electric activity of various formations of the brain and the spinal cord, down to the activity of individual cellular elements. This refinement in physiological research has been made possible by the

use of so-called microelectrodes, extremely thin metal filaments or glass capillaries filled with a salt solution, which are brought into contact with the object of the investigation. The state and activity of the nerve cells are expressed in terms of the electric potentials they generate. These potentials are detected by microelectrodes (a fraction of a micron in diameter) that are either inserted into the cells or brought into contact with them. Suitable physical instruments amplify the potentials hundreds of thousands of times over and record them automatically, after which they can be subjected to objective and accurate scientific analysis and assessment. Considerable headway has already been made in studying the functions of the nervous system by electrophysiological methods, and there is every reason to expect even more notable results in the near future. Indeed, it will probably be no exaggeration to say that this achievement has been just about as important to the physiology of the nervous system as techniques for the study of the atomic nucleus have been to physics.

To give a fuller picture of modern physiological experiments involving electrophysiological techniques, we should mention that electrodes of different diameters are used by physiologists not only to probe and record the electric activity of various nerve structures, but also, if need be, to stimulate those structures with an electric current. In most cases certain electrodes are used to stimulate nerve cells; others, to measure potentials. But sometimes the same electrodes are used alternately to stimulate structures and to measure their potentials.

The efficient use of electrophysiological techniques in studying various problems of the physiology of higher nervous activity requires that a small surgical operation be performed first. This has as its purpose the careful "grafting" of various contact and immersion electrodes in diverse points of the surface of the cerebral cortex or deep-seated subcortical formations. A considerable number of electrodes are grafted in this way; sometimes dozens may be applied to the same animal. To prevent them from moving after the operation, they are fastened to cranial bone. Highly complex physiological experiments may thus be carried out, since the animals enjoy a relative freedom of movement and there are practically no departures from the normal state of their health.

The advanced and refined electrophysiological techniques of the present day have in this way furnished physiologists with new effective methods of studying the various organs and systems of the organism; above all and most successfully, the functions of the nervous system and the sense organs. In investigations of the functions of the higher areas of the central nervous system these methods are supplementary to the principal one, the classic Pavlovian conditioning method. They have, however, the advantage that they make it possible to study not only the ultimate manifestation of conditioned and unconditioned responses, but also the intermediate nervous processes that take place in various links of the central nervous apparatus of these reflexes; these are, moreover, studied directly. Hence, the extensive use of electrophysiological tech-

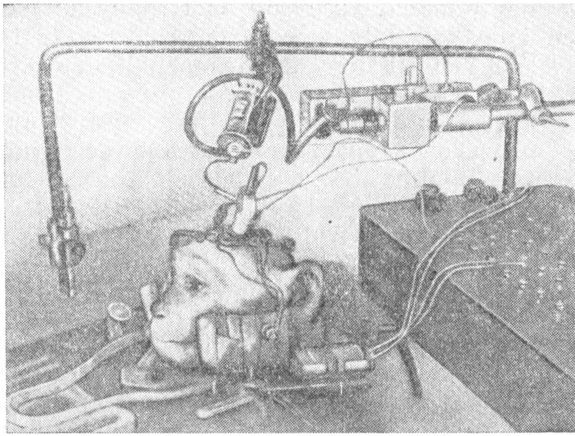

Fig. 1. A monkey with electrodes introduced into the brain (H. H. Jasper)

niques (separately or in combination with classic methods) by scientists in the Soviet Union and other countries in investigating various problems of the physiology of higher nervous activity and, especially, the most topical, cardinal problems: the structural and functional principles of the conditioned connection and the structural and functional principles of various forms of cortical inhibition.

Pavlov considered the formation of a conditioned reflex to be a process of the establishment of a chronic nervous connection between two points in the brain, excited by the coupled action of corresponding stimuli one or several times. This is the conditioned connection, a stable nerv-

ous phenomenon, a product of a higher nervous synthesis, with qualitatively specific features distinguishing this connection from the related, more elementary, distinctly temporary, fleeting phenomena in the activity of the nervous system, phenomena known as the development of pathways, facilitation, the summation reflex, dominance, etc. "While the summation reflex represents a momentary, transient phenomenon," Pavlov wrote, "the conditioned reflex is a chronic phenomenon, gradually becoming stronger under the above-mentioned condition; it is a characteristic cortical process." [1]

The conditioned connection arising between the light and food centres of the brain as a result of the combined action of these stimuli on the organism is shown schematically in Fig. 2. Light can now produce a food reaction, i.e., a food conditioned reflex, for the very reason that the excitation that has arisen in the brain centre of the light signal is conducted via the newly-formed conditioned connection to the food centre of the brain and excites it. It goes without saying that, like any scheme, this is only a simplified picture of a phenomenon that is in reality highly complex, but it does give some idea of the newly-formed nervous connection that forms the basis of a qualitatively new type and higher class of reflexes, the conditioned reflex, which is the focal phenomenon in the whole area of higher nervous activity.

The most topical problems of higher nervous

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[1] I. P. Pavlov, *Psychopathology and Psychiatry,* Foreign Languages Publishing House, Moscow, p. 257.

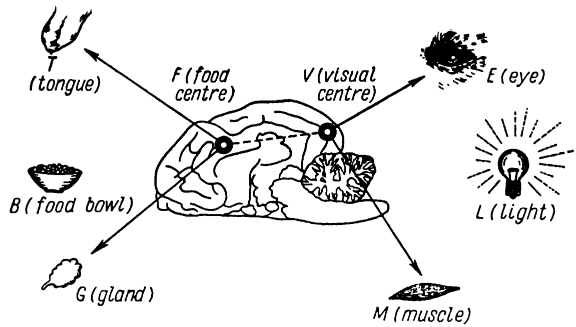

Fig. 2. Conditioned food reflex to light

EVM—arc of unconditioned orientating motor reflex to flashing of lamp (**L**); **TFG**—arc of unconditioned food salivation reflex to food in bowl (**B**); **VF**—conditioned reflex connection between light and food reaction, coupled in cerebral cortex

activity, which have commanded the close attention of investigators ever since the theory of conditioned reflex activity first arose, include the problems of which area or organ of the central nervous system is the organ of conditioned reflex activity and what the architecture of the conditioned reflex is, what functional features of the nerve cells are at the root of the formation of the conditioned reflex, and what delicate structural changes in the body of the nerve cells and in their processes constitute the material channel of the conditioned connection.

Pavlov's views on these problems are well known. He held that it was the cerebral hemispheres that were the organ of conditioned reflex activity in the higher organisms. With respect to the first of the problems listed above, he suggest-

ed in the latter years of his work that the conditioned connection linked different points of the cerebral cortex, points in the cortex representing inborn reflexes. Pavlov did not consider it established that subcortical nerve formations could effect a true conditioned connection, although he did not deny such a possibility. "It is not impossible," Pavlov wrote, "that sometimes, under certain special conditions, conditioned reflexes are formed extra-cerebrally, in other parts of the brain." [1]

Whereas in Pavlov's view the coupling function of the brain in the higher animals and man is vested in the cerebral cortex, some contemporary scientists are of the opinion that conditioned reflexes may be formed in all sections of the central nervous system, including the spinal cord.

The American physiologists P. S. Shurragger, E. A. Culler, W. N. Kellogg, and others interpret their findings as evidence that the spinal cord of the higher animals, isolated from the higher centres of the central nervous system by complete transection, can develop a conditioned reflex. In their experiments with dogs operated upon in this way they for several hours paired the repeated (up to 1,000 times and more) stimulation of the tail by a weak electric current with the stimulation of a rear foot by a strong current. It was found that after such training the shock to the tail begins to produce a contraction of the muscles of the leg. Although the phenomenon was unstable, persisting for no more than

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[1] I. P. Pavlov, *Complete Works,* 1949, Vol. 3, p. 169 (in Russian).

ten minutes following the termination of the paired shocks, and differed fundamentally from a true conditioned reflex, the American investigators deemed it possible to call it a spinal conditioned reflex.

T. N. Nesmeyanova and N. M. Shamarina at our institute repeated the experiments of the American physiologists and subjected the results to a careful analysis. They demonstrated that the paired shocks to the tail and the foot were by no means essential for producing so-called spinal conditioning: the repeated stimulation of the tail alone could cause the flexing of the hind leg muscles. The phenomenon described by the Americans thus lacks one of the most important characteristics of the conditioned reflex connection: the need for the excited state of at least two nerve centres to coincide in time. What kind of reflex activity of the spinal cord are we, then, faced with in these experiments?

A detailed analysis of this atypical phenomenon, misnamed spinal conditioning, has shown that it is closely related to the phenomenon described long ago by the Russian physiologist N. Y. Vvedensky and named by him hysteriosis. The phenomenon appears to be based on the following mechanism. The repeated stimulation of the receptor area of some reflex (regardless of whether this is or is not paired with the stimulation of the receptor area of another reflex) produces a quite stable rise in the excitability of corresponding nerve structures, followed by the gradual enlargement of the zone of increased excitability. Owing to this, the excitation impulses arising in the central nervous elements of the

activated reflex spread easily to other central nervous elements and thereby give rise to the atypical reaction.

From this standpoint it is possible to offer a satisfactory explanation of another fundamental feature distinguishing the atypical reactions described above from a conditioned reflex. Whereas the conditioned reflex is at first generalized and then gradually becomes more precise and concentrated, atypical reactions are at first localized and then gradually become more and more generalized, which is reflected in the fact that the stimulation of some section of the skin produces several atypical reflexes instead of one. The area of increased excitability may be assumed to increase gradually, with the rise in the number of stimulations, so that it embraces the structures of ever new reflex reactions. A more or less significant increase in the excitability of nerve structures as a result of their systematic activation or activity is a feature common to all sections of the nervous system. Unquestionably, increased excitability, along with other phenomena common to the nervous system, such as the development of pathways, the summation reflex, and dominance, plays an important role in forming the conditioned connection wherever these phenomena take place in the higher areas of the central nervous system, areas whose cells possess the specific faculties of developing and registering patterns. As for the metaphysically-inclined physiologists mentioned above, they have quite mechanically drawn an equal sign between elementary nervous phenomena in the spinal cord and the conditioned reflex.

The above-mentioned hypothesis of spinal conditioned reflexes has a very limited following in contemporary neurophysiology.

Far more widespread are views about coupling functions vested in lower areas of the brain. What is more, it has been suggested in recent years that certain parts of the brain located below the cerebral cortex play the principal and final role in conditioned reflex activity, while the cortex plays the secondary role of an "intermediate station" along the route of the nervous impulses. Such views appeared following the discovery of the so-called reticular formation of the brain (see Fig. 18).

The structure of the reticular formation is not altogether typical of the greater part of the central nervous system and was described by histologists as far back as the end of the past century. The name was applied by them to diffuse masses of cells of all types and sizes, divided by nerve fibres running in all directions and forming something like a nerve network. In the area of the brain stem (a term embracing the medulla, pons Varolii, and midbrain) and the interbrain the masses of reticular cells are situated between thick bundles of ascending and descending nerve tracts and anatomically more or less clearly defined nerve nuclei and nucleoles. They thus fill the gaps between these specific formations of the central nervous system, imparting a somewhat irregular laminated structure to the above-mentioned parts of the brain. Many aspects of the macro- and micro-structure of the reticular formation are insufficiently clear, and morphologists of the nervous system are at pres-

ent engaged in heated discussions about defining and characterizing the reticular formation more exactly in ana'omo-histological terms and referring various central nervous formations to it. As to its functions, nothing at all definite about them was known until recently. It was only fifteen or twenty years ago, thanks to the above-mentioned latest achievements of electrophysiology, which made it possible to study the deep-seated formations of the brain experimentally, that the functions of the reticular formation likewise became the object of systematic experimental research. During this comparatively short period of time physiologists in many countries have succeeded in accumulating a wealth of diverse factual data confirming the exceptionally important role of this formation in the activities of the entire central nervous system and receptors.

The work of Magoun, Moruzzi, Jasper, Bremer, Fessard, Gastaut, Dell, Amassian, Hernandez-Peon, Granit, Lindsley, and many others has established that the reticular formation exerts a great influence on the functional condition and activities of all sections of the central nervous system without exception, from the spinal cord to the cerebral cortex, as well as on the functional condition and activities of nearly all the sense organs. This was established by experiments of high precision, involving the direct electrical or chemical stimulation of structures of this formation and their reflex excitation or, on the contrary, destruction. The changes in the condition and activities of various areas of the brain and the receptors are determined by recording either

their electric activity or reflex reactions (in their natural manifestation) involving them.

As for the character of the influence itself, the experiments revealed that it is not necessarily the same. The data accumulated for the present justify the conclusion that the influence of the bulk of the reticular formation boils down to improving the condition and stimulating the activity of the above-mentioned central formations and receptors, to activating or, to use the customary term, to energizing them. On the other hand, the small domains of the reticular formation situated primarily in the medulla and midbrain exert a basically opposite influence, i.e., inhibitory. In the light of these data many physiologists have advanced new explanations of the mechanism of such phenomena as attention, alerting, sleep, consciousness, emotional states, etc.

All the data concerning a powerful and versatile invigorating and activating influence of the reticular formation upon the state of various receptors and areas of the central nervous system, including the cerebral hemispheres, far from conflicting with Pavlov's ideas and the basic principles of his teachings, are in complete harmony with them, and this applies even to the clearly exaggerated estimates, by many investigators, of the strength and significance of this influence. The great physiologist attached exceptional significance to the role of the subcortical (i.e., lying below the cerebral cortex) nerve formations in the activity of the brain as a whole, attributing to them, specifically, the role of something in the nature of a source of energy for the cortex,

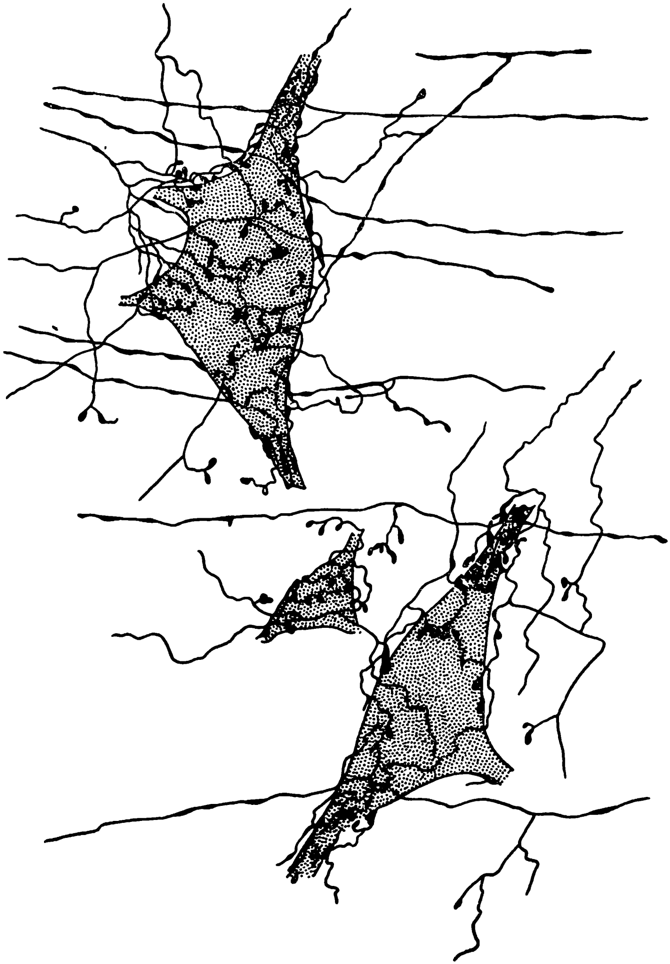

Fig. 3. Nerve cells of reticular formation under the microscope

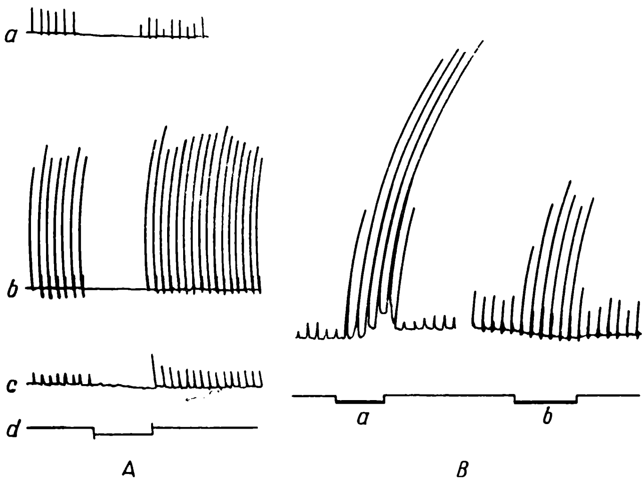

Fig. 4. Influence of reticular formation on the activity of various brain centres

A—inhibition of flexor (a), patellar (b), and nictational (c) reflexes upon excitation of the inhibiting part of the reticular formation; d—excitation mark; B—enhanced motor reactions of the cortex (a) and of patellar reflex (b) upon excitation of the stimulating part of the reticular formation (Magoun)

maintaining the tonicity and capacity to work of its cells at the proper level and charging them with vim and vigour. Nor do the new findings about the functions of the reticular formation conflict with Pavlov's ideas about the close interaction between the cortex and the subcortical formations, and about the leading role of the cortex in that interaction.

The fact is that Magoun, Moruzzi, Jasper, Bremer, Hernandez-Peon, French, Segundo, and

others established definitely that the reticular formation itself is constantly under the strong influence not only of various receptors, but also of some of the central formations, such as the cerebellum and the cerebral cortex. It has been demonstrated, for instance, that by stimulating certain regions of the cortex or the cerebellum it is possible to alter the pattern of the electrical activity of the reticular formation. Noteworthy too is the fact that it has proved possible, in experimental conditions, to show that the cortex can cause excitation of the reticular formation, while the latter, when activated, can in turn influence the cortex. Accordingly, there is something like a cycle of interaction between the cortex and the reticular formation, a phenomenon that is rather widespread in the activity of the central nervous system.

The rapid accumulation of experimental findings concerning the functions of the reticular formation and its role in the central nervous system posed the question quite soon of the relation of the reticular formation to the most complex and important activity of the brain: the process of coupling and of effecting conditioned reflexes. Relevant data were obtained for the most part in experiments in which the process of the formation of conditioned reflexes was accompanied by the direct registration of the electric activity of the cortex and the reticular formation of the brain stem (Yoshii, Gastaut, Fessard, Magoun, Morrell, and others). In these experiments it was established that the development of a conditioned reflex produces changes in the electric activity of both the cortex and the reticular

formation, the latter changes, according to some investigators, occurring earlier and being the more significant and long-lived. These and certain other, earlier established and less important data lent support to the theoretical postulate that the conditioned connection is coupled in the reticular formation and other subcortical formations rather than in the cortex (Gastaut, Fessard, and others); it is only in a subsequent subcortical formation that this connection is projected, as it were, into the cortex ready-made.

Since it is not possible to give detailed consideration here to the facts and interpretations mentioned briefly above concerning the role of the reticular formation in conditioned reflex activity, we shall have to confine ourselves to a few cursory remarks.

There is no denying the importance of the general invigorating influence of the reticular formation on the state of the cortex and, hence, on the process of the formation of conditioned reflexes in it. As for the contention of some scientists that the formation of conditioned reflexes takes place primarily in the reticular formation, while the cortex is but something like a "dependent" of it, this is directly at variance with many definite facts that are common knowledge. These facts were obtained in Pavlov's laboratories, but even apart from that the above contentions are refuted very clearly by the new experiments of Magoun, Morrell, Trofimov, Kogan, and others. The American scientists Magoun and Morrell, unlike Gastaut, Fessard, and Yoshii, have demonstrated that the changes in the electric activity

of the reticular formation during conditioning are far less pronounced and stable than the changes in the electric activity of the cortex, the former disappearing soon after conditioning, whereas the latter persevere. Similar results have been obtained by L. G. Trofimov and co-workers, while A. B. Kogan has established by electrophysiological methods that a patch of the cortex separated completely from the reticular formation is capable of developing and effecting conditioned reflexes, let alone interacting with other parts of the cortex.

To summarize what has been said here about the relation of the reticular formation to conditioned reflex activity, it should be noted that by its invigorating and activating influence on the cortex, a primarily trophic influence that supports the vigour and activity of the cortical structures, the reticular formation does indeed play an indirect, but highly important part in conditioned reflex activity. It is not impossible that the reticular formation, like certain other subcortical nerve formations, is indeed capable of forming primitive conditioned reflexes, which play some sort of secondary role in the conditioned reflex activity of the brain as a whole. But reliable new electrophysiological findings, in complete agreement with the wealth of data obtained by the classic conditioned reflex methods, support the major principle of Pavlov's teaching, namely that the cortex in the higher organisms is the principal organ of conditioned reflex activity, the organ that develops the most highly perfected and complicated conditioned reflexes, which make possible delicate and exact adapta-

tion to the environment, to the changing conditions of life.

It may safely be said that two problems loom largest among the host of problems relating to the study of higher nervous activity in animals and man. These are the problems concerning the mechanism of the coupling of the conditioned connection and its internal inhibition. It is the solution of these problems that will mean a decisive advance in our understanding of the work of the brain. Little wonder therefore that these problems command the most interest among the neurophysiologists of the world.

We know that one sure way of gaining an insight into a complicated biological phenomenon is by studying its history. That is why it is so important to trace the evolution of those adaptive mechanisms that, at the level of the higher animals and man, take the form of the coupling of the conditioned reflex connection. Pavlov considered that the living organism adapts itself to its environment by means of inborn connections with environmental factors and connections developing during the existence of the individual organism. The rudimentary ability of pre-nervous individual adaptation inherent in primitive forms of life attains a high level of development in the nerve cells that appeared in the process of evolution, cells that are the principal vehicles of the adaptive ability in more complicated animal organisms. From this moment on individual adaptation to changing surroundings is achieved by reactions similar to the conditioned reflex, and these subsequently acquire the character of conditioned reflex activity. "Individual adaptation,"

Pavlov wrote, "exists throughout the animal world. This is the conditioned reflex." [1]

Physiology today has at its command a great mass of exact data making it abundantly clear that in the process of the evolution of the nervous system, as its structure became more and more differentiated and its functions specialized, the ability to effect the coupling of conditioned reflex connections has developed unequally in different areas of the central nervous system. It has degenerated gradually in the ancient, i.e., in the lower and middle, centres, disappearing in them completely at the level of the higher animals and man, whereas, on the other hand, in the young, i.e., the higher, centres it has been making most rapid progress, attaining its greatest creative potency in them in the higher animals and man. What is the general biological property of living matter that forms the basis of the acquisition of individual experience by living beings and serves as the foundation of conditioning, attaining a high level of development in the nerve cells produced in the process of evolution? Unfortunately, this fundamental problem has been studied very inadequately not only with respect to the long chain of the evolution of living matter, but even with respect to the last links of that chain: the nerve cells of the higher centres of the central nervous system.

Pavlov believed that the extraordinary reactivity and ability to impress inherent in the nerve elements of the cerebral hemispheres was the

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[1] I. P. Pavlov, *Complete Works*, 1949, Vol. 3, p. 450 (in Russian).

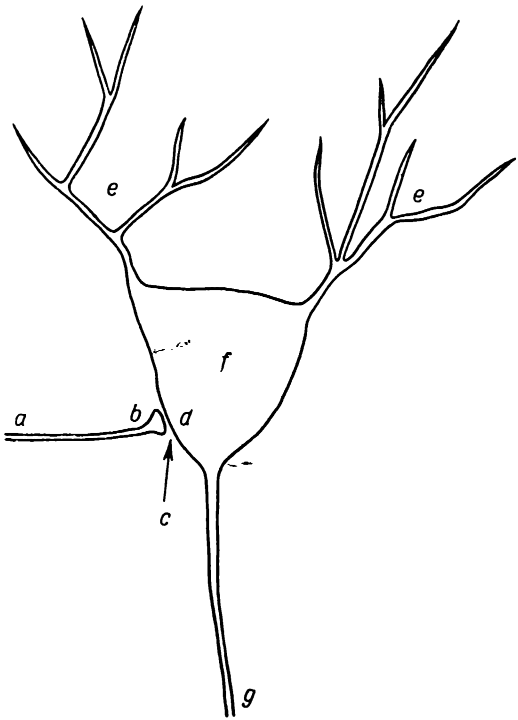

Fig. 5. Scheme of synapse: point of contact of process of one nerve cell with body of another

a—presynaptic fibre; **b**—synaptic knob; **c**—extracellular space; **d**—surface membrane of cell; **e**—short processes of cell (dendrites); **f**—body (soma) of nerve cell; **g**—its long process (axon)

property thanks to which they coupled the conditioned connection. On this subject he wrote: "This connection in the cerebral hemispheres probably owes its emergence to their extremely high reactivity and ability to impress, and is a permanent and inherent property of this part of the central nervous system." [1] It may be assumed that short-lived and transient phenomena like the development of pathways, the summation reflex, and dominance (which are related genetically to the conditioned reflex and are inherent to a certain extent in all nerve formations), when occurring at the highest level of the central nervous system, undergo a sharp qualitative change, becoming a chronic phenomenon, i.e., a conditioned connection, precisely thanks to the above-mentioned properties of the cortical nerve cells.

As for the problem of the relatively delicate structural and physico-chemical changes in the nerve tissue that form the material basis of the conditioned connection, here Pavlov, lacking direct facts, confined himself to the hypothetic assumption that the changes in the extremely fine ramifications of the nerve cell processes or in the membranes separating them could be regarded as such a basis of the conditioned connection. "The scene of this coupling faculty," Pavlov wrote, "are probably the junctional points of neurons (and, specifically, of the cerebral cortex)..." [2] Elsewhere [3] he was even more

[1] I. P. Pavlov, *Psychopathology and Psychiatry,* Foreign Languages Publishing House, Moscow, pp. 286-287.

[2] I. P. Pavlov, *Complete Works,* 1949, Vol. 3, p. 288 (in Russian).

[3] *Ibid.,* p. 356.

explicit on the same subject: "Coupling, the formation of new connections, is attributed by us to the separating membrane, if it exists, or simply to the tapering ramifications between the neurons, between the individual nerve cells." Views very close to these are expounded by several present-day neurophysiologists: J. Konorski, J. C. Eccles, I. S. Beritashvili, and others. They assume that the conditioned connection is coupled either by the formation of new synapses (points of contact between nerve cells), or by the activation of existing potential synapses, or by an increase in the synaptic surface through repetitive stimulation.

In recent years some neurophysiologists (M. G. Larrabee and D. W. Bronk, D. P. Lloyd, J. C. Eccles and W. Rall, P. G. Kostyuk, and others) have established by electrophysiological investigations of the process of synaptic transmission in the spinal cord that the passage of a series of rhythmic impulses through a synaptic contact between two nerve cells considerably enhances the excitability and conductivity of that contact. This makes the contact easily penetrable for subsequent stimulating impulses for scores of seconds, if not for many minutes. The phenomenon is accompanied by a sharp enhancement of the reflex function. Known as post-tetanic potentiation, this phenomenon at present holds the interest of many neurophysiologists.

As a matter of fact, such a phenomenon in neuromuscular synaptic transmission was established and investigated a long time ago by Schiff, Vvedensky, and others. But the enhancement of synaptic transmission by the prelimina-

ry repeated stimulation of a presynaptic nerve fibre, established on neuromuscular preparations, was not utilized until recently to gain an insight into the mechanism whereby the conditioned connection is coupled. As soon as it was established with respect to synaptic junctions between nerve cells, it was suggested immediately that post-tetanic potentiation developing in the synaptic junctions between the cells of the higher centres of the central nervous system could be the basic principle behind the coupling of the conditioned connection. This is the viewpoint of Eccles, Kostyuk, and certain other neurophysiologists. The assumption has become all the more attractive now that Eccles has attributed post-tetanic potentiation to plastic changes in the synaptic apparatus—namely to a swelling of the synaptic knob, to protoplasmic changes in it, an increase in its volume, and a resulting shrinkage of the junctional space. It may be that the "extremely high reactivity and ability to impress" of the nerve cells of the higher centres of the central nervous system boils down precisely to a pronounced propensity on their part for such plastic changes.

The important role of nerve element, functions in enhancing the excitability of these elements and in changes of a plastic or structural character in them is also corroborated by a number of other facts obtained by conventional techniques of histological and physiological research. Since these facts are obviously related to the coupling of the conditioned connection, they deserve brief mention here. First of all, mention should be made of the old data of Ramon y Ca-

jal, Ariens Kappers, G. E. Coghill, and others. These indicate that nerve element activity causes the formation of new synaptic contacts between the terminal arborization of the axon of one neuron and the cell-body and dendrites of another, thus increasing the number of such contacts, while the disuse of elements produces the very opposite results: far from synapses being formed, existing ones undergo atrophy. The experiments of T. N. Nesmeyanova, F. A. Brazovskaya, and Y. N. Yordanskaya at our institute established that the atrophy of the lower section of the transected spinal cord, with most of its nerve cells perishing, a phenomenon noted long ago by Sir Charles Scott Sherrington and others, is actually due not so much to its severance from the rest of the central nervous system as to the disuse of its nerve elements. Systematic training of the transected spinal cord, its regular activation by reflex activity not only prevents such atrophy and the depletion of its cellular composition, but enhances the excitability and vitality of the nerve cells, maintaining them at a high level. Likewise highly indicative in this context are the results of K. S. Abuladze's experiments. The stimulation by acid of the mucous membrane of a patch of the tongue, brought out by surgical means to an external position, at first produces but slight reflex salivation. However, the subsequent regular training of the reflex causes a very pronounced and stable enhancement of it within a few days.

All these facts add up to clear evidence of the important morphogenetic function of training, or of the systematic activity of nerve struc-

tures, as well as evidence of the role of this factor in bringing about a stable rise in their excitability and vitality. And quite obviously all these morphological and functional changes are of exceptional importance to the coupling of the conditioned connection in the higher centres of the central nervous system.

It is to be hoped that a deeper penetration into the functions of the nerve cell—the "atomic nucleus" of present-day neurophysiology—will enable us to get to the bottom of the mechanism of conditioned reflex coupling.

The supremely effective role of conditioned reflexes in adaptation is achieved not only by the speed and firmness of their coupling, but also by the faculty to disconnect and suppress stimuli that have lost their signalling value. Special investigations brought Pavlov to the conclusion that the use of a conditioned stimulus without reinforcement (the so-called extinction of the conditioned reflex) leads not to a destruction of the temporary connection, but to its more or less complete functional blocking by means of the process of internal inhibition. In which departments of the nervous system does this inhibition arise and what is its mechanism?

The study of the functions of the reticular formation, discussed at some length above, made it possible to single out sections of that formation that have a primarily inhibiting effect on other parts of the brain and spinal cord, including the cerebral cortex. We would like to note in passing that it was the great Russian physiologist I. M. Sechenov who discovered the inhibiting centres of the brain. The existence of special

inhibiting mechanisms deep inside the brain prompts several scientists (Jouve, Roitbak, and others) to consider the activity of these subcortical formations to be responsible for the extinction of conditioned reflexes. The participation of certain sections of the reticular formation in the process of internal inhibition is quite probable; however, in our view, its role is of secondary importance. The fact is that internal inhibition makes possible a most refined analysis of environmental phenomena, with the singling out of important signals from a multitude of stimuli that are either of no consequence to the organism or have lost their signalling value. It is hard to believe that this most delicate analysis is performed by subcortical centres of the brain. Indeed, many facts could be adduced in support of the claim that it is first and foremost cellular structures of the cerebral cortex that provide the material medium in which internal inhibition takes place.

Systematic investigations at our laboratory (Y.M. Pressman, M. Y. Varga, M.I. Struchkov, F. K. Daurova, Y. A. Romanovskaya, and L. I. Chilingaryan), as well as the experiments of other scientists, justify the assertion that internal inhibition arises initially not in the cortical point where the conditioned stimulus (light, sound, etc.) acts and not in the cortical point where the unconditioned reflex (food, defensive, sexual) is represented, but in the elements of the conditioned connection itself, possibly in the cortical assemblage of interneurons. It is noteworthy that decortication in the case of higher animals makes the orientating reflex practically

inextinguishable. This is one of the unconditioned reflexes that undergo comparatively rapid extinction in animals whose cortex is intact.

What is the more intimate, cellular mechanism of internal inhibition and, for that matter, of the other modifications of inhibition in the higher areas of the central nervous system? Many aspects of it are for the present still obscure. Some investigators associate the inhibition mechanism with the activation of nerve-cell dendrites, or short processes (Beritov); others, with the activity of special inhibitory synapses that produce a specific chemical inhibitory transmitter substance (Eccles). In our opinion, the participation of inhibition in the delicate analysis of environmental signals and in shaping the organism's responses, in other words the coordinating function of inhibition, should be considered in conjunction with its protective function discovered by Pavlov. The capacity of the nerve cells for renewed excitation can be maintained only provided the effects of previous stimulations are systematically eliminated. The highly reactive cells of the cortex are especially in need of continual restoration of their capacity to work, of their normal physico-chemical composition. An example of the restorative inhibition of nerve cells is provided by our daily natural sleep, during which inhibition spreads to a great mass of the structures of the brain.

In the conscious state the inhibition of the nerve cells is of a fractional, mosaic character. Nevertheless, we consider that this mosaic character does not deprive inhibition of its protective-restorative functions. What happens when a

conditioned signal is not reinforced with unconditioned stimulations? Evidently, the conditioned stimulus in that case loses its importance for the organism and becomes useless and unnecessary. Accordingly, its action on corresponding cortical cells is blocked by inhibition. It may be assumed that the stimulation of the nerve cells, in accordance with the principle of the self-regulation of the physico-chemical state, activates the reverse mechanisms of cellular inhibition. So long as we reinforce the conditioned connection, i.e., increase the excitation of the interneurons of the conditioned connection by the action of the unconditioned stimulus, excitation proves stronger than the mechanisms of inhibition. But then we stop applying the unconditioned stimulus. Repetition of conditioned signals now causes training; it strengthens the inhibitory mechanisms, above all in the intermediate cellular elements of the conditioned connection. Here we again encounter the role of training, the systematic activity of nerve structures, but this time it is a case of the training of mechanisms that hamper, rather than facilitate, the excitation of the nerve cells. The mounting activation of the inhibitory mechanisms gradually produces a complete functional blocking, or inhibition, of the conditioned connection. The dual nature (coordinating and protecting) of inhibition has two important consequences in the case of the extinction of the conditioned reflex: on the one hand, the organism ceases to react to a useless signal, i.e., it distinguishes that signal from other environmental phenomena, and, on the other hand, the nerve cells no longer waste energy in

vain and are able to restore their normal physico-chemical composition, their high capacity to work.

It can scarcely be denied that the complicated process of the extinction of a conditioned reflex involves a host of structures situated at different levels of the central nervous system. An important part in this process is probably also played by the reticular formation of the brain. We consider it necessary to note only one fact here: cortical elements of the conditioned connection, most probably the interneuron assemblage, serve as the initial point of inhibition in the extinction of a conditioned reflex. The inhibition of a conditioned reflex in the absence of reinforcement is precisely a case of internal inhibition, i.e., a process arising within the conditioned connection; it is not a result of the excitation of other reflex structures, as is maintained by P. K. Anokhin, J. Konorski, and others. The key to understanding the mechanism of internal inhibition should be sought in the processes of the self-regulation of the physico-chemical state of the nerve cells, processes that have lately commanded the close attention of biochemists (V. A. Engelgardt and others).

The coupling of the conditioned reflex and its internal inhibition are examples of the two main aspects of higher nervous activity: the synthesis of stimuli acting upon the organism and the analysis of those stimuli, i.e., the singling out of the signals, the phenomena of consequence to the animal or man. It is precisely internal, individually acquired inhibition that makes possible the high resolving (differentiating) power

of the cortex, its analytical activity. If one signal is reinforced with an unconditioned reflex, while another signal is not, a dog can be made to distinguish 100 metronome beats per minute from 96, a circle from an ellipse with an 8:9 ratio of semi-axes, a tone of 500 vibrations per second from a tone of 498 vibrations, and other very similar mechanical, temperature, and olfactory stimuli.

The cerebral cortex discharges its analytical function in a dialectical unity with continual synthetical activity. The formation of a single conditioned reflex, discussed above, is an example of relatively elementary synthesis. The more advanced and complex synthetical activity of the cortex is exemplified by its ability to integrate into a single whole the entire picture of an experiment, when conditioned stimuli are applied in a certain order for several days in a row. Here, in other words, we have an ability to automatize, as it were, a complicated chain of different types of activity (the "dynamic stereotype" or the systematic element in the work of the cerebrum). Higher nervous activity thus presents a picture not of a set of separate conditioned acts, but of complex systems of reflexes arising from the animal's or man's previous experiences. One "triggering" stimulus is now enough to set off the whole chain of systematized conditioned reflexes.

This remarkable property of the cerebral cortex is referred to by some authors as an "action acceptor", or a "motor task formulated in the brain", or "the animal's programme of action". We see no reason for the present to give

up the Pavlovian term "dynamic stereotype". Nor is this a mere question of semantics. The notion of a systematic element in the work of the cortex helps us to understand how the reflex stereotype is formed and how it is corrected, supplemented, or changed under the influence of changing external conditions, i.e., it helps us to think physiologically.

Pavlov's teachings have taken us a long way towards understanding such formerly mysterious phenomena as sleep, dreams, hypnosis, and the mechanisms responsible for pathological conditions of higher nervous activity in animals and man. These phenomena are considered from the standpoint of Pavlov's materialistic teachings in numerous popular articles and booklets, and there is therefore scarcely a need to dwell upon them here. What does appear to be necessary, however, is to speak, if only briefly, of Pavlov's concept of man's two signal systems.

In animals higher nervous activity is confined to responses to direct sensory (visual, auditory, tactile, etc.) signals of the environment. "This is what we, too, possess as impressions, sensations and notions of the world around us, both the natural and the social—with the exception of the words heard or seen. This is the first system of signals of reality, common to man and animals." [1] But in man, in connection with the advent and development of work and social life, "there emerged, developed and achieved extraordinary perfection signals of the second order,

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[1] I. P. Pavlov, *Psychopathology and Psychiatry,* Foreign Languages Publishing House, Moscow, p. 378.

signals of these initial signals, in the shape of speech—spoken, auditory and visible".[1] This second, qualitatively different system of signals of reality, typical only of man, is "specifically ours", it "made us men", and plays an exceptional role in our conscious life. These signals of signals "represent an abstraction from reality and make possible the forming of generalizations; this constitutes our extra, *specially human, higher mentality* creating an empiricism general to all men and then, in the end, science, the instrument of the higher orientation of man in the surrounding world and in himself."[2]

The second-signal system (speech) enables man to coordinate and join his efforts with the activities of fellow men in collective work, i.e., serves above all as a means of communication. The birth and evolution of the second signal system brought about a qualitative change in the accumulation of man's individual experience. Whereas an animal has at its command only the stock of impressions of reality that it has acquired individually, man in the process of his individual existence proves to be "armed" with the experience of all the preceding generations, drawn from stories, books, and the monuments of material (including industrial) culture. Animals acquire from preceding generations only genetic experience: a limited number of inborn unconditioned reflexes. All their other habits have to be acquired anew each time. Man, thanks to his second signal system, becomes the posses-

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[1] *Ibid.*, p. 388.
[2] *Ibid.*, p. 296.

sor of the knowledge accumulated by the human race over thousands of years.

Up to now we have been speaking of the second signal system as a means of communication between people. We must now consider it as an instrument of thinking. A characteristic feature of the word is its function of generalization, of abstraction from reality. V. I. Lenin wrote in his *Philosophical Notebooks:* "The senses show reality; thought and word—the universal. Every word (speech) already universalizes."[1] We would like to point out that it is the function of abstraction inherent in the word that makes human thinking as active as it is. Indeed, the surrounding world can be changed only by someone capable of visualizing that world as different from what we directly perceive. The faculty for abstraction from reality is therefore essential if the human mind is not just to reflect the surrounding world, but is to create it. With the evolution of the second signal system, the passive adaptation to the environment, so characteristic of animals, gave way to an effective alteration of that environment by human activity.

Unfortunately, we still know very little about the specific physiological mechanisms of the second signal system. Literally the first steps only have been taken in this field. The physiologist M. M. Koltsova has thus established that to a baby words are initially specific signals of singular phenomena. For instance, the word

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[1] V. I. Lenin, *Collected Works,* Foreign Languages Publishing House, Moscow, 1963, Vol. 38, p. 274.

"mummy" at first denotes one woman only: the baby's mother. Time is needed for the word "mummy" to come to denote father's mother (the child's grandmother), the mothers of other children, and the cat with its kittens, i.e., for it to become a generalized signal of the second signal system. According to Koltsova's data, the generalizing function of the word arises in the process of the formation of multiple conditioned connections in response to one and the same word stimulus. If most of these conditioned connections are inhibited artificially, the word loses its abstract character and for a time becomes an ordinary conditioned signal. It need scarcely be pointed out how tremendously important both theoretically and practically is the further study of the physiological mechanisms of the second signal system.

Advances in the physiology of higher nervous activity are full of promise for many branches of learning: medicine (above all, psychiatry, neurosurgery, neuropathology, and anaesthesiology) and pedagogy, philosophy and psychology. Firm traditional links exist between the physiology of higher nervous activity and these sciences. New and extremely promising contacts are also arising with certain technical subjects, such as cybernetics.

Progress in electronics by the middle of our century had given rise to most complex automatic devices. It soon became obvious that further headway in automation and remote control, in improving the reliability of automatic systems, and in the most rational organization of automated industries was impossible without close

contact with the physiology of the brain, without a deeper understanding of the principles of cerebral activity. The cybernetics experts therefore began to look hopefully to neurophysiology, seeking to gain a real understanding of the higher functions of the central nervous system.

What can there be in common between a mechanism, an automaton, and a living organism? After all, the "dead" parts of automatic devices have neither metabolism nor excitability. They can neither follow the laws of evolutionary development nor transmit features through heredity....

The following can, however, be said in answer to the question formulated above. The study of the neurophysiological principles of the coupling of conditioned connections, of memory phenomena, etc., including the biochemical ionic-molecular mechanisms of excitation and inhibition processes, is an important trend in the modern physiology of higher nervous activity, but not the only trend. Another possible approach to the subject is to disregard the biological nature of nervous phenomena and to concentrate on the principles and regularities of brain activity that can be simulated on an inorganic basis. At this point the physiology of higher nervous activity joins up directly with mathematics or, rather, with those of its sections that form the theoretical foundation of cybernetics.

These two trends of research—the microphysiological and the synthetical—complement each other. No matter how deeply we may probe the physiology of the cell, an understanding of its

work will not by itself explain the activity of the brain as a whole. Individual elements of complex systems do not possess the properties of the systems: the nerve cell cannot think, and the radio valve cannot compute. The brain, like automatic devices, has qualities that arise only as a result of the interaction of a multitude of elementary structural units. Pavlov in his day dreamed of the time when the incredible complexity of brain activity would be covered by "the majestic formulas of mathematical equations". An understanding of the basic principles of the functioning of the brain makes it possible to construct models of them. These models may be either logical (in the form of mathematical formulas) or physical (in the form of various automata, or "hardware"). Models present nervous phenomena schematically, but they provide a means of experimentally testing our notions about the functional "architecture" of reflex acts.

On the other hand, the study of the principles of higher nervous activity helps in the designing and programming of various automatic devices that can "learn", "remember", and "regulate themselves". This union of physiology and cybernetics is particularly full of promise for the problem of reliability. Hence the increased significance of research into the compensation of impaired functions of the central nervous system. Whereas in the past this section of physiology "catered" primarily for clinical medicine, nowadays physiological findings are also of interest to the physicist and the engineer. And, conversely, the study of faults in the operation

of automatic devices may suggest to the physician what lies behind certain pathological conditions and how they can be cured.

What are the most essential and predominating principles underlying the organization of the work of the brain that make it so highly reliable and so resistant to injurious influences? This is what we propose to discuss in the following chapters.

3 PROTECTIVE INHIBITION

The two main states of living nerve cells known to modern science are excitation and inhibition. The excitation of nerve cells increases the activity of the organs with which those cells are connected. Inhibition, on the other hand, reduces the activity of those organs or even halts it altogether. It is important to note that even the simplest response of an organism is impossible unless the two states arise simultaneously.

Supposing you bend an arm. This means that the cells connected with the flexing muscle have been excited. Excitation impulses travelling along the nerve fibres reach corresponding muscles, and they contract. But what about the arm? Has it actually bent? Yes, but only provided that a process of inhibition developed simultaneously in the nerve centre of the extensor muscles, only provided that the contraction of the flexors coincided with a relaxation of the antagonistic muscles. Certain diseases upset these normal relationships: excitation spreads to both groups of nerve cells, muscles are strained more and more, but the limb remains motionless.

No less a role is played by excitation and inhibition processes in higher nervous phenomena.

Supposing that before giving a dog food we light a lamp. After a few such combinations the mere lighting of the lamp will begin to excite the dog's food centre: the animal will begin licking its chops, looking into its food bowl, and secreting saliva. It will do this, regardless, of whether the lamp burns brightly or faintly. But supposing that we now continue giving the dog food only after a flash of a bright lamp, while the lighting of a dim lamp is not reinforced with food. In that case we find that the response to the dim lamp soon vanishes. Special experiments reveal that this disappearance of the reflex is associated with the development of the process of inhibition in certain nerve elements. It is the continual interplay of the excitation and inhibition of nerve cells that makes possible the remarkable, precise, and flexible activity that delights us so in the playing of a pianist, or the actions of an airman, or the virtuoso skill of a master craftsman.

"Our entire nervous activity," Pavlov wrote, "consists of two processes, of excitation and inhibition, and our whole life is a constant meeting, relationship of these two processes. . . . The relationship between excitatory and inhibitory processes, the balance between them determines our whole behaviour, normal and pathological." [1]

The excitation of nerve cells entails significant changes in their chemical composition. The work of the Soviet biochemists A. V. Palladin, G. Y. Vladimirov, V. S. Shapot, and others has

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[1] I. P. Pavlov, *Selected Works,* 1949, pp. 320 and 547 (in Russian).

shown that the period of excitation is marked by a decrease in the content of those chemical substances in nerve tissues that, according to modern science, are sources of energy (such as adenosine triphosphoric acid). At the same time there is a build up of metabolic "dross", specifically ammonia. This substantially affects metabolism and reduces the activity of enzymes, living chemical catalysts. The use of refined radioisotope techniques has revealed that during excitation there is a gradual suppression of the metabolism of the nucleic acids which play an important part in the process of protein synthesis, i.e., in the process of the renewal of the cell's chemical composition. Quite obviously, living cells are in need of the constant restoration of their ability to function, of their normal physico-chemical composition. Otherwise there is the danger of the overexcitation, exhaustion, and death of the nerve cells and, hence, the death of the organism.

It must be put to Pavlov's great credit that he discovered the protective-restorative role of inhibition, the process that is so important in regulating and coordinating central nervous activity. Pavlov demonstrated convincingly that inhibition is not a period of inactivity of the nerve cells. Inhibition is a highly active process, but this activity is of a specific kind. During inhibition the cells are cut off, as it were, from external activity and cease to respond to stimuli. Their activity is now directed at restoring their normal condition, their energy potential. Investigations by biochemists have fully borne out Pavlov's idea. It has been shown that during inhibition there is a build up of chemical substances that are

sources of energy and a drastic decline in the waste material of the life process: ammonia, lactic acid, and inorganic phosphorus.

In what cases does the protective inhibition of nerve cells arise? A striking example of protective-restorative properties is furnished by what is known as transmarginal inhibition. If we develop a conditioned food reflex to the ringing of a bell, the food response in terms of salivation will, within certain limits, be proportional to the intensity of the sound. But when that intensity reaches a certain limit, salivation will begin to decrease and then cease altogether. This means that our stimulus has become excessive, intolerable for the nervous system; there is thus a danger of overexicitation of the nerve cells. Accordingly, the effect of the sound was curbed by the protective barrier of transmarginal inhibition.

Transmarginal inhibition arises especially quickly in animals whose organism has been weakened by disease, nervous breakdown, excessive nervous tension or in animals with a congenital deficiency of the nervous system or weak type of higher nervous activity.

Pavlov discovered the protective function of inhibition when studying the higher nervous (conditioned) activity of the cerebral cortex. Experiments over a period of many years have led us to conclude that the protective function of the inhibition process is reflected in the activity not only of the cortex, but of the nervous system as a whole (possibly even in all the excitable tissues of the organism); it is manifested not only in functional disturbances of brain activity (breakdown, overstrain, pressure of insuperable tasks),

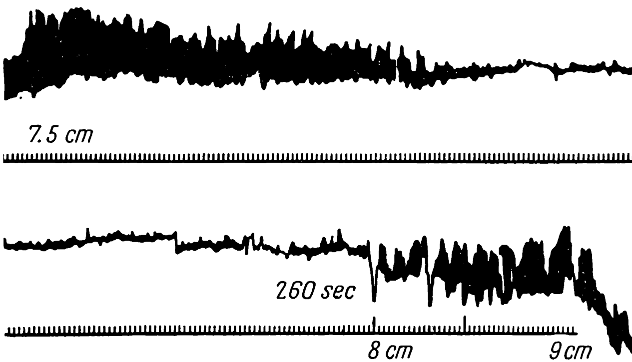


Fig. 6. Record of reflex flexing of dog's leg in response to electric stimulation

but in organic lesions too, when trauma, haemorrhage, or infection damage the very structure of the nerve tissue.

Nerve cell inhibition was first observed by Sechenov. He found that very intense stimulation of the sensory nerves of a frog suppresses its spinal reflexes, such as the flexing of a leg.

Later Vvedensky performed the following experiment. He cut out a frog's muscle, with the nerve belonging to it, and began stimulating the nerve with rhythmic electric shocks. The muscle contracted obediently in response to each stimulation of the nerve, but ceased to contract when the shocks became very frequent. The same thing was observed when the shocks were infrequent, but intense. Why is this so? Does the muscle simply "tire" and a condition of fatigue arise? Experiments did not confirm such an assumption: no sooner was the rhythm of the shocks altered

to make them infrequent, or the current intensity reduced, than the muscle at once resumed its contractions. Vvedensky gave the phenomenon he had discovered the name of "pessimum". Backed by the theoretical concepts of Pavlov, we suggested that the effect observed by Sechenov and Vvedensky was connected with the protective role of inhibition.

The protective function of inhibition may be observed especially clearly in pathological cases of nerve centre disturbances. Fig. 6 is a record of the contractions of a dog's leg after injury to its spinal cord. One can see from the figure that stimulation with a strong current caused inhibition of the reflex movements, suppression of the reflex. But as soon as the experimenter reduced the current intensity, the movements reappeared.

In the experiments carried out at our laboratory protective inhibition was observed in cases of the most diverse injuries of the central nervous system: transections, local hypothermia, compression, disturbances of the blood supply to the spinal cord, the brain stem, and the cerebral cortex, and the general suppression of the higher centres of the central nervous system under the influence of severe traumas and burns (traumatic and burning shock). Understandably enough, various injuries to the brain and spinal cord weaken the nerve cells drastically. In these circumstances even moderate stimulation cannot be tolerated by them, and that is why protective transmarginal inhibition arises so quickly and distinctly in the damaged structures.

Experimental research leads to the conclusion that the protective function of inhibition has a

universal, general physiological significance and is inherent in higher and lower centres of the nervous system, down to its elementary formations.

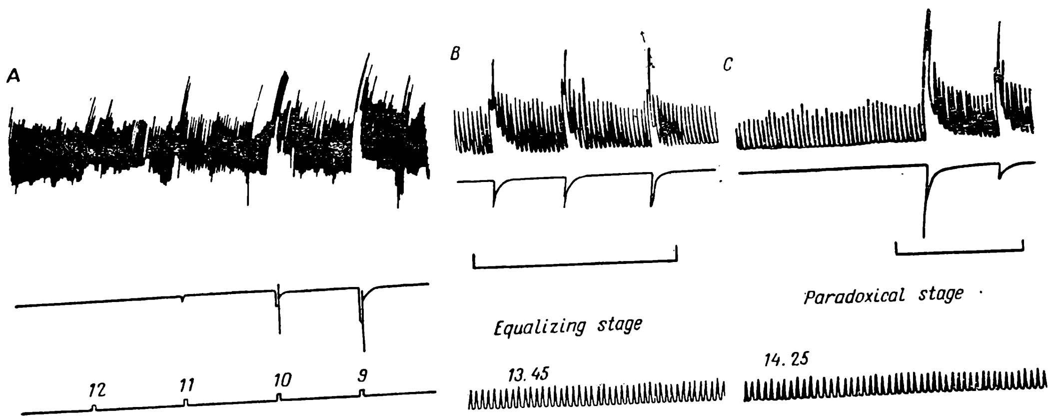
It is highly characteristic of transmarginal inhibition that the relationship between the magnitude of the response and the intensity of the external stimulation is upset. In the foregoing it was pointed out that ordinarily the magnitude of an organism's response corresponds to the intensity of the stimulus. The stronger the stimulus, the greater the response: the more intense the contraction of muscle, the more abundant the salivation, the more pronounced the rise in blood pressure, etc. The transition to inhibition upsets these "proper intensity relations". The sequence of the changes that take place has been studied especially thoroughly and systematically by the Vvedensky and Pavlov schools. Fig. 7 shows the dynamics of the changes of a rabbit's respiratory and motor responses with the development of traumatic shock caused by destruction of the muscles of the right rear foot.

In the lower part of the figure there are marks denoting 2.5 second time intervals and a record of the stimulation of the animal's left foot with an electric current. The figures denote the distance between the coils of the induction machine: the smaller the figure, the stronger the current. It is not hard to see that prior to the trauma the responses were the greater, the stronger was the electric stimulation of the skin of the left hind limb (*A*). As the shock developed, the responses began to be of the same magnitude (*B*) and then became distorted (*C* and *D*): mod-

erate stimulation had a greater effect than intense stimulation. This was followed by the disappearance of all responses and the onset of the last, inhibited stage, betraying profound suppression of the nervous centres. Consequently, nervous centres in the state of transmarginal inhibition are capable of responding to relatively weak stimuli, while strong stimuli heighten inhibition and prove ineffective.

Distorted, wrong responses to environmental influences naturally impose severe limitations on the organism's ability to adapt itself to its conditions. At the same time, it is the suppression of responses to strong stimuli that saves the nerve cells from complete exhaustion and death In this way the external adaptive behaviour of the nervous system, in the event of transmarginal inhibition, is "sacrificed", as it were, in order that the nerve cells themselves might be saved.

This regularity is especially conspicuous in certain human psychic disturbances. Infectious diseases and chronic intoxication of the organism by the products of upset metabolism may greatly weaken the central nervous system, causing transmarginal inhibition to arise in it as a "physiological measure of protection" (Pavlov). The outward behaviour and external activity of such a patient undergo a marked change: he cannot work, his responses to the world around him become distorted, he loses touch with human society. But while "losing" in adaptive behaviour, the brain, gripped by transmarginal inhibition, ensures the restoration of the normal functions of the nerve cells and makes possible subsequent recovery, it "saves itself".


A
12
11
10
9
B
Equalizing stage
13.45
C
Paradoxical stage
14.25

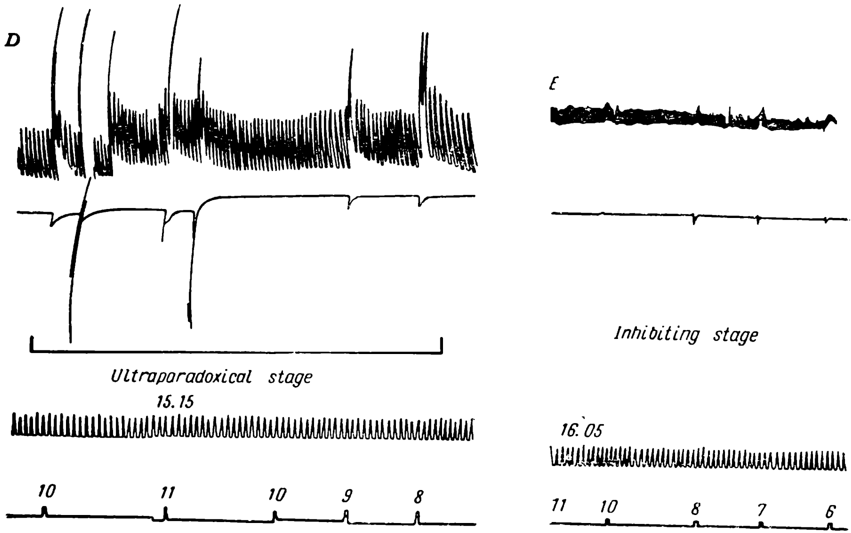


Fig. 7. **Transmarginal inhibition of respiratory reactions (upper recording) and left rear foot** movements (second recording from top) in traumatic shock

A, B, C, D, E—parts of experiment

Laboratory findings show what the danger to the central nervous system is in the event of transmarginal inhibition proving inadequate, not arising in time, or being eliminated by the experimenter.

Fig. 8 gives records of a rabbit's responses at a later stage of severe traumatic shock. As a result of the trauma, the responses were for a long time suppressed to the extent of a phase of complete inhibition (*A*). Suddenly the responses reappeared, but evoked only by very strong stimuli (*B*). This might have seemed a favourable sign, a sign that the nervous system had partly restored its functions. However, this was a restoration of functions directly preceding the animal's death. There is reason to think that in this case we observed the exhaustion of transmarginal inhibition, its breakdown. Deprived of their protective inhibition barrier, the nerve centres quickly used up their last resources and went out of action altogether.

Highly indicative facts are reported by L. V. Krushinsky, who studied the motor stimulation and convulsive attacks of white rats in response to strong auditory stimulation. The scientist demonstrated that the prolonged action of sound stimuli with short (5-10 sec) intervals produces no effects in any way endangering the animal's life.

The excitation observed in this case develops against the background of transmarginal inhibition and is therefore of low intensity, since the transmarginal inhibition produced by the action of the auditory stimuli continuously reduces the degree of the excitation of the nerve cells. If,

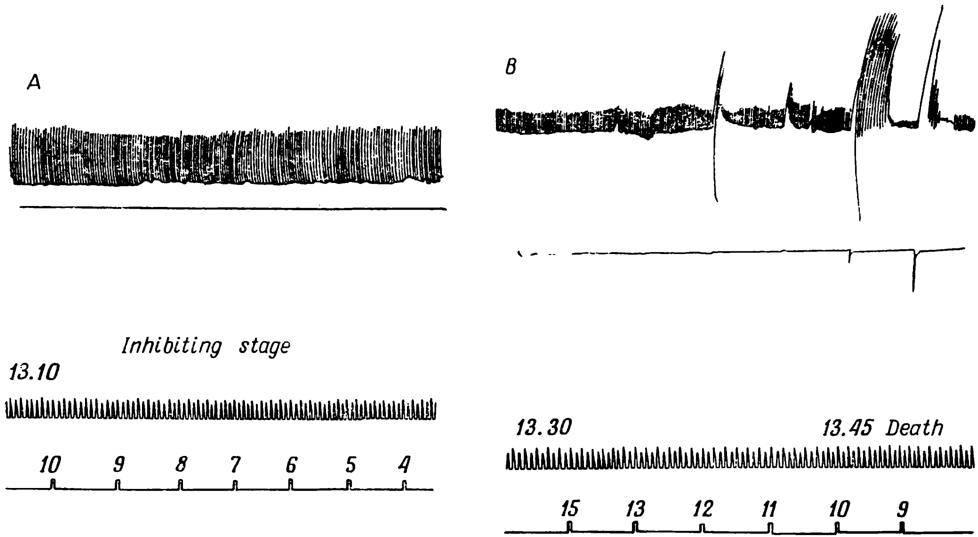


Fig. 8. Disappearance of transmarginal inhibition in final stage of traumatic shock in rabbit
A, B—parts of experiment

however, after 10-15 minutes of auditory stimulation, a longer (3-5 min) interval is observed and the action of the auditory stimuli is then resumed, excitation develops that is more intense than that observed before the interval. During the interval the central nervous system apparently frees itself from transmarginal inhibition and its capacity to work increases; hence the more intense excitation in response to stimulation after the interval. According to Krushinsky's data, this excitation in 12 per cent of the cases resulted in the death of the experimental animals, the post mortem revealing far-reaching fatal changes in the brain matter.

Up to now we have spoken primarily of the protective, defensive role of transmarginal inhibition. It is also necessary to point out its *restorative* and, in pathological cases, *curative* effect. Investigations have shown that in various injuries of the central nervous system the rational prescription of moderate doses of soporifics and sedatives can do much to hasten the restoration of the impaired functions. The diagrams in Fig. 9 give the time that was needed for the restoration of the flexing reflexes of the hind limbs, urination, and the vascular reflexes in dogs that had experienced spinal shock. It was found that a mixture of soporific drugs (urethane, veronal, and bromide) in doses considerably extending the period of daily slumber can almost halve the period needed for recovery.

The effects of exceedingly strong stimuli, dangerous to the nervous system, are thus neutralized by protective transmarginal inhibition. But strong stimulation is not the only factor by

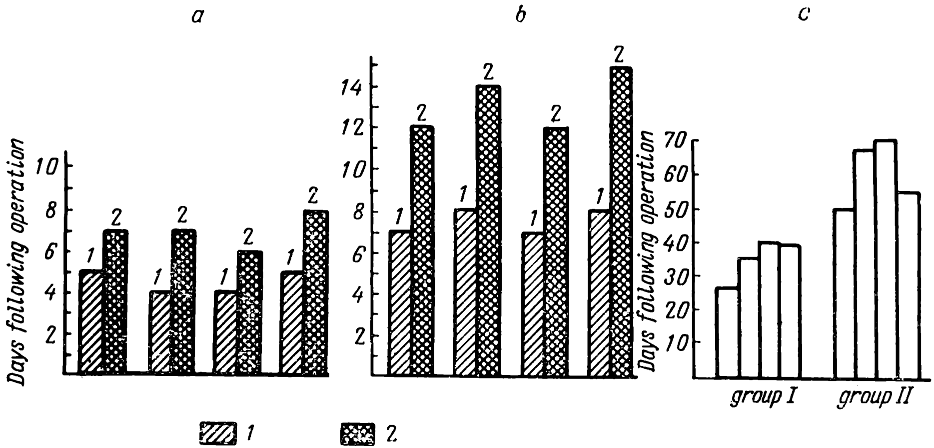


Fig. 9. Normalization of impaired functions hastened by soporifics

a—flexor reflexes of rear limbs; **b**—urination; **c**—vascular reflexes in treated (group I) and control (group II) dogs; 1—treated dogs; 2—control dogs

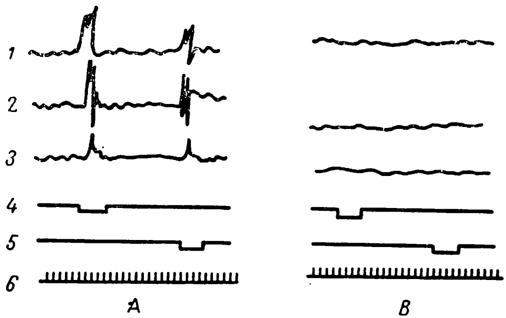


Fig. 10. Inhibition of rear foot and tail reactions in dog under the influence of weak stimuli

A—prior to stimulation; B—after weak stimulation. Key to figures: 1—right foot; 2—left foot; 3—tail; 4—stimulation of left side; 5—stimulation of right side; 6—time in seconds

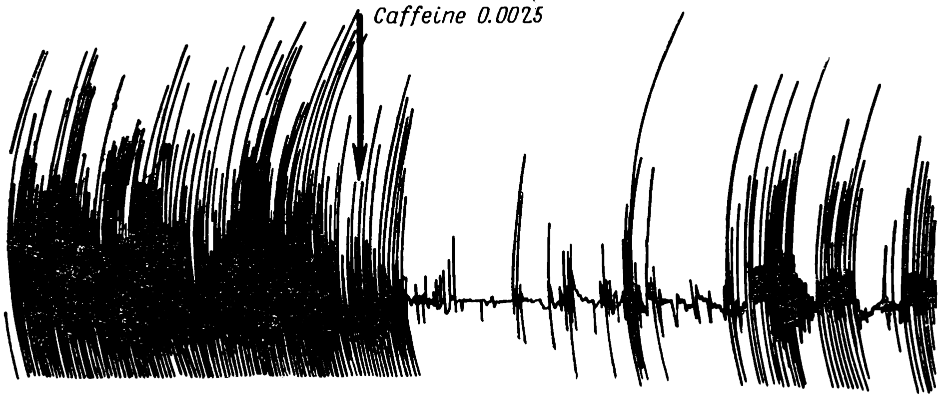
any means that gives rise to transmarginal inhibition in the central nervous system. Far more important to brain activity is the inhibition that arises in response to weak stimuli.

An interesting fact has been described by T. N. Nesmeyanova and N. M. Shamarina of our institute. By special techniques they obtained a stable rise in the excitability of a section of a dog's spinal cord below its transection. In these conditions the stimulation of the skin of the animal's right or left side produced reflex reactions of the tail and hind limbs (Fig. 10). During the following days weak electric stimulation was applied to the limbs, tail, or skin of the rear half of the body. When, after this, attempts were made to evoke motor reflexes of the legs and tail,

they were found to be inhibited. Could this have been due to overexcitation and fatigue of the spinal cord or to the transmarginal inhibition, with which we are now familiar? The facts did not bear out such an assumption. For one thing, it was only weak stimuli that had an inhibiting effect. For another, a sharp increase of the current intensity again produced movements of the legs and tail. Here, evidently, was a case of some other type of inhibition, not transmarginal, since it would be eliminated by a strong stimulus.

The inhibiting effect of weak stimuli may be observed even in the simplest living organisms. For example, the amoeba, a cell leading an independent existence in water, ceases to move, retracts its pseudopodia, and assumes a spherical shape under the influence of weak concentrations of chemical substances. It is enough to increase the concentration of the salt or acid for the amoeba to pass into an excited state and to begin moving vigorously in an effort to swim away from the source of chemical irritation.

A number of investigations have shown that small doses of drugs stimulating the nervous system (caffeine, strychnine, adrenalin) distinctly enhance inhibition, their effect being opposite to that of medium doses. Fig. 11 shows the record of part of our experiments with caffeine. When a rabbit in the excited state is given a small dose of caffeine, the effect is soothing. Could this be because we have overexcited its nervous system and the additional stress has produced transmarginal inhibition in it? No, this is not so, since a bigger dose of caffeine, far from weakening,


Caffeine 0.0025

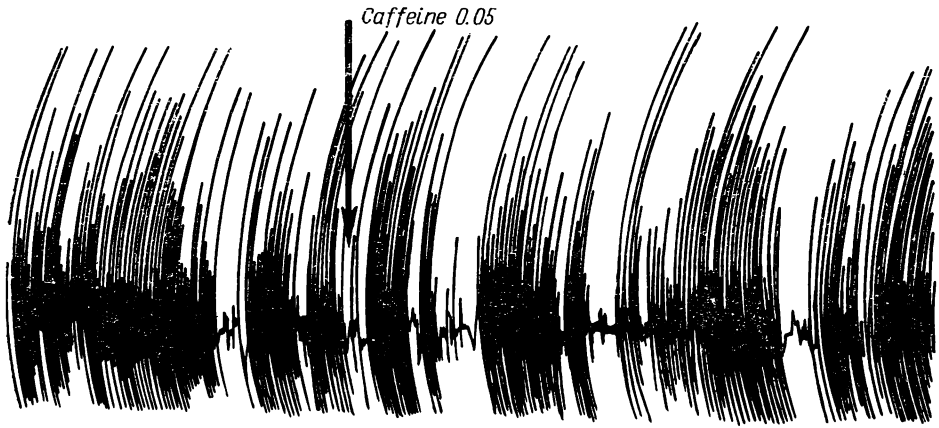


Fig. 11. **Effect of caffeine on rabbit's motor activity**

heightens the animal's motor excitation (lower diagram).

In physiology it is known that this or that reaction takes place only in response to stimulation of sufficient intensity (idea of threshold). A dog, say, will jerk away its paw only if the intensity of the electric current applied to its paw exceeds a definite value. Research carried out in recent years appears to suggest that reactions to weak subthreshold stimuli are restrained by an inhibition process ("primary" inhibition) that takes part in regulating the threshold, in fixing the level of excitability most expedient for the organism.

The process of nerve-cell excitation is thus regulated by inhibition, which limits it, as it were, on either side. Transmarginal inhibition protects the cell from excessive, superintense excitation, stipulating its limit, while primary inhibition is related to the initial moment of the stimulation process.

The latter type of inhibition rids the reacting system, as it were, of the need to get excited about minor matters, matters of little consequence; it serves as a means of combating "interference", physiological "static". In this case, as in many others, the living organism functions according to the principle that, in automatic control theory, has come to be known as a disturbance switch off controller.

Up to now we have been discussing inhibition that is primary, that arises "from the outset" under the influence of weak stimuli. Let us call this preventive inhibition, thereby underlining the fact that it prevents the process of excitation,

whereas transmarginal inhibition arises *as the result* of excitation and is engendered by it. Not every type of inhibition that follows excitation is, however, transmarginal. This fact again is illustrated best by the action of comparatively weak stimuli upon the nervous system.

Let us subject an animal or human being to the action of some recurring stimulus: sound, light, or irritation of the skin. At first the action of our stimulus will have several effects pointing to an excited state of the nervous centres: a change in the biocurrents of the brain, in the activity of the sweat glands, in the lumen of the blood vessels, a contraction of muscles, etc. These changes are characteristic of the biologically important orientating reaction, the "alerting" reaction. But with the passage of time the stimulus will cease to produce these reactions. Special experiments have shown that it is the process of inhibition—not transmarginal in this case, either—that enables the organism to get accustomed to a stimulus in this way. Should the stimulus now be increased, the reaction will reappear.

Can it be that recurrent stimulation has exhausted the nerve cells, proving excessive for them, beyond their endurance? No, the meaning of adaptation phenomena (habituation phenomena) is different. They rid the central nervous system of the need to react to unimportant stimuli that are useless to the organism, they enable the organism not to "waste" energy on this.

Let us return to the food reflex experiment. By pairing the flashing of a lamp with the appearance of the food bowl we conditioned our

dog. The lamp alone now, without the food bowl, causes the dog to salivate, to lick its chops, to make typical movements. But let us now alter the course of the experiment by continuing to flash the lamp without producing any food. The lamp will flash two, three, ten times, and finally the dog will stop looking eagerly into the food bowl: the food reaction is extinct. As soon as the lamp has become an unnecessary, a false signal, its food effect is "switched off" by the inhibition process.

The inhibition process enables the organism to pick out the signals of greatest importance and consequence for it at a given moment. Let us assume that a dog has been trained so that its food reflexes are evoked by the flashing of a lamp, by the scratching of its skin, and the gurgling of water. Suddenly a bell rings. If we now test our usual signals immediately after the bell, their action will be found to have been drastically attenuated, if not reduced to naught.

What has happened? The new stimulus (the bell) produced an orientating reaction, the "what's this?" reflex, a turn of the head, pricking up of the ears, etc. After all, the bell could herald some important event, either favourable or dangerous to the animal. In its brain there therefore arose a seat of sufficiently strong excitation, the central mechanism of the orientating reflex. All other reactions, including the food reflexes developed by us, are, accordingly, inhibited. After a certain period of time these reflexes will be re-established, they will reassert themselves in full.

These last examples serve to illustrate the

dual role of inhibition. On the one hand, it ensures the delicate, precise, and biologically expedient functioning of the brain, imparting accuracy and refinement to the excitation process and imposing restrictions upon it. At the same time and parallel with this, inhibition makes for the economical expenditure of energy by the nerve cells and for the timely restoration of their energy potential. This was very aptly described by Pavlov, who wrote of the cells of the cortex: "The most vigilant signaller has played its important role and, for a time, while it is not needed, its rest is carefully guarded." [1]

Inhibition of the cortical cells arises whenever the cells have gone through the excited state. Dusser de Barenne and McCulloch in 1934 employed an electric current to stimulate the section of the cortex causing the extension of the radiocarpal joint in a monkey. If the first stimulation was followed by a second 13 seconds later, there was no reaction. But as soon as the interval between stimulations was lengthened, the reactions became constant in magnitude.

We believe that all forms of inhibition in the normally functioning nervous system have protective-restorative properties. Every transition of nerve cells into the state of inhibition is used for their, so to speak, preventive maintenance. Even brief inhibition enables nature to facilitate "running repairs", restoring the capacity to work and normalizing physico-chemical composition. It is this that accounts for the remarkable inex-

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[1] I. P. Pavlov, *Psychopathology and Psychiatry*, Foreign Languages Publishing House Moscow, p. 98.

haustibility, efficiency, and reliability of the nerve cells, which is such an amazing feature of the central nervous system.

We anticipate a possible objection of the reader at this point. But surely, he may object, inhibition is at times not easy. What a strain it is sometimes to wait for something, to retard one's reactions or even suppress them deliberately! What possible rest and recuperation can this involve? Before replying to these objections, let us establish where exactly the difficulty lies in suppressing reactions.

Let us suppose a tracker dog sees a criminal. The criminal's appearance and smell are for the dog a signal triggering off the reaction of attack; they set up a powerful seat of excitation in corresponding nerve centres. Nevertheless, the dog lies still, because under the influence of its training a second powerful seat of excitation has arisen in its brain, one that can be removed only by the command to attack. If the second seat were clearly stronger than the first, it would completely suppress the dog's aggressive defense reaction: the animal would lie perfectly still and its nervous system would experience no particular stress. The whole point is that both seats are sufficiently strong; the second one cannot suppress the aggressive excitation in the brain centres, but only prevents that excitation from going out to the effector organs. It is this simultaneous powerful excitation of a considerable mass of nerve cells that is a difficult burden for the nervous system, in some cases straining it beyond the breaking point. The "breakdown" occurs not because the system could not endure

the inhibition, as some people think, but because inhibition could not arise and could not make itself felt sufficiently.

It is quite obvious that the mechanism we have described differs fundamentally from the case of the stimulus losing its signalling effect, as in the extinction of a conditioned reflex. Unfortunately, in our physiological literature the term "internal conditioned inhibition" is used with reference to any inhibition acquired in the process of an animal's individual experience, any trained retardation of responses. Accordingly, phenomena of very different origin, such as the extinction of conditioned reflexes and the case of the dog just described, come under the category of internal inhibition.

It is by no means our claim that the mechanism of inhibition cannot be damaged. Experimental practice provides us with many instances of the development of a chronic weakness of inhibition, its deficiency. What we do maintain is that the inhibition process itself is never difficult, exhausting, or destructive for the organism, since inhibition is above all rest, recuperation, and protection for the highly reactive nerve structures.

Another objection may arise at this point in the mind of the attentive reader. Our continual references to the restorative role of inhibition, he may feel, are at variance with the above-mentioned cases of inhibition arising before excitation, arising in nerve cells that have not worked yet and have not experienced functional deterioration. What is the purpose of recuperation when something has not yet had the chance

to experience fatigue? Pavlov too, it should be noted, put this question to himself and to his co-workers, when discussing the protective function of inhibition. At the present time there are strong reasons for thinking that the primary inhibition of cells that have not been at work not only frees them from responses to unimportant (say, very weak) stimuli, and not only thereby prevents energy expenditures in vain, but, as a preventive measure, increases the energy potential, stability, and functional capacity of these cells.

The well-known Soviet scientist D. N. Nasonov has demonstrated that the excitation of nerve cells enhances such a property of their protoplasm as the ability to capture particles of pigment. Nasonov's followers have found that use of weak stimuli, far from increasing, diminishes coloration below the level characteristic of the unstimulated cell, this phase of reduced sorption coinciding in time with the phase of initial excitation decline. S. N. Romanov subsequently observed a highly interesting fact: nerve cells in the stage of faint coloration prove far more resistant to the action of additional influences—including harmful ones, such as strychnine—than cells that were not exposed to weak stimulation and that have an excitability normal for them.

There is also a second fact that deserves mention. It was said in the foregoing that very small doses of caffeine do not evoke an excitation process in the central nervous system and, in fact, have a primary inhibiting effect. In experiments with white mice we were able to show

that the central nervous system of mice that had received small doses of caffeine, as well as an inhibiting bromide, was far more resistant to oxygen deficiency than the brain of control animals. The results of such experiments are given in the following table.

Survival of White Mice in Hermetically Sealed Vessels

Group of mice	Number of mice			
	Less than 1 hour	From 1 hour to 1 hour 29 min	From 1 hour 30 min to 1 hour 59 min	2 hours and longer
Control mice	10	10	0	0
Mice that received caffeine (0.05 mg)	2	9	7	2
Mice that received bromide (2.5 mg)	2	8	9	1

There are thus facts confirming that primary inhibition, i.e., the inhibition preceding excitation, also possesses protective properties.

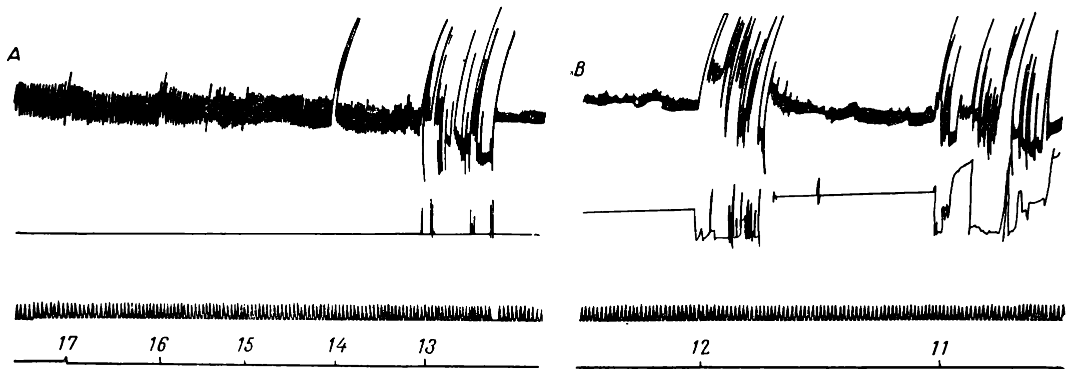
When speaking of preventive inhibition, we exemplified it by cases of inhibition arising in certain nerve cells, in the centres of the orientating reflex, the food and defensive reflexes. There are moments, however, when inhibition spreads to extensive areas of the brain, not infrequently to its greater part. A case in point is our daily natural sleep, a period of general rest, when the central nervous system recuperates most fully. Evidently, sporadic inhibition while the organism is awake—"preventive maintenance without

suspension of operations"—is not enough to maintain the normal efficiency of the nerve cells. That is why nature submits the brain every night to a more thorough overhaul.

We must, however, at this point indicate a substantial difference between "preventive" inhibition during sleep and the transmarginal inhibition of overexcited nerve cells. Whereas in transmarginal inhibition the external activities of the nervous system are sacrificed in order to save it from exhaustion and destruction, inhibition during sleep is marked by a combination of protective-restorative processes with a constant readiness to resume external activities. Fig. 12 gives the kymograms of the respiratory and motor reactions of rabbits to painful stimuli during partial sleep, or hypnosis (*C*), and a state of drowsiness induced by small doses of soporifics (*D*). It is evident that although the responses of the rabbits are suppressed (the animal that was awake responded to an excitation of 13 cm, whereas the hypnotized rabbit responded with a motor reaction only to stronger excitation, viz. 10 cm), the reactions exhibit a proper force relationship: their magnitude is the greater, the stronger the stimulus. This means that an inhibited nervous system continues to respond adequately to external influences; when the stimuli, finally, reach a certain intensity, inhibition disappears altogether and the animal wakes up. The reader will recall that in transmarginal inhibition, on the other hand, responses were suppressed all the more, the greater the intensity of the stimuli. Strong stimuli, far from eliminating transmarginal inhibition, deepened it.

It should be noted that even in the event of powerful, destructive influences upon the organism, inhibition does not at once acquire the character of transmarginal. By gradually increasing the trauma (in our case the blows dealt by a hammer to the muscles of the right rear leg), we are able to observe all the main "defense lines" of the central nervous system (Fig. 13). Before the trauma the rabbit's reactions obeyed the rule of force relationships (*A*). Following the first moderate trauma, there arose inhibition of the type that arises during sleep (not transmarginal): the reactions were weakened, but were still related to the strength of the stimulus (*B*). After a period of time the reactions became completely normal (*C*). But now the rabbit was subjected to another trauma, much more severe than the first. We may assume that protective properties of "preventive" inhibition are now inadequate, the excitation of the nerve cells exceeds the limit of their functional capacity, and transmarginal inhibition arises in the central nervous system. This gives us a picture of the consecutive stages of transmarginal inhibition: the equalizing, the paradoxical, the ultraparadoxical, and the inhibitory (*D*, *E*, *F*). Inhibition becomes deeper and deeper, and with it the general condition of the animal becomes worse. Finally, transmarginal inhibition too disappears (*G*). The reactions that were absent reappear, followed by exhaustion and the animal's death.

Numerous experiments with diverse influences upon the central nervous system make it possible to note a certain sequence in the changes in functional condition with the rise in the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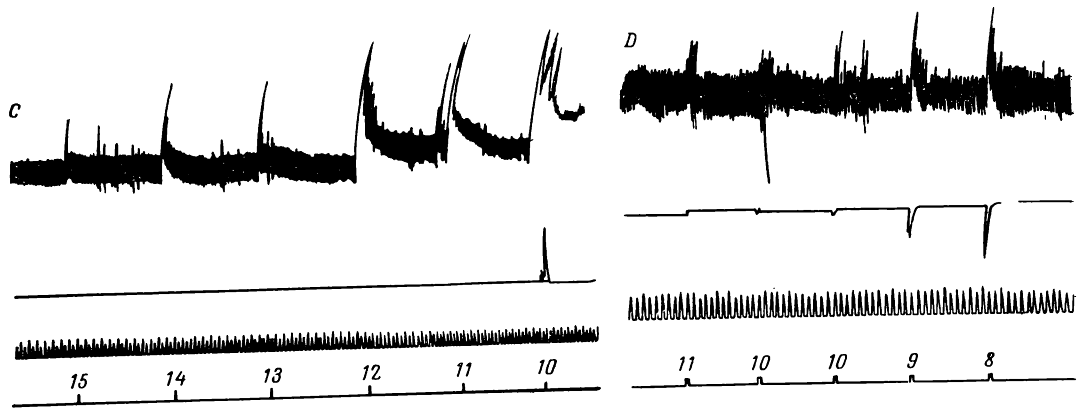
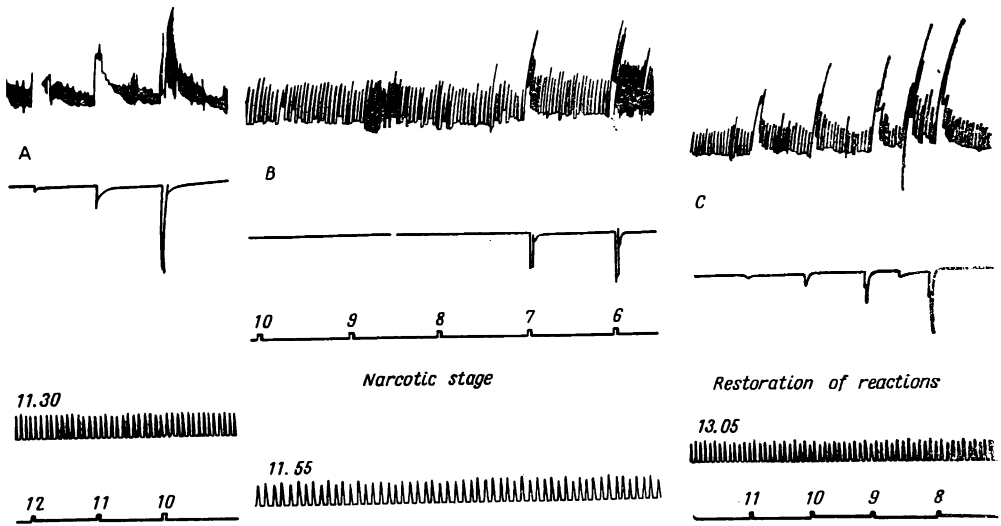


Fig. 12. Respiratory and motor reactions of rabbit when awake (*A* and *B*), hypnotized (*C*), and drowsy under the influence of small dose of soporific (*D*)

Recordings from top to bottom: respiration, foot movement, 2.5 sec time marks, and electric stimulation marks (figures indicate distance between inductor, coils, smaller figures therefore corresponding to higher current intensities)


A
B
C
10
9
8
7
6
Narcotic stage
Restoration of reactions
11.30
11. 55
13.05
12
11
10
11
10
9
8

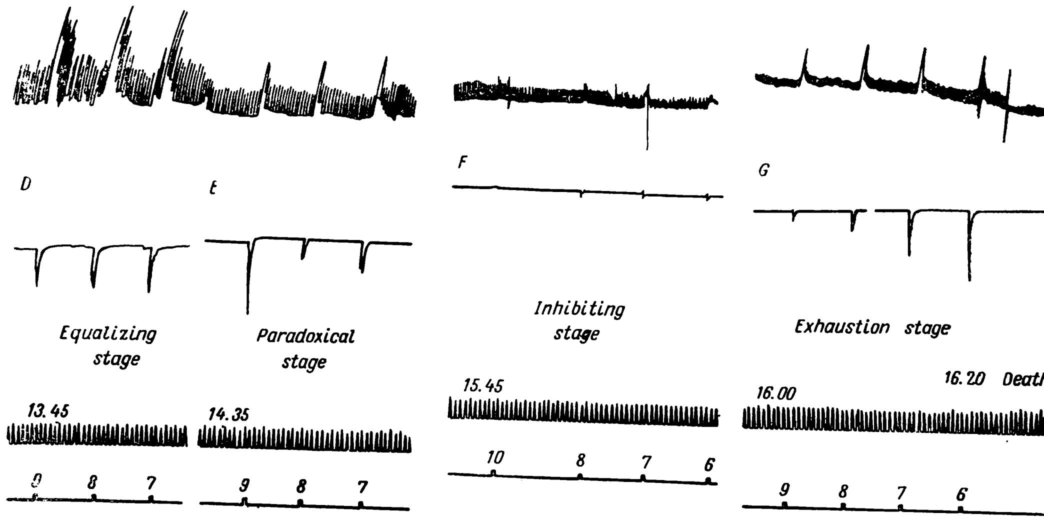


Fig. 13. Change in respiratory and motor reactions of rab bit with increasing severity of trauma
Meaning of curves same as in Fig. 12. **A, B, C, D, E, F, G**— parts of experiment

strength of the external stimulus. This sequence was very clearly in evidence in studies of the effect of different doses of the typical stimulant caffeine (Fig. 14), although the proposed scheme of its action is by no means confined to the action of this drug alone. Very small (subminimal) doses of caffeine at once generate inhibition without preceding excitation. Small doses give rise to a phase of excitation, which then gives way to a period of inhibition. It is important to note that this inhibition is not transmarginal. In its physiological characteristics it is similar to the primary inhibition produced by subminimal doses. Medium doses of caffeine produce prolonged excitation. And only large doses occasion transmarginal excitation, which sets in the faster, the larger the dose. Such is the logical sequence of the two principal modifications of protective inhibition.

It should be pointed out that every animal has its own "scale" of subminimal, small, medium, and large doses. This provides the means for singling out four main types of reactivity among animals, and these are shown schematically in Fig. 15.

In the case of the "weak" type preventive, protective inhibition is quickly followed by slight and short-lived excitation, which soon gives way to transmarginal inhibition. In the "highly excitable" type a rapid transition to the phase of very strong excitation is observed after relatively small doses, owing to the insufficiency of preventive inhibition. However, this excitation "explosion" soon gives way to transmarginal inhibition of responses. The "strong balanced mobile"

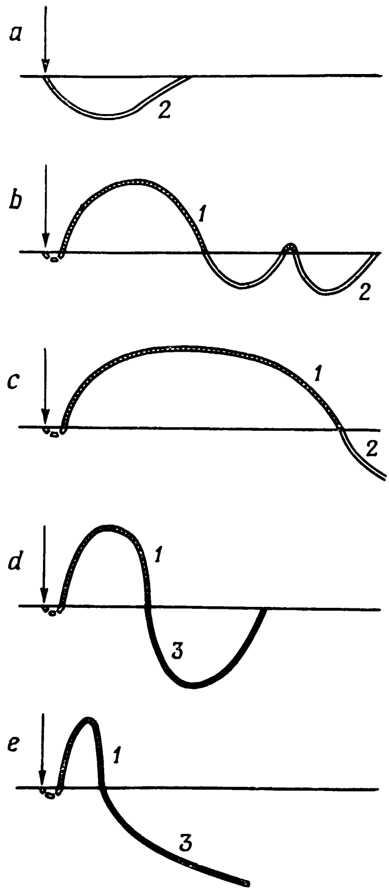


Fig. 14. Changes in functional state of higher centres of central nervous system of rabbit with rise in caffeine dose

a—subminimal dose; b—small dose; c—medium dose; d—large dose; e—toxic dose. 1—excitation; 2—inhibition not accompanied by distortion of conditioned responses; 3—transmarginal inhibition

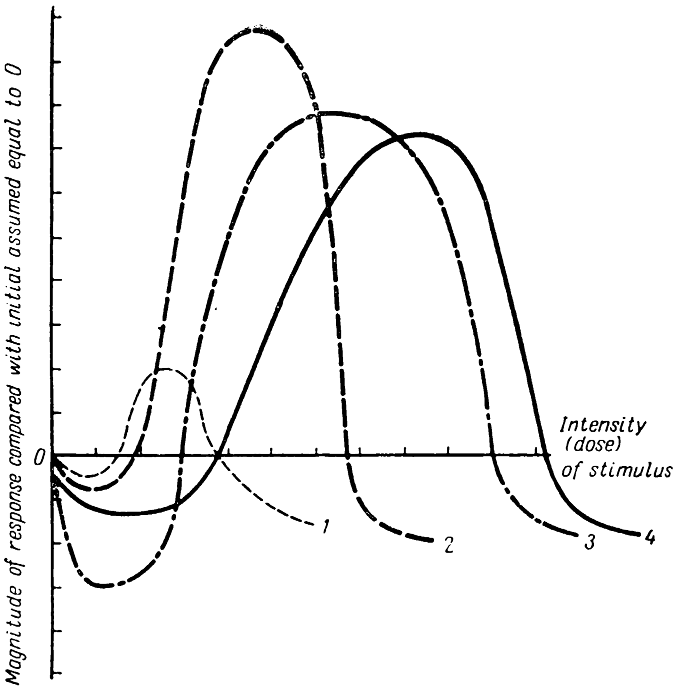


Fig. 15. **Main reactivity types**

1—weak; 2—strong excitable; 3—strong balanced mobile; 4—strong balanced inert

type exhibits the most profound preventive inhibition, although it is not prolonged. It is followed by a sharp rise in excitability, which for a long time does not give way to transmarginal inhibition. A striking feature of the "strong balanced inert" type is the slow change of phases, with a gradual growth of their amplitude.

Below we shall consider the fact that each of the above-mentioned phases is determined by the interaction of antagonistic physiological mechanisms, one of which ensures the excitation of the live reacting system, and the others, its autostabilization (the mechanisms of preventive and, later, of transmarginal inhibition).

In this way the transition from inhibition to excitation is only the outward picture of the phenomenon. During the excitation phase the mechanisms of preventive inhibition, far from ceasing to operate, clearly increase their activity up to a certain point. Behind the "façade" of excitation, as well as of inhibition, there takes place an intense "conflict" of the mechanisms of reactivity and autostabilization.

What are the mechanisms of inhibition in the central nervous system? Unfortunately, there is much that is still obscure, unexplored in this field. Little wonder that Pavlov called the problem of acquired conditioned inhibition the "cursed problem" of the physiology of higher nervous activity. Nevertheless, modern science has at its command a certain number of facts and theoretical generalizations concerning the specific mechanisms of the inhibition of simple and complex reflexes. The deep-seated factors behind the excitation and inhibition processes

are physico-chemical transformations, the specific features of ionic reactions. These, however, are problems we shall not go into here, chiefly because these metabolic processes, as specific processes of a living organism, can scarcely be utilized in the designing or operation of automatic devices. It seems to us to be more expedient and appropriate, therefore, to discuss the inhibition mechanism in relation to the *structure* of nervous reacting systems and the *types of connection* between individual nerve elements.

In recent years some scientists (the Australian physiologist Sir John Eccles and others) have come to the conclusion that the nerve cell has two types of connections with the processes of other cells. If excitation from other cells reaches connections (synapses) of the first type, the cell under investigation is excited. But if the connection involved is of the second type, the cell becomes immune to excitation, it is inhibited. Since every cell has a host of synapses of both types, its excitation or inhibition depends upon the proportion of one type to the other.

An important circumstance should be mentioned at this point. The nerve cell is sometimes regarded as a switch that can be in one of two positions: excitation or inhibition, "yes" or "no", 0 or 1, + or —. Such a notion appears justified in reference to the state of the long process of the nerve cell, its axon (Fig. 16). Indeed, if the excitation of the nerve cell has reached a certain point, impulses of propagating excitation appear at the "output" in the axon. On the other hand, if the cell is inhibited, there is no impulse transmission along the axon. But this "all-or-nothing"

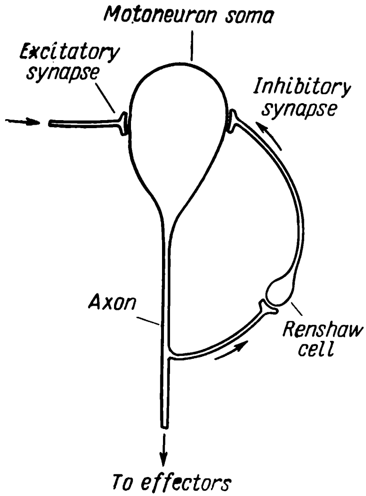


Fig. 16. Self-regulation of motoneuron excitation

principle does not reflect the state of the cell body itself.

The interaction of the inhibiting and exciting synapses produces a most complicated conflict of antagonistic tendencies in the nerve cell. This conflict is all the more complex because of the influences and changes due to causes other than the connective (synaptic) machinery. Here we refer to the changes in the living substance of the cell associated with the blood supply, the influx of nutrients and oxygen, the removal of waste, and chemical influences through the blood. As a result, the state of the cell is characterized by a series of dynamic transitions from extreme excitation to deep inhibition, by a whole

gamut of changes in its functional properties. We speak of this to make the point that the nerve cell is, as it were, a "relay" of a special type, with properties capable of experiencing a colossal range of changes. This changeability accounts for the exceptional refinement and expedience of the switching on or off of the mechanisms regulated by a given cell.

It is noteworthy that the existence of the inhibiting synapses makes for a certain self-regulation of the nerve cells. Fig. 17 gives a schematic picture of the motoneuron *B,* whose excitation ultimately causes a muscle to contract. The long process of this cell gives rise to a side branch connected with the Renshaw cell *C*. A process of the latter reverts to the body of the motoneuron, acting upon it through the inhibiting synapse. The whole system has been designed by nature in such a way that moderate impulse propagation along the axon does not excite the Renshaw cell. If, on the other hand, the excitation of the motoneuron becomes too strong, the brake comes into play and reduces the level of excitation.

Quite recently T. C. Eccles, P. G. Kostyuk, and others demonstrated that there is still another mechanism for preventing excitation in the nerve cell. For the sake of simplicity, we shall explain it with the help of the same Fig. 17. The excitation impulses, through the branch of the long process, activate the cell *D,* through the process of which they reach the synapse exciting motoneuron *B*. As a result of this, the synapse loses its excitatory properties. In this case the motoneuron *B* "avoids" the incoming excitation from

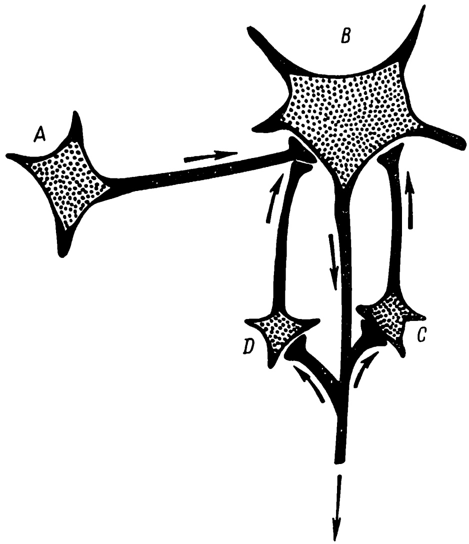


Fig. 17. Autoblocking of nerve cell "input"
A, B, C, D—nerve cells forming a self-regulating system

cell *A* not through the development of a state of inhibition inside *B,* but through the *blockage* of the inputs of the reactive system. It is hard to find a more graphic example of the protective role of inhibition. At the same time there is no escaping the conclusion that such safety fuses have only a definite range of action. If they were always able to keep excitation in check, we would not encounter cases of the overexcitation and exhaustion of nerve cells.

Apart from such comparatively simple micro-fuses, the central nervous system has complex

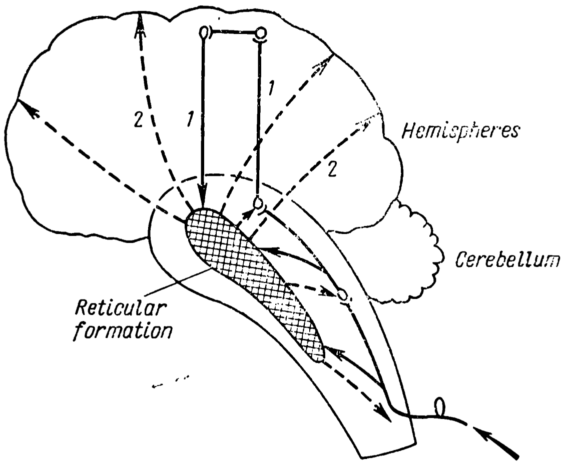


Fig. 18. Regulation of functional state of central nerve formations by reticular formation

1—influences upon reticular formation, 2—reticular influences upon brain

regulators of the excitation and inhibition processes.

Research during the past 10-15 years has led to the discovery and careful study of the functions of the so-called reticular formation, a concentration of nerve cells in deep-seated parts of the brain. It has been found that all the nerve pathways carrying excitation impulses to the brain from the receptors (the retina of the eye, internal ear, tactile formations of the skin, etc.) have lateral projections into the reticular formation (Fig. 18). The latter, under the influence of these stimuli, has great sway over the state and

level of excitability of most diverse areas of the central nervous system, ranging from relay points along the routes of travelling impulses to the "end stations", i.e., cortical cells. The higher centres of the brain are thus under a twofold influence: along the main pathways, which have long been known to physiologists, they receive signals from the sense organs (visual, auditory, tactile, etc.), while through the reticular formation there is constant "adjustment" of the level of excitability and regulation of the activity of these centres. If the cortex is compared to the screen of a television set, one can say that the classical pathways feed the cortex with the picture and sound, whereas the reticular formation regulates the brightness and definition of the picture, the illumination of the screen, and the volume of sound. It must be added that the reticular formation itself is under the influence of the cortex, and the relationship between the cortex and the reticular formation is cyclical and interdependent, with a certain supremacy of the cortex. This ensures the most expedient participation of the reticular formation in the work of the brain, a participation depending upon the signal value of the stimuli acting on the organism.

It is quite obvious that the reticular system plays an important part in the mechanism of central inhibition, in the propagation of excitation processes, in the concentration of attention, in the transition from sleep to consciousness, in the phenomena of hypnosis, and in pathological conditions of brain activity. Some scientists have come to believe that individual sections of the

reticular system exercise a primarily inhibiting or primarily stimulating influence. This question still requires clarification, and we shall therefore not dwell upon it here. We felt it important merely to describe one of the specific mechanisms whereby the inhibition of central nervous formations is effected.

Particularly great difficulties arise in the study of the mechanism of the inhibition of conditioned reflexes, the highest form of the organism's adaptation to its environment. Schematically the main links in the conditioned reflex arc appear to be the following (Fig. 19): the receptor of the stimulus (in our case, of an auditory signal), the effector of the inborn reflex (food or defensive), and the intermediate links of the temporary nervous connection. Let us assume that we stop reinforcing the signal: we ring the bell without producing any food. The conditioned reflex is inhibited and becomes extinct. But where does inhibition arise first in that case: in the signal receptor, in the centre of the unconditioned reflex, or somewhere else? Experimental facts provide us with a certain measure of information on this point.

F. K. Daurova staged the following experiment at our laboratory: she combined an auditory signal with food and with the stimulation of a dog's paw by an electric current. A double conditioned reflex was soon formed: in response to the signal the dog lifted its paw and looked into its food bowl, while salivating. The experimenter then ceased giving the dog food in combination with the auditory signal, whereas the electric shocks were continued. The food reflex

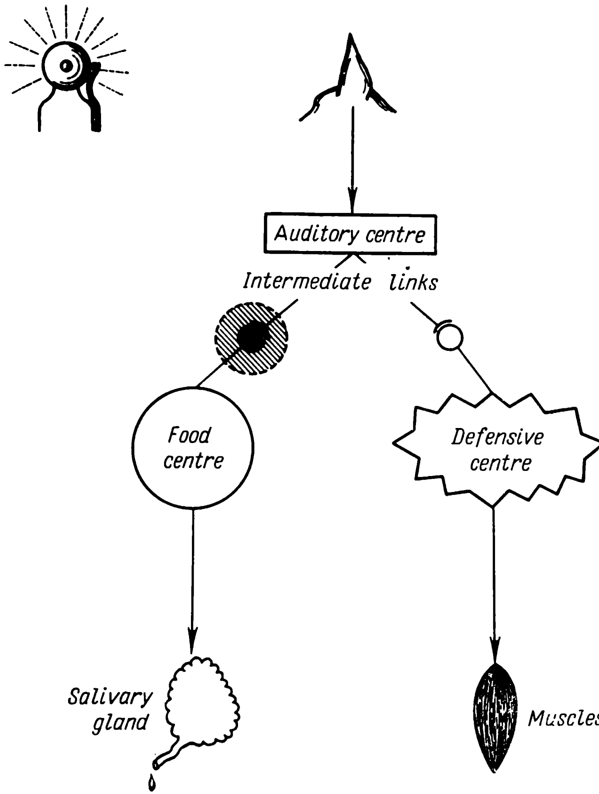


Fig. 19. Arc of double conditioned reflex. Shaded spot shows point of origin of inhibition during extinction of food reaction

soon became extinct. In response to the bell the dog now only lifted its paw, displaying no signs of a food reaction. Quite obviously, the internal inhibition of the food reflex did not arise in the centre of the conditioned signal, since that signal continued to be received by the animal, producing a defence reaction.

Perhaps, then, inhibition develops in the centre of the unconditioned reflex? Other experiments, however, cast doubt on this too. Y. A. Romanovskaya and L. I. Chilingaryan extinguished the defence reflex in response to the bell and at the same time determined the excitability of the area of the cortex corresponding to the stimulated paw. It was found that at the moment when the paw reaction had ceased, the excitability of the motor centre remained high. Only later did the excitability of the motor centre fall below its initial level. It may therefore be assumed that the inhibition process originates in intermediate links of the conditioned connection, spreading from there, with further inhibition, to the centre of the unconditioned reflex and the signal receptor.

It is not hard to see the advantage to the organism from this sequence in the development of the inhibition process. The blockage of communications, while breaking a temporary connection no longer needed by the organism, leaves open the possibility of further use of both the receptor and the effector centres, which greatly extends the regulative functions of the cortex.

We thus see that in different specific conditions central nervous formations are inhibited by different mechanisms, various nerve structures

within definite limits playing either a primarily inhibiting or a primarily inhibited role. Such a "division of labour" does not conflict with the principle of the defensive-protective function of inhibition. This is principally because protective inhibition is inherent in the very nature of living nerve tissue. The nerve fibre is amazingly indefatigable. Excitation impulses can travel along it in an endless stream, yet the properties of the nerve remain practically unchanged. All this is true, however, provided we are dealing with a normal, undamaged nerve. No sooner is a crystal of a chemical substance applied to a section of the nerve, or is it treated with cold, or subjected to the action of a sufficiently strong electric current than the section begins to undergo profound changes: an initial decline of excitability, temporary excitation, and repeated profound inhibition. Vvedensky made a deep study of the changes occurring in a nerve that is damaged. The facts he established led him to advance a theory of the transition from excitation to inhibition and vice versa. The great Russian physiologist named this the theory of parabiosis (parabiosis—"next to life"), thereby implying that profound inhibition is like an intermediate phase between the normal state of the nerve tissue and its death. Earlier we pointed out that the biological meaning of Vvedensky's parabiosis consisted in the protective-restorative properties of inhibition, whatever part of the nervous system it arose in.

The process of inhibition is therefore characteristic of every nerve formation and, possibly, of every living tissue of the organism. But how,

in that case, are we to understand the existence of special inhibition apparatus, special inhibition cells (of the Renshaw cell type), and special inhibition synapses? The fact is that the *property of inhibitability,* like the property of excitability, is pronounced to a *different* degree in *different* nerve structures. In some structures inhibition arises very readily, and in the overall activity of the central nervous system they therefore play a predominantly inhibitory role. Other structures are marked by a preponderance of excitation, with the transition to inhibition more difficult. These structures play the role of activators of nervous responses. It need scarcely be explained that the *relative specialization* of the nerve elements *in excitation and inhibition processes* makes the nervous system and its highest department, the brain, exceedingly flexible and labile, imparting an infinite diversity of nuances to their activity.

A reference should be made here to a principle of the operation of the central nervous system that will be discussed in detail in the next chapter. In the process of the historical evolution of living beings the mechanisms of inhibition have undergone continuous perfection and become more complicated. The ancient and cruder mechanisms have not disappeared altogether, but have been relegated to the background, making room for later acquisitions. Thanks to this, highly developed organisms have become able to make rational use of mechanisms of different degrees of complexity.

Let us return to the case of the nerve fibre. In order that the central nervous system should

function efficiently, it is necessary for the nerve to serve as a reliable and undefatigable conductor of impulses. Nature has removed from the nerve the function of inhibition and transferred it to other, specialized formations, the junctional points of the fibre with the body of another nerve cell or with an effector organ, such as a muscle. But let us assume that, as a result of injury, the exposed nerve conductor is subjected to the action of external temperatures, is traumatized by a bone splinter, and experiences an oxygen deficiency through impairment of the blood supply. Clearly, in this new situation excitation impulses would exhaust the damaged and weakened section of the fibre. Accordingly, the ancient mechanism of inhibition, latent in the nerve tissue itself, comes into play. A local reversible blockage of the excitatory impulses is formed, and the conditions thus arise for preserving the vital functions of the nerve until the organism repairs the damage done by the injury.

There is reason to think that something like this takes place in the nerve cell itself. The mechanisms of its connection with other cells (synapses) are so adjusted that weak stimuli first of all switch on inhibiting devices, thanks to which the cell is protected from unnecessary excitation over minor causes. This, however, is not simply an absence of sensitivity. In response to weak "subthreshold" stimuli, the cell undergoes a process of preparation for forthcoming activity, with a prophylactic rise of the energy potential, which is evidenced by the cell's increased resistance to strychnine and to oxygen deficiency under weak stimulation. When the

incoming excitatory impulses exceed a certain value (excitation threshold), the activating synapses gain the upper hand over the inhibitory, and an excitation process develops in the cell, spreading along its axon. The inhibitory feedbacks to which we referred above always restrict and restrain the excitation process, preventing a convulsive discharge. What is more, during the excitation period the activity of the inhibitory mechanisms, far from stopping, increases continuously. If the influx of excitatory impulses is relatively small, it gradually proves insufficient to maintain the excited state of the cell, is suppressed, and becomes extinct. Adaptation and habituation set in, which constitute the first line of defence against overexcitation and breakdown.

Now let us consider another case. The influx of excitatory impulses mounts. The inhibitory synapses prove unable to counteract the excitation of the nerve cell. In this case the more ancient and universal mechanism of transmarginal inhibition is brought into play. It is still difficult to say at present where this inhibition is localized in the excitatory synapses or in the cell bodies themselves. The one thing that is clear is that the cell itself does not remain aloof from these developments. This is illustrated graphically by the sharp rise in the readiness of the cellular protoplasm to assume a coloration during the secondary decline in excitability.

The picture is made much more complicated by the fact that transmarginal inhibition arises by no means simultaneously in the elements of different centres of the central nervous system.

The specialized electrophysiological investigations of V. S. Shevelyova have shown that in the event of such strong influences on the organism as penetrating radiation, prolonged stimulation with electricity, and mechanical injury, inhibition arises first of all in the knots of the sympathetic nervous system, which regulates the so-called vegetative functions: the blood circulation, respiration, digestion, etc. This is followed by blockage of the centres of the hypothalamus and cerebellum, which are likewise closely associated with the vegetative functions. It is only after this that inhibition develops in the cortical nerve cells. The changes listed have the features of a pathological process, since the dislocation of vegetative functions is bound to affect the state of all the parts of the brain, including the cortex. At the same time the blockage arising at relatively low levels and indirectly inhibiting the higher centres of the brain for a time makes it unnecessary for them to use their own mechanisms of extreme defence measures: transmarginal inhibition. This gives the cortex a certain reserve of time to mobilize the defensive powers of the organism, and it is able to act as the supreme organizer of the campaign against the pathological changes.

By means of these examples we have been trying to show that the existence of special inhibition mechanisms and the unevenness of the development of inhibition in various centres of the central nervous system are not at variance with the concepts about the universal nature of the protective-restorative properties of the inhibition process.

The protective-compensatory function of inhibition and the utilization of every case of transition to the inhibited state for "preventive maintenance" in order to restore the capacity of the nerve cells to work are thus the first important principle of the reliability of the brain. This principle is backed up by the combined activity of most diverse mechanisms, ranging from the inhibition inherent in elementary nerve formations to the complex systems of the interaction of excitatory and inhibitory synapses, the activating and suppressing influences of the reticular formation of the brain stem, and the apparatus of the internal inhibition of conditioned reflexes.

4

LATENT RESERVES

The evolutionary process that living beings have been going through for millions of years has been accompanied by the ever greater specialization of the nervous centres. A very distinct division of "duties" may be observed in the higher animals and man among the central nerve formations, each of which controls certain of the complex organism's functions. For instance individual segments of the spinal cord are connected with definite parts of the body: areas of the skin, groups of muscles, and internal organs. Higher up, in the medulla, there are specialized centres of respiration and blood circulation; damage to these centres is at once fatal to the animal. Still higher, in the diencephalon, physiological analysis reveals apparatus controlling the body temperature and the gas composition of the blood, the food centre, and the centres of thirst and sexual activity.

Research over the past few years has disclosed the extremely complicated internal structure of these centres. Indeed, it has left the impression that each centre consists of two main parts that have opposite influences upon the regulated function. Highly indicative in this

respect are the experiments with the food centre, which appears to consist of two centres: a centre of hunger and a centre of satiety. If by means of electrodes inserted deep into the brain matter we stimulate electrically the centre of hunger, an animal that has been fed to satiety will return to its food bowl and continue eating. Stimulation of the satiety centre, on the other hand, makes a hungry animal indifferent to its food. Similar results are obtained when these centres are destroyed artificially. An animal with a destroyed centre of satiety becomes extremely gluttonous and grows terribly fat, whereas an animal deprived of its hunger centre can perish from exhaustion in a cage full of food. Analogous data have been obtained in studying the centre of thirst, the respiration centre (inhalation and exhalation sections), and certain others. It is not quite clear whether there really exist only positive and negative sections within each or whether it is actually a case of different parts of a single centre having different physiological characteristics, differing in excitability and inhibitability, a case of a quicker or highly difficult transition from excitation to inhibition and vice versa. A great deal here will have to be established by further experiments.

Some scientists are inclined to divide the entire central nervous system into "+centres" and "— centres", into excitatory and inhibitory centres. However, by no means all the experimental findings fit into such a scheme. For example, it was found that the stimulation of one and the same point of the reticular formation of the medulla may evoke either inhibitory or excita-

tory effects, depending upon the functional state of the nerve cells. At the same time the relative division of nerve structures into primarily excitatory and primarily inhibitory appears to be a highly expedient principle of classifying regulative formations, since their joint activity in opposite directions maintains the vital "constants" well: the optimal values of the body temperature, the blood pressure, the level of metabolism, and the content of sugar, oxygen, and carbon dioxide in the blood circulating through the body.

The specialization of the nerve centres was demonstrated very clearly and convincingly in experiments involving the so-called "self-excitation" of animals, first staged by J. A. Olds and P. Milner in 1954. Thin electrodes were grafted in various parts of the brain of white rats. Current was fed to the electrodes only provided the rat pressed a special lever with its paw. As a result, some extremely interesting phenomena were observed. With one arrangement of the electrodes in the brain, rats would spend hours beside the lever, pressing it up to 7-8 thousand times an hour. But with a different arrangement of the electrodes, a rat would only press the lever once and never touch it again. By altering the food excitability of the rats, by giving them chemical substances called hormones, by studying the significance of their diet and sexual cycle, and by the post-mortem examination of the position of the electrodes in the brain, the scientists found that the animals had pressed the lever repeatedly if the electrodes had been in the satiety section of the food centre or in the centre of sexual activ-

ity. If the animals, however, had refrained from self-excitation, this meant, as a rule, that the electrodes had been in the defensive centre, whose excitation is accompanied by emotions of pain, rage, or fear.

This "division of labour", or pronounced specialization of the nerve centres, is also characteristic of the highest part of the brain, the cerebral cortex. For example, in the area of the central fissure, on the boundary dividing the frontal from the parietal lobe, we find the effector motor centres and the terminal station of the nerve impulses arising in movements; it is here that the so-called kinaesthetic analyzer has its cortical representation. This is the destination of impulses from sensitive formations embedded in muscles, tendons, and joints. Situated in the posterior central fissure is the tactile analyzer, which receives the tactile signals from the skin receptors. It is noteworthy that the size of the cortical areas associated with the task of regulating the movements of certain organs corresponds to the complexity of the organ's functions rather than to its absolute size. Fig. 20, reproduced from a book by the Canadian physiologist W. Penfield, shows schematically the size of the cortical areas representing the organs of speech, the hands, feet, torso, etc. It is evident that the control of the lips, tongue, and wrist (the organ of human labour) involves a far greater mass of cortical cells than does the control of the torso and feet. The cortical part of the visual analyzer is situated in the occipital lobes of the cerebral hemispheres; the cortical part of the auditory

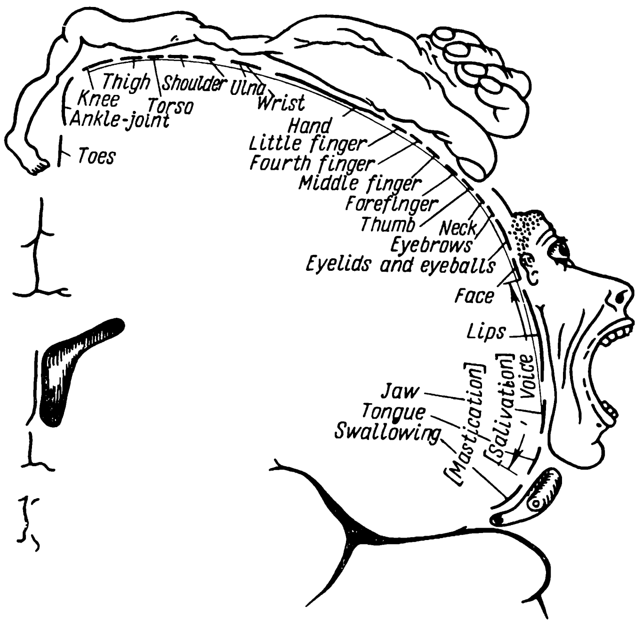


Fig. 20. Various organs represented in the motor zone of human cortex (W. Penfield and T. Rasmussen)

analyzer, in the temporal lobes. Under the influence of social life and collective work there arose centres of speech functions in the human cortex. It is these centres that enable us to receive word signals, verbal and graphic, as well as to produce them.

Numerous investigations show that the process of the evolution of living beings is accompanied by the increasing specialization of

the nerve centres. For instance, in the poorly-developed cortex of the cerebral hemispheres of birds there is practically no strict localization of function; in the case of the ungulata and beasts of prey localization becomes more definite, while in man it is most clearly defined. In mature animals the localization of functions is more pronounced than it is in their young. It is interesting to note that such a relatively young function of the human brain as speech, which arose recently, is associated with the activity of definite areas of the cortex less rigidly than the reception of direct sensory (visual, auditory, tactile, etc.) signals.

The progressive specialization of the nerve centres undoubtedly played an important part in the evolution of the regulative activity of the brain, making it swifter, more flexible, and accurate. At the same time it presents a certain hazard to the general reliability of the central nervous system. Indeed, when a highly specialized centre goes out of action, this entails the loss of a certain function and, hence, a profound and irreparable disturbance of brain activity. How has nature got out of this difficulty, how has she overcome this contradiction? It appears that in the process of evolutionary development the higher centres of the brain, along with a "division of labour", have acquired and retained a very high plasticity, a faculty of the nerve centres *to substitute for one another*. This principle of cortical activity is most pronounced in animals with a simple organization.

The American scientist K. S. Lashley studied the effect of the surgical removal of various

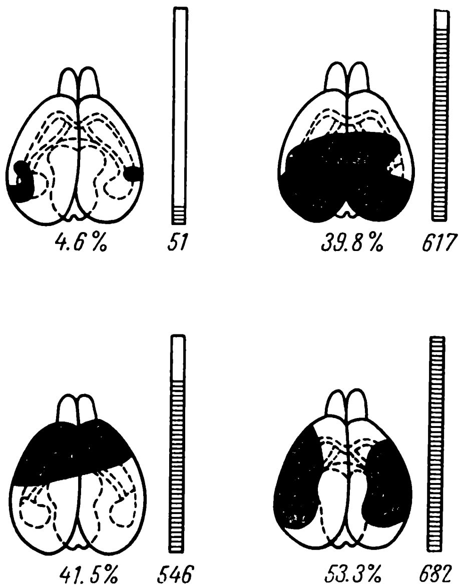


Fig. 21. Dependence of number of errors upon mass of removed cortical matter (K. S. Lashley)

Removed areas are shown in black; figures under the brain indicate percentage of decortication in relation to total surface area of the cortex; figures under the columns show number of errors in testing rat in maze

parts of the cortex upon the ability of rats to find their way out of a maze. He established that the correct or erroneous actions of the rats depend not on the site of the damage, but on the total mass of the cortex removed. The diagrams in Fig. 21 show that the removal of a small mass of the cortical substance leads to a small number of errors, which however increases steadily with the removal of larger areas. These experiments led Lashley to the conclusion that all the parts of the cortex are of equal value to the organism.

A serious conflict thus arose in the study of the brain. On the one hand, numerous experiments involving the excitation and damaging of individual areas of the cortex pointed to a definite specialization of the nerve centres, especially in the higher animals and man. On the other hand, the observations of physiologists and clinicians indicated that the impairment of functions as a result of damage to individual cortical zones is often temporary and reversible. Much clarity was introduced into this complex and involved problem by the work of Pavlov.

The investigations in question involved the use of both the old technique of removing various parts of the cortex and the method of conditioned reflexes, the development of a food reaction to auditory, light, and other similar conditioned signals. It had been noticed before Pavlov's experiments that the removal of the occipital lobes of the cortex altered a dog's behaviour substantially. The animal's sight remained intact: it was able to avoid obstacles and turned to a bright light. But at the same time

it ceased to recognize its master and remained indifferent to the sight of a running cat. "It sees, but does not understand", was said of such animals. The objective Pavlovian method of conditioned reflexes made it possible to get to the bottom of these phenomena. It was found that a dog whose occipital lobes had been removed could be conditioned if light were combined with feeding. After a time the dog would salivate in response to light alone. If, however, we were to try to condition the dog to respond to a complex visual signal, such as an object of definite shape or its movement in space, we would find that no temporary nervous connection is formed even after a large number of pairings.

Quite analogous results were obtained when the auditory zone, situated in the temporal area of the cortex, was removed. After such an operation a dog would still be able to distinguish noise from a definite tone and a loud sound from a weaker one, but the ability to distinguish tones, let alone semitones, would vanish completely. On the basis of these experiments Pavlov came to the conclusion about the *dynamic localization* of functions in the cortex. Pavlov assumed that every cortical analyzer—the visual, auditory, olfactory, etc.—consists of two main parts: the nucleus of the analyzer and its peripheral elements. In the occipital regions of the cortex, for instance, there is a concentration of nerve cells specializing in the reception of visual signals. This is the nucleus of the visual analyzer, and it is essential for the fine discrimination of light stimuli. But apart from this

nucleus, other, at times far-removed areas of the cortex, have dispersed visual cells.

The findings of several scientists (a great deal has been done in this field by the Soviet psychologist and neuropathologist A. R. Luria) justify the assumption that in normal conditions the dispersed elements of the analyzer assure its contact with other cortical centres. Thanks to the dispersed elements, visual, auditory, and other stimuli are incorporated in the systems of nervous connections that form the basis of the complex acts of behaviour of animals and man. The peripheral elements of the analyzer perform the "secondary treatment" of the signals first received by the nucleus. Should the nucleus of the analyzer be damaged, the dispersed elements assume the functions lost by the corresponding brain centre. True, they are unable to replace the nucleus of the analyzer altogether; without the nucleus their activity becomes cruder and more primitive, but it is the mobilization of latent reserves that enables the organism to make good the loss of the principal receptor centre.

Pavlov's views have been corroborated by the latest electrophysiological experiments. The use of sensors to measure action potentials from various points of the cortex makes it possible to record the electric potentials arising when the sense organs are stimulated. If sound stimuli are employed, the active points will be found to be most numerous in the temporal regions, where the nucleus of the auditory analyzer is situated. The further the sensors are from the epicentre of the auditory area, the

rarer and weaker will be the electric responses to the sound stimuli. Modern electronic techniques have made it possible to chart something in the nature of a map of the central and peripheral elements of the analyzer and to obtain graphic evidence of the "superimposition" of the periphery of one analyzer upon the periphery of another, that is of the overlapping of various analyzer systems. What is more, electrophysiological techniques have clarified our notions about the cortical centres that have no clearly-defined boundaries at all and therefore cannot be pin-pointed by the method of removing parts of the cortex. This applies specifically to the localization of the cortical centres of the internal organs. The analyzer of the signals from the internal organs evidently has no clearly-defined nucleus like that of the auditory or visual centre. It is represented by elements scattered through various parts of the cortex. Electrophysiological investigations, however, have not only backed up Pavlov's concept of "dispersed elements", but have enriched science with fundamentally new information. The study of the cortical analyzers by registering electric potentials has revealed that the stimulation of one and the same sensory nerve, or receptor, produces electric responses in two areas that are far removed one from the other. There is reason to think that such cortical "duplication" has a twofold biological meaning. On the one hand, effector organs may be drawn into the reactions of the organism to the most diverse factors through interaction with different regulative formations of the cortex. On the other hand,

double, if not multiple, representation in the cortex assures a great reliability of the higher regulation of vitally important functions of the organism.

Thanks to the theory of the dynamic localization of functions in the cortex, it has not only been possible to reconcile the conflicting results of experiments involving cortical stimulation and the removal of various regions of the cortex, but to discover the remarkable adaptability of the living organism to possible damage of its "control panel".

Investigations over a period of many years have made it possible to extend Pavlov's principle of dynamic localization to other parts of the central nervous system, specifically to the spinal cord. The partial transection of the spinal cord in dogs causes a profound disturbance of the functions of standing and walking. This is quite understandable, since the surgeon has cut the conducting fibres from the brain to the muscles and from the muscles to the brain. At the same time damage was done to the nerve centres of the spinal cord itself. The dog "does not feel" the lower half of its body and cannot "control" its limbs. With the passage of time, however, the motor functions are restored to such an extent that a dog operated upon can hardly be distinguished from a healthy animal (Fig. 22). What has happened? The regeneration of the conducting fibres is practically impossible. Although nerve cell processes are capable of growth, a barrier of cicatricial supporting tissue has arisen in their path and the destroyed nerve cells of the spinal cord are for-

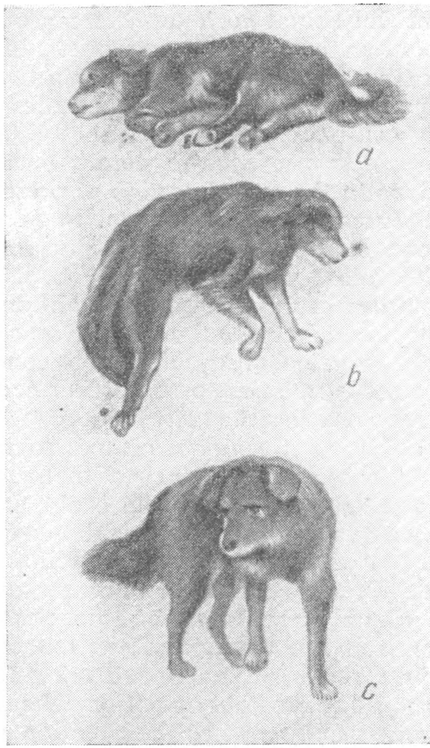


Fig. 22. Restoration of functions of standing and walking in dog after median transection of spinal cord
a—2 days later; **b**—15 days later; **c**—30 days after operation

ever lost to the organism. There can therefore be only one answer to the question formulated above: in the spinal cord too there are reserve roundabout pathways for excitation impulses, and there is a reserve of nerve cells in the spinal cord capable of taking over the duties of the destroyed centres.

The principle of the dynamic localization of functions in the spinal cord is at present supported by some Soviet scientists. Not long ago it was corroborated once again by the electrophysiological experiments of L. S. Gambaryan, who demonstrated that, in addition to the well-known conductors of muscular sense, there are in the dorsicolumns additional conducting tracts from the muscles to the higher centres of the central nervous system.

The ability of the nerve centres to readjust their functions is truly amazing. In the foregoing we pointed out that in the brain there are centres innervating the flexor and the extensor muscles. Let us now perform the following experiment. Under anaesthesia let us sew the tendons of an animal's flexor muscles to its extensors, and the tendons of the extensors, to the flexor muscles of that leg. During the first few days following the operation the animal will be quite helpless: when the situation requires of it that it bend its leg, the excitation of the flexing centres will cause it to be extended. This, however, will be a temporary phenomenon. Some days later the dog will have learned to use this leg no worse that the other three. The nerve centres will have been "retrained": the flexing centres will have assumed the duties of

the extensors, while the extensors will have acquired the properties of their antagonists.

What is more, it is possible to sew together nerves that are quite different in the character of their influences, such as the nerves of the brachial plexus of a front leg and the vagus nerve, which transmits regulating signals to the heart, the stomach, and other internal organs (J. Erlanger, P. Anokhin, and others). In the latter case some quite remarkable paradoxes were observed. The stimulation of the skin of the foot would cause not the flexing of its muscles, but coughing and vomiting movements. Conversely, the foot would move in accordance with the periodic contractions of the stomach. The dog would appear to have become a complete invalid. But time is a great healer, and the aptitude of the nerve centres for "retraining" is enormous. The vagus nerve centre gradually becomes a regulator of limb movements, while the motor centres of the leg "learn" to control the lungs, heart, and stomach.

What is it that made possible these miraculous transformations of the nerve centres and played the key role in their readjustment? This will be described later in the book. In the meantime, let us sum up what has been said.

The second basic principle of the reliability of the central nervous system of animals and man is the combination of the high specialization of the nerve centres with their flexibility and plasticity, the ability of these centres to undergo a dynamic readjustment of their functions and to replace damaged or completely destroyed structures, as well as the existence of reserve conducting tracts.

5

INDEPENDENCE AND CENTRALISM

Let us remove a dog's cerebral cortex. When the animal recovers from the immediate effects of so severe an operation, we find that its behaviour has experienced a substantial change. The dog does not recognize its master, it does not react when called. Its world has become meagre and primitive. Indeed, it can perish of hunger in a room where there are hunks of meat strewn about and bowls of water. The decorticated dog has completely lost the ability to learn, to develop conditioned reflexes. The thousands of stimuli that used to prompt it to perform complicated actions—the sight and odour of food, the barking of other dogs, the approach of a cat, the sight of an open door leading into the street—have ceased to have any effect upon it. But the dog has not lost its ability to move. It roams the room for hours, fleeing from sharp or hot objects, chewing food, if the food is put in its mouth. The dog has been deprived of the supreme cortical regulators of its behaviour. All its movements are now governed by the activities of the lower, subcortical motor centres. Their functions are simpler, more stereotyped and primitive, but these centres go on working.

Now let us transect the spinal cord of another dog. The back half of the dog's body will be paralyzed; the feet will drag along the ground. The signals from the diencephalon, the midbrain, and the medulla no longer reach the muscles of the caudal extremities. Yet if an electric current is applied to a rear foot, the dog will jerk the foot away. This happens because the centres of the spinal cord situated below the point of transection continue to function. The movements have become cruder and more mechanical, but they do take place, since the spinal centres operate.

Now let us cut the nerves leading to the muscles. If we now again stimulate the skin of the foot with an electric current, pinch it, or prick it with a needle, the foot will remain motionless. The muscles are, however, alive, and, most important of all, they have not become incapable of contracting. It is enough to apply an electric current to the muscle tissue itself, to observe its contraction. Moreover, a muscle deprived of connection with the central nervous system becomes more sensitive to the direct action of chemical stimuli, hormones, supplied to the blood by the endocrine glands. Left to itself, it lives and operates with the aid of the most ancient mechanisms of chemical regulation and its own reactivity to direct stimulation.

The mechanisms of automatic self-regulation that arose millions of years ago have been retained by the higher animals. A heart removed from the organism will contract for hours if blood enriched with oxygen is made to flow through its vessels. A segment of the small in-

testine brought out under the skin continues its peristaltic movements thanks to the "local" nerve network that permeates the intestinal wall. The vessels of a rabbit's ear deprived of all nervous connections with the organism will contract and dilate under the influence of chemical substances introduced into the blood. But how simple and crude the reactions of the muscles, heart, and vessels appear, when they are controlled only by their own mechanisms or the lower spinal centres!

Twofold, threefold, and fivefold regulation means something more than just the simple duplication of the functions of some centres by others. Every new level of regulation makes the work of the effector organs more complicated, more refined, and more perfect; it makes that work more useful and valuable to the organism as a whole. This applies above all to the cerebral cortex, the highest regulator of functions.

Workers at our laboratories (N. S. Djavadyan, V. S. Kulikova, T. A. Maltseva, A. A. Markova, Y. M. Pressman, Y. A. Romanovskaya, P. V. Simonov, B. D. Stefantsov, S. A. Chesnokova, and many others) have carried out a comprehensive study of the changes in the various functions of the organism following decortication. The experiments revealed that all these functions are retained: the animals walk, their hearts beat, their lungs are ventilated, they digest their food and void urine. But how simplified the activities of the internal organs become! Fig. 23 shows charts illustrating the magnitude and dynamics of reflex gastric juice secretion in a dog fed with meat, bread, and milk. Already in

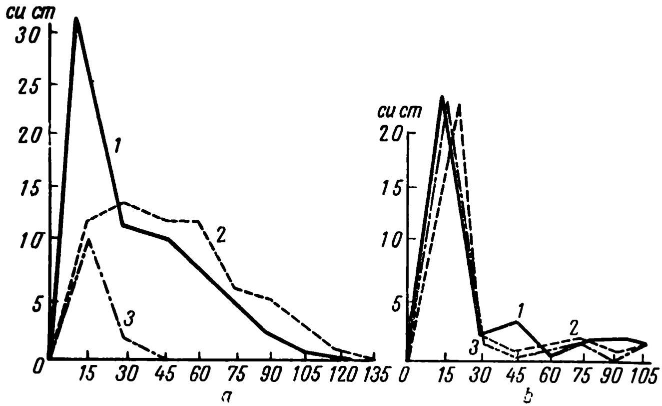


Fig. 23. Effect of bilateral decortication on the activity of gastric glands in a dog fed with meat (*1*), bread (*2*), and milk (*3*)

a—normal; b—after total decortication. Amounts of gastric juice in cu cm are plotted as ordinates; the time in min, as abscissas

Pavlov's classic experiments it was established that in a normal dog every type of food produces a specific pattern of secretion. Following bilateral decortication, this delicate adjustment of gastric juice secretion to the character of the food vanished: meat, bread, and milk all began to produce identical secretion.

There remained the possibility that the deterioration in stomach activity was not due to decortication, but had been caused by severe operative trauma. A control experiment was staged. A dog has only one stomach, but it has twin salivary glands on each side. Let us remove the cortex of one hemisphere and observe how

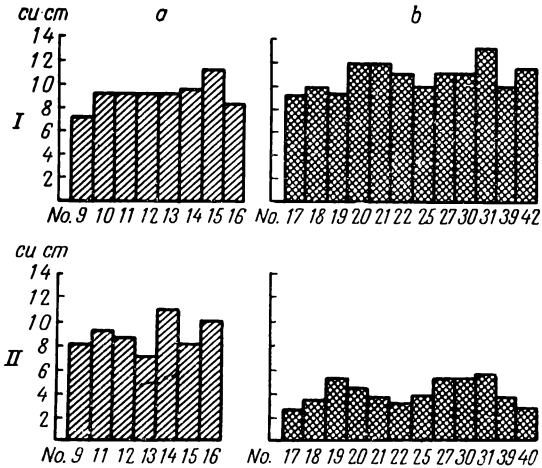


Fig. 24. Reflex salivation (columns) in dog in response to 30 g of rusks before and after removal of cortex of left hemisphere

I—right parotid gland; II—left parotid gland. **a**—before operation; **b**—after operation. Amounts of saliva in cu cm are plotted as ordinates; test numbers, as abscissas

the activity of the salivary glands is affected. Fig. 24 shows that whereas on the healthy side the work of the salivary gland has not changed, the secretion of the gland deprived of cortical regulation has been drastically suppressed. This means that we are dealing not with an operative trauma, but with the effects of the decortication of one half of the brain.

A deficiency in the regulation of the functions of the internal organs becomes especially apparent when additional exertion is required of

the organism, when it is subjected to extra strain. Even small motor excitation produces intense palpitation of the heart and panting in decorticated dogs, which tire extremely quickly. They are also less resistant to such harmful factors as infection, loss of blood, and penetrating radiation. The well-being of decorticated animals is deceptive. The preservation of the main vital functions is but apparent, concealing their weakness and inadequacy.

Existing concepts in neurophysiology about the different levels of integration in the central nervous system, Pavlov's conception of the cortical representation of unconditioned reflexes, the experimental findings of a large group of research workers, and the extensive data of other investigators have made it possible to build up the notion of the "multistoreyed" structure of the inborn unconditioned reflex arc. According to this notion, excitation is transferred from the afferent pathways to effector pathways in various parts of the brain (from *I* to *V* in Fig. 25). Every reflex—the defensive, food, orientating, sexual, etc.—has its own centres, its own representation at various levels of the central nervous system. When higher centres are cut out, this does not entail a complete loss of the corresponding function, but makes it cruder and more primitive.

An unconditioned reflex must be represented in the cortex for the response to be incorporated in a system of conditioned reflex connections. It is the cortical centres that make possible the defensive, food, and similar responses to auditory and light signals, to distant heralds of effects

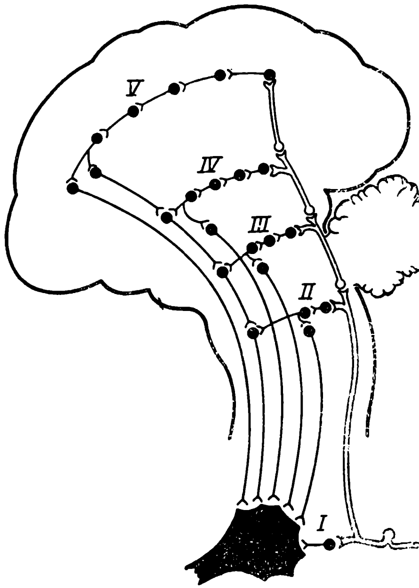


Fig. 25. The "multistoreyed" structure of the unconditioned reflex arc

I, II, III, IV, V—levels of the brain

important to the organism. In Pavlov's laboratories his desciples and followers (particularly notable work has been done in this field by K. M. Bykov) have demonstrated that the activity of any internal organ can be called forth or altered by a conditioned reflex mechanism. In decorticated animals the conditioned regulation of internal organs disappears.

Does this mean that unconditioned reflexes interact only at the cortical level? No. Since

every unconditioned reflex is represented in subcortical areas of the brain, certain forms of interactions between reflexes are also possible at the subcortical level. N. Y. Vvedensky and A. A. Ukhtomsky's school in its day established and subjected to a comprehensive study the important general principle of the activity of the central nervous system that later came to be known as dominance. It was found that the formation of a seat of strong excitation in one of the brain centres causes the inhibition of other reactions, the stimulations usually producing these reactions acquiring the property of fortifying the dominant seat. When, earlier, we considered the question of the external inhibition of conditioned reflexes (p. 78), we mentioned a case that can actually serve as an example of cortical dominance. But dominance is a universal principle of the work of the central nervous system. A dominant seat of excitation can also be set up in subcortical formations and even in the spinal cord (Fig. 26).

When a syringe with milk is emptied into a rabbit's mouth, the animal sits still and swallows the milk. But when a stable excitation of the defensive centre, with the features of defensive dominance, is induced in the same rabbit by special methods, its reactions change drastically. The feeding procedure with the introduction of the syringe into the mouth now produces violent motor excitation: the rabbit refuses to eat and tries to break loose. Only isolated swallowing movements can be observed.

The inborn reflexes of decorticated animals yield to certain training. The first few days after

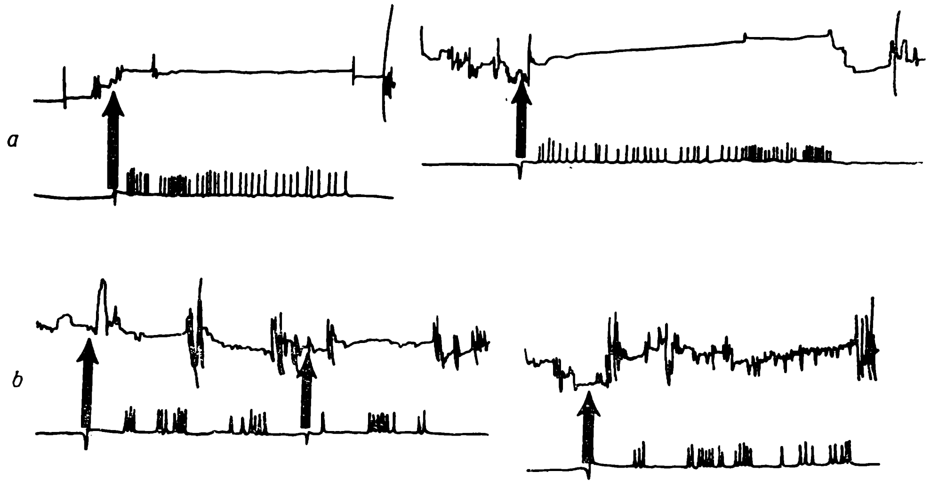


Fig. 26. Reactions of decorticated rabbit to introduction of food into its mouth under ordinary conditions *(a)* and under conditions of defensive dominance *(b)*

Top recording: motor reaction. Bottom recording: swallowing. Arrows indicate moment when syringe is introduced

the operation a rabbit, released from his cage, stumbles against surrounding objects. In about a month the animal learns to manoeuvre between them after lightly touching an obstacle with the tips of its whiskers. But when we irritate the whiskers of a sitting rabbit, there is no reaction of turning. Nor does the mere sight of an obstacle cause the running rabbit to turn, until it contacts the obstacle with the tips of its whiskers. On the seventh-ninth day following the operation the decorticated rabbit develops a motor reaction to the smell of food. As soon as a bowl filled with beets or grass appears in the cage, the rabbit experiences motor excitation, starts running about the cage, beating the floor with its hind paws, and smelling the air vigorously. In the days that follow the rabbit will come up to the food bowl, strike it with its front paws, and push it with its snout, but will not eat the food.

Not infrequently, decorticated animals will exhibit reactions very similar to conditioned reflexes. If a decorticated rabbit is subjected repeatedly (five-six times a day for four-six weeks) to painful stimulation of the ear, the animal begins to bend its head to the ground. The same response can then be evoked by touching the ear with a dull stick or a finger. Touching other parts of the body does not produce this reaction. Nor is it produced by the other stimuli (auditory and light) that always accompanied the pricking.

Decorticated animals thus exhibit two types of complex motor reactions. First, there are the general, diffuse movements that do not culminate

in a biological effect (the eating of food or the removal of the destructive agent). Secondly, there are the standard, automatic responses to stimuli directly connected with food or pain: the movement of the head upon irritation of a section of the skin, which has been pricked, the avoidance of an obstacle after touching it with the tips of the whiskers, etc.

What is it that the decorticated animal has lost? It has lost the faculty for delicately specialized responses to distant heralds of influences important to the organism; it has lost the faculty for full-fledged conditioning.

If we regard the conditioned reflex as a result of the synthesis, or combination, of two or more unconditioned reflexes, then experiments with decorticated animals enable us to judge what is introduced into the structure of the conditioned reflex by the subcortical centres of the brain and what belongs to the cortex exclusively.

In the process of coupling the conditioned reflex is known to pass through three main stages. The first of these is the stage of generalized reactions, in which the reflex is caused not only by the signal that was combined with the food or pain, but by many other stimuli, especially by such that are like the main one in character (for example, not only by the bright lamp that was switched on before feeding, but also by a weak lamp, by a flashing light, and even by a bell, all of which never coincided with the animal's feeding). This is followed by a stage of highly specialized reactions only to the stimulus that was combined with the food or pain (in our case the bright lamp). It should be noted

that this stage is characterized not only by a high standard of perfection and accuracy in analyzing the external signals, but by similar high standards in the performance of the effector organs. If the conditioned reflex developed is a motor one, the movement—in the stage of specialized reactions—will be most economical, expedient, and coordinated. Finally, the conditioning process is crowned by the automatic stage, in which the conditioned reaction acquires the features of a stereotyped, "memorized" response, resembling an inborn reflex.

In a definite sense it may be said that the process of the establishment of a new conditioned connection is each time a recapitulation, as it were, of the adaptive activity of living beings over thousands of years. Indeed, the diffuse, "disorderly" reaction in the form of general, poorly-coordinated excitation is highly characteristic of primitive groups of animals. Later animals acquired the ability to respond with precise reactions to very definite signals. The stimuli that for millions of years had retained their meaning for the organism (food, pain, an individual animal of the opposite sex) became signals of inborn unconditioned reflexes.

Our consideration of the interaction of the centres of unconditioned reflexes at different levels of the central nervous system leads us to formulate three important principles.

1. Although the simple forms of interaction between reflexes of the dominance type are universal and characteristic of all the centres of the brain and the spinal cord, there are substantial differences between the manner in which

these interactions take place at higher and lower levels of regulation.

2. In the undamaged organism the interaction of unconditioned reflexes at the lower and middle levels is always controlled by the higher levels and practically cannot be detected in naked form. Even such a "purely spinal" reaction as the familiar patellar, or knee-jerk, reflex is greatly influenced by higher centres right up to the cerebral cortex.

3. The process of the coupling and fulfilment of a conditioned reflex involves all the storeys of the realization of the unconditioned reactions concerned. Each of these storeys provides for a certain aspect of the conditioned act, the subcortical centres chiefly creating the general background activity, the energy "charge", and ensuring the biological direction. The general supervision over the use of the lower centres in effecting conditioned reflexes rests with the cortical level of coupling.

We have thus considered the participation of various brain centres in realizing unconditioned reflexes, in the dynamic relationships arising between unlike unconditioned reflexes, and in conditioned reflex activity. It is appropriate now to ask: what does the central nervous system gain from the combination of the relative independence of the lower centres with their subordination to higher regulative formations? First of all, this sharply enhances the reliability of the central nervous system and, hence, of the organism as a whole. The multiple duplication of regulation makes it possible, in an emergency, for the functions of lost or damaged links to be

"intercepted" by the centres of other levels, which are intact. Let the function in question be less elaborate—the important thing is that it will continue to be discharged and will fulfil its role in the animal or human organism.

But the duplication implied is a duplication of a special kind. The higher levels of regulation do not simply repeat the work of the lower; they impart new properties, a new quality to a function and give it a higher degree of flexibility and perfection. The higher the level of regulation, the closer the connection of each function (locomotion, respiration, blood supply, etc.) with the current activity of the organism as a whole, with the specific conditions of the environment.

Without repeating the activities of the lower brain centres or taking over their duties, the higher centres incorporate this or that function in the general adaptive reaction of the organism. We speak of this at such length because some authors visualize the cortex as some screen on which all the internal organs and all their parts are represented. It is hard to imagine how the cortex has the chance, in that case, to control man's external adaptive behaviour, including the launching of artificial Earth satellites and the creation of atomic power stations. Similarly, it is not clear what is left to the lower levels of the brain and what they are for, in general, in a highly-developed organism. Obviously, we have here a simplified presentation of the problem.

Some time ago we advanced the idea that what are anatomically projected into the cortex are *not individual organs and not individual functions* in their ultimate effector expression,

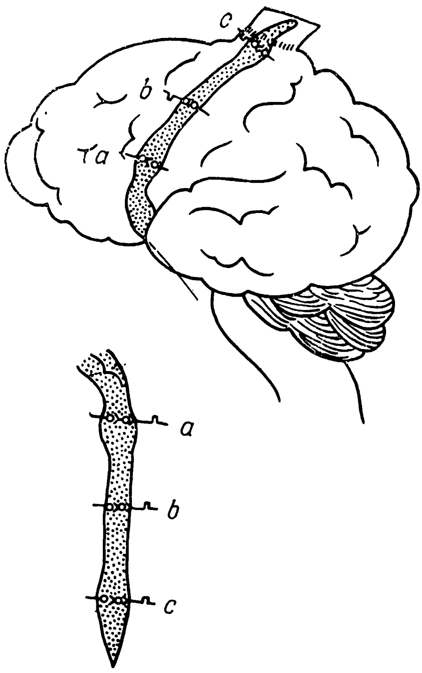


Fig. 27. Schematic picture of spinal cord projection in cortex

a, b, c—various reflex arcs coupled in spinal cord and areas representing them in cortex

but *lower centres of the central nervous system.* This idea is represented graphically in Fig. 27. By virtue of this arrangement, the cortex effects the generalized, integrated regulation of diverse functions of the organism through subordinate centres of the brain and spinal cord, making use of these specialized formations. Nature has freed the higher brain centres from elementary work, enabling them to engage in complicated creative activity.

The flow of information was distributed accordingly. Although the signals from the internal organs do reach the cortex, they do not bring about the excitation of the higher structures that form the basis of thought and speech: in normal conditions we do not feel our stomach, heart, or intestines. On the other hand, the external signals from the organs of sight and hearing are constantly in the "bright spot of the consciousness" (I. P. Pavlov), for the lower brain centres are unable to assess the real meaning of these signals, which may herald important events.

The third important factor assuring a high reliability of the work of the brain is thus the multistoreyed structure of the unconditioned reflex arc, the combination of the relative independence of the lower regulative formations (down to the mechanism of the self-regulation of organs) with their constant subordination to higher brain centres.

6

THE "SUPREME ORGAN" OF RESTORATION AND DEFENCE

In the previous chapters we have dwelt at length on the role the cortex plays in the normal adaptive activity of the higher animals and man. The experiments of physiologists and the observations of physicians appear to furnish weighty evidence in support of the view that the cortex also plays an important part in the restoration of impaired functions when the organism is subjected to very strong destructive factors (mechanical trauma, injury, burn).

Nevertheless, several scientists—among them, first and foremost, the German physiologist Bethe—until recently maintained the very opposite. By amputating the legs of frogs, birds, guinea-pigs, and dogs, Bethe and his followers came to the conclusion that the restoration of the impaired functions of standing, posture-maintenance, and walking is instant and automatic, not requiring any training. Later sections of the cortex of these animals were removed, and in this way it was found that the restoration of functions supposedly does not depend upon the higher centres of the brain. The results, obtained chiefly with lower vertebrates and birds

were declared to be equally valid for higher animals and man.

A quarter of a century ago we decided to check Bethe's findings and try to clarify this point of major theoretical and practical importance. The idea of such an investigation and its first results received warm support and approval from our teacher Pavlov in his day. With our co-workers (A. I. Karamyan, V. D. Dmitriyev, R. O. Barsegyan, B. D. Stefantsov, N. M. Shamarina, V. N. Drozdova, Y. A. Romanovskaya, L. S. Goncharova, Y. V. Maksimova, T. G. Urganjan, N. I. Nezlina, S. N. Ivanova, and many others), we produced various disturbances of the motor functions of animals (primarily dogs). This was achieved by the criss-cross sewing together of nerves, the fastening of the tendon of one muscle to the tendon of another, the severance of the nerves of some foot, the complete amputation of two paws, the partial dissection of the spinal cord, the destruction of the organs of equilibrium (the so-called labyrinths), the removal of the cerebellum, and other injuries. After such operations the scientists carried out close observations and comprehensive investigations of the resulting disturbances and the process of their elimination.

First of all, it was found that the restoration of the impaired functions is not an instant readjustment of the activity of the central nervous system, but a complex process of systematic training, exercise, and the development of new motor habits. Fig. 22 shows the gradual restoration of the functions of standing and walking in a dog that underwent a partial transection of

the spinal cord. Even these preliminary observations cast doubt on the views of Bethe's supporters that compensation is automatic readjustment of motor functions. The most interesting and clinching facts were, however, obtained by surgical decortication. It should be pointed out that, unlike Bethe, we performed not a partial removal of individual sections of the cortex, but complete decortication, as a result of which the experimental animal was completely deprived of its cerebral cortex. It was found that decortication leads to a *renewed disturbance of earlier restored functions;* moreover, these functions *are never again restored* in decorticated animals, no matter how long we wait for this to happen. The corresponding pictures in Fig. 28 show that decortication brought about the repeated impairment of the functions of standing and walking, recovered after a partial transection of the spinal cord. It is important to note that these disturbances were not a consequence of the decortication procedure itself, which of course is a case of severe surgical intervention. For one thing, control experiments involving the decortication of healthy dogs reveal that decorticated dogs stand on their feet well, walk about, and, indeed, differ little outwardly from normal animals. Secondly, the decortication of dogs operated upon earlier does not simply impair their movements, but upsets *the very functions* damaged by the first operation. Finally, the removal of the cortex of one hemisphere shows that the repeated impairment of earlier re-established functions takes place primarily on the side corresponding to the decorticated hemisphere.

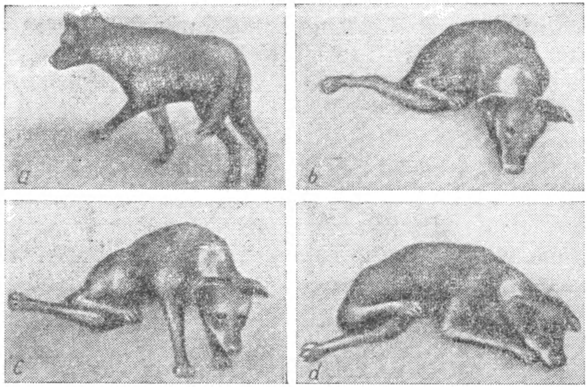


Fig. 28. Effects of decortication in dog earlier subjected to partial transection of spinal cord

a—one month after transection; **b, c, d**—after total decortication

These experimental results were corroborated by another series of experiments. In this series the animals were first decorticated, following which the motor functions were impaired in various ways: the spinal cord was dissected, paws were amputated, nerves were re-sewn. It was established that the decorticated dogs *had completely lost the faculty to restore impaired functions.*

Experiments over a period of many years, involving more than 100 dogs, which lived from a few months to several years after complete decortication, have led to the conclusion that *the cerebral cortex plays a vital and vigorous role in compensating impaired motor functions in adult higher mammals.* Accurate experimental

findings made it possible not only to refute the mistaken contention of Bethe's supporters, but to reveal some of the reasons for that misconception.

The fact is that the experiments of these investigators—Bethe himself included—were staged without due consideration for the age of the animals or the level of their organization. Physiologists have established that the younger the animal, and the lower and simpler its organization, the smaller the role played by the cortex in the activities of the organism. In insects, for instance, the central mechanism of the nervous system is in the form of a chain of ganglia, while in frogs, lizards, and birds the forebrain is known to be relatively poorly developed. Experiments performed at our laboratory have shown that in pups, rabbits, birds, frogs, and reptiles, unlike adult dogs, the removal of the hemispheres (in frogs and lizards, the forebrain) does not lead to the complete loss of restored functions and that disturbances re-established by the operation disappear with the passage of time. These facts show that the question of the restoration of impaired functions should be approached as a complex biological problem, with due consideration for the path traversed by living beings in the course of their evolution.

A detailed study of the process of the restoration of functions in experimental animals has made it possible to identify three main periods, or stages, in the state of the damaged nervous system. In the first few hours and days following the trauma (dissection or destruction of the spinal cord and nervous tracts) there arises a

phase of the suppression, or inhibition, of the functions of the central nervous system. This inhibition is defensive and protective-curative; it protects the sensitive nerve cells from overexcitation, exhaustion, and death, ensuring the period of rest needed for the restoration of the structures affected to this or that extent by the trauma. It must be remembered that, in addition to the nervous impulses from the site of the lesion, the cells are subjected to the action of the products of the decomposition of the dead tissues, an impaired blood supply, etc. This phase of inhibition later gives way to a period of increased excitability, of increased activity by the nerve formations drawn into the pathological process. This very important period is apparently characterized by the mobilization of secondary, "reserve" tracts, their training, the readjustment of interaction between nerve centres, the coupling of new connections between centres, and the development of new habits. Gradually the central nervous system becomes as efficient as it was. However, the training and perfection of the newly-formed mechanisms continue for a long time, until the impaired functions have been restored to a high degree.

Quite clearly, medical treatment in cases of injury to the human central nervous system should be conducted with due consideration for these phases in the restoration of functions. In the first period it is necessary to ensure, maintain, and in certain cases somewhat enhance protective-curative inhibition, since premature stimulation of the affected nerve structures can tax them beyond endurance. On the other hand,

the period of increased excitability should be used in every way to establish and train the compensating mechanisms. This is accomplished by means of massage, prescribed exercises, physical therapy, and the proper medicines. The experiments of T. N. Nesmeyanova, F. A. Brazovskaya, and Y. N. Iordanskaya at our institute demonstrated that the systematic training of the nerve structures of the spinal cord of dogs below the point of transection by moderate electric stimulation, the passive bending of the feet, and massage not only improve the functions of these structures, but also to a certain extent prevent degenerative changes in the nerve cells. Indeed, one is often amazed by the truly extraordinary compensatory potential of the living organism. To establish the existence of this potential and draw upon it is the most important duty of the medical practitioner.

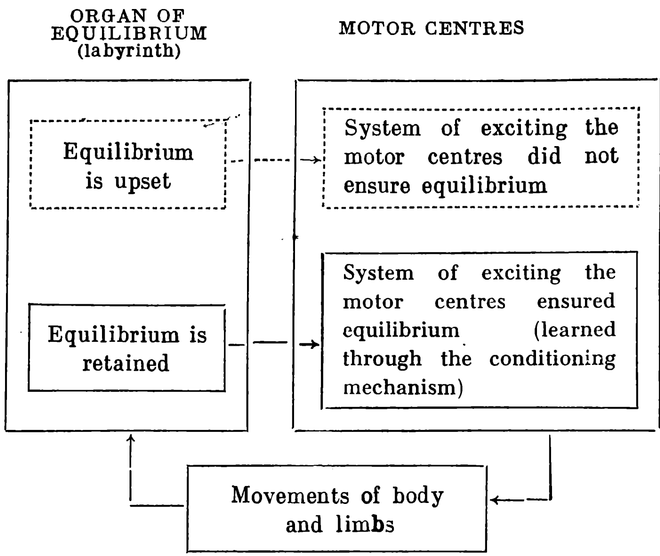
Scientists have often sought to establish the supreme and commanding link in the complicated process of the restoration of impaired functions. In recent years the Soviet physiologist P. K. Anokhin has greatly elaborated upon Bethe's idea of the "creative role of afferentation", i.e., of nerve impulses signalling to the brain about pathological changes produced by a trauma and, subsequently, about the progress of recuperation.

Indeed, information plays a very big part in compensation phenomena. The investigations of Anokhin and his co-workers have shown convincingly that the impulses informing the brain of disturbances that have arisen issue not only and not so much from the damaged organ itself,

but from the sensitive formations that are most affected by the dislocation. Thus in the event of the partial removal of the stomach, the signals will come from the lower sections of the intestinal canal, which will be receiving food not quite suitable for absorption. It is these impulses that will give an impetus to the mobilization of the mechanisms facilitating better chemical and mechanical processing of the food. Similarly, the restoration of the functions of standing and walking in an animal with an amputated foot takes place under the influence of signals from the labyrinth (the organ of equilibrium) rather than under the influence of signals from the stump of the removed foot.

Compensation is a process of gradual approach to the complete restoration of the impaired function. During this period the brain centres taking part in the compensation phenomena operate like complex systems of multiple feedback. The dog whose foot has been amputated is unable to keep its balance. It tries to get up, sways, and falls. This produces nervous impulses in the receptors of the internal ear, the organ of equilibrium; the impulses signal what has happened and make the animal repeat its attempts to keep its balance on three feet. In this way the signals from the internal ear serve as an impetus and give a start to the formation of new, changed relationships in the central regulators of standing and walking. These changed relationships assume the outward form of new motor acts, which in turn produce changed impulses from the internal ear. When the animal succeeds in keeping its balance for some interval

of time, the signals from the organs of equilibrium inform the brain that the necessary effect has been achieved, the conditioning mechanism then helps to learn the precise motor reaction of the body and feet, as well as the distribution of muscular activity, ensuring that the posture is retained. We have attempted to depict schematically the process whereby the position of the body in space is re-established.



The feedback mechanisms have long commanded the close attention of physiologists. As far back as 1826 Bell pointed to the important role of sensory impulses from the muscles in

effecting motor acts. Subsequently the problem of physiological feedback was dealt with by Sechenov, Samoilov, Magnus, Sherrington, Bernstein, Anokhin, Granit, Wiener, and others in their writings. The importance of the feedback principle to the adaptive activity of animals prompted Anokhin to subject to criticism the notion of a reflex as of a triple act effected according to the pattern: external signal—work of central mechanisms—response of animal (Descartes, Sechenov, Sherrington, Pavlov, and others). Anokhin considers every reflex act certain to contain a "fourth reflex link": "feedback afferentation", which signals about an accomplished or unaccomplished biological effect. Although Pavlov's teachings did contain the idea of a "fourth link" in the form of reinforcement (food, electric current, etc.) or the absence of reinforcement, the role of this link, in Anokhin's opinion, was not sufficiently appreciated and the reflex arc remained "uncoupled".

We feel that Anokhin's controversy with classic neurophysiology is due to a certain extent to the fact that regulative systems are being confused in this case with their activity, i.e., the reflex. The reflex arc incorporates three structural links: (1) the afferent (sensory) part, consisting of the receptor (eye, ear, nerve mechanisms in the skin and muscles), the pathways by which excitation impulses travel to the brain, and the corresponding nerve centres; (2) the central mechanism transmitting the impulses from the afferent to the effector part, and (3) the effector section, which, in turn, consists of the effector nerve centres, pathways, and effec-

tor organs. That the *anatomical* structure of the reflex is tripartite will not be challenged by Anokhin himself.

But the term "reflex" has a different meaning when it is used to denote the *functional unit* of the adaptive activity of animals and man. Can it be, perhaps, that in this context the reflex act consists of four rather than of three components? Perhaps Pavlov really did miss the fourth link? We believe, however, that this is not the case either.

The living organism in the Pavlovian view is not a stereotyped machine like a piano, which responds with a sound every time a key is struck. The living organism is a dynamic system in constant activity, the purpose of that activity being to maintain certain biological constants: its physico-chemical composition, its integrity. It is indeed permeated with feedback cycles that maintain optimal levels of the sugar content in the blood (state of satiety), the gas composition of the blood, the blood pressure, and, finally, the integrity of the organism, bearing in mind the possibility of damage to it by external destructive agents.

Pavlov understood stimulation (the push starting a reflex) to mean *a disturbing influence on an initially closed system:* pain or its portent, hunger or excitation of the food centre by a conditioned food signal. The second link in a reflex, according to Pavlov, is the central organization of activity directed at abolishing the deviation that has arisen. The third link in a reflex is the reaction partly or completely abolishing the deviation: the eating of food or the avoidance of

the electric current. Pavlov spoke repeatedly of the balancing of environmental influences as the basis of adaptation. It should be noted in passing that hunger too is a result of an environmental influence: of the absence of food in the environment.

In this way the existence of closed feedback cycles in the living organism does not conflict with the tripartite scheme of the reflex; on the contrary, it is in good agreement with that scheme, since the reaction of the cyclical system consists of *three* components: the disturbing deviation—activity—the restoration of the stationary state. Nor is this contradicted by the fact that not every reflex act is crowned by a *complete* biological effect. The absence of an effect serves as an impetus to repeated reactions, to the development of complex reflex chains. The principle of the "cycle" accounts fully for the maintenance of the constants (the content of sugar and oxygen in the blood, etc.) already produced by evolution, but cannot account for the *formation* of these constants, since a closed regulating cycle always presupposes some "programming" principle.

Phenomena similar to the restoration of the functions of walking, described above, take place in the event of the compensation of any damage to the central nervous system, effector organs, or sensory apparatus. Obviously, the "readjustment" of the nerve centres following the criss-cross sewing of the median nerve of the foot to the vagus likewise takes place under the influence of impulses signalling disturbances of the motor functions and the activity of the internal

organs: the heart, stomach, and lungs. But does this furnish any grounds for speaking of a "creative" role of impulses from the periphery? We think not.

In compensation phenomena, as in all adaptive acts of the living organism, signals from the outer world and from inside the organism play a very big part. To put it more simply, there could be no adaptive activity at all without external prodding. This was stated very definitely and convincingly by the father of Russian physiology Sechenov in his day. Any inborn or acquired reflex is certain to have an afferent (i.e., informative, directed to the brain) part in its arc. But information as such is meaningless in the absence of machinery to receive it and to transform it into effector signals. The nerve centres of the brain and, above all, the cerebral cortex are the cardinal and really creative unit determining the success or failure of compensation. But then, let "Mr. Fact", as Pavlov used to say, pronounce judgement on this.

Let us perform the criss-cross sewing together of the median and vagus nerves of a dog, wait until the impaired functions have been fully restored, and then remove the cortex. Fig. 29 (*c* and *d*) shows that *compensation has disappeared* in this case! The foot that could hardly be distinguished from a healthy one a short time ago now collapses helplessly in walking. Have the impulses from the sensory formations ceased? Does not the brain receive information about the recurrence of the trauma? All this continues, but the dog's organism has now been deprived of the supreme organ of compensatory adapta-

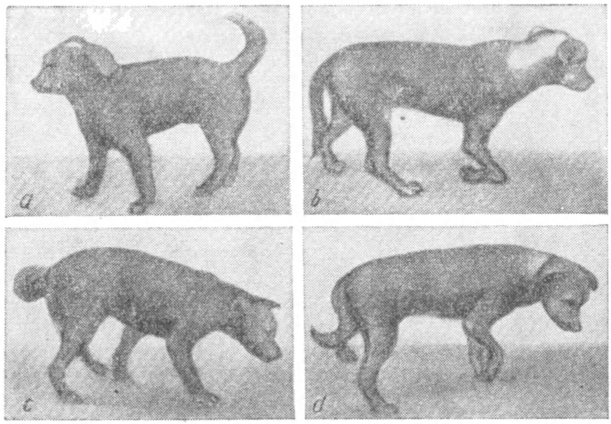


Fig. 29. Loss of compensation following decortication

a—dog Radius prior to decortication; c—dog Takhits prior to decortication; b—after decortication; d—after decortication

tion, and the animal is doomed to remain an invalid forever.

How does the cortex participate in the process of the restoration of impaired functions? A great deal here requires further experimental study. For the present it is possible only to give a general schematic picture of the process, like that shown in Fig. 30.

In the foregoing it was pointed out that the participation of cortical centres in unconditioned reactions makes them more delicate, accurate, and refined. Sir Charles Sherrington, the major British neurophysiologist, relatively long ago arrived at the notion of the higher centres of the brain serving as a source of continual bene-

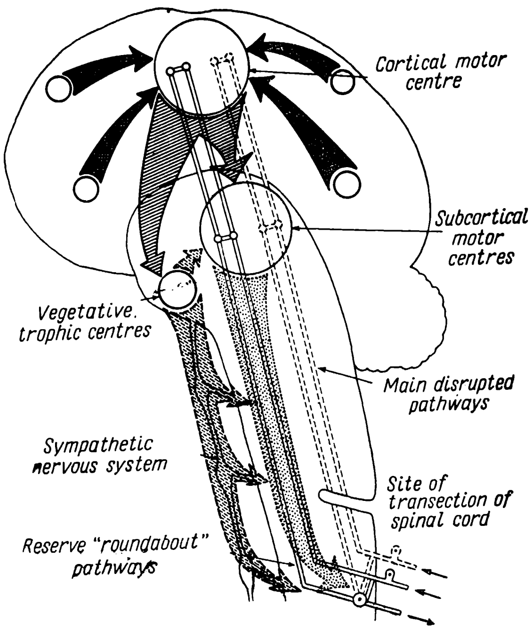


Fig. 30. **Cortical influences on the restoration of impaired functions of the spinal cord**

ficial and tonic influences on the motor centres of the spinal cord. J. F. Fulton, elaborating upon Sherrington's views, established that the motor area of the cortex, especially in the higher animals, should be referred to these sources too. According to the direct electrophysiological experiments of Adrian and Moruzzi, the pyramidal pathways linking the cortex with the motor centres of the spinal cord exhibit a constant electrical activity, moreover not only when the animal is awake, but also when it is asleep under anaesthesia. The moderate intensity of these corticospinal impulses does not produce the excitation of the motor centres that causes muscles to contract. There is reason to think that the effect of these continual impulses is to maintain the spinal centres in an active state, ready for prompt reaction.

Cortical representation of unconditioned reflexes thus has a direct regulating influence on lower centres (solid-line shading in Fig. 30). Physiologists have found, however, that, parallel with this "triggering" influence, which activates corresponding organs, the higher brain centres also exert an indirect influence on those organs. This influence does not engender activity, but improves the efficiency of the nerve centres, sense organs, and muscles, stimulating metabolism in them and improving the supply of the blood. Such an influence has come to be known as vegetative-trophic. L. A. Orbeli, the outstanding Soviet physiologist, has demonstrated that this influence is exercised through the sympathetic nervous system, whose higher centres are situated in the brain.

In recent years several physiologists, foremost among whom it is necessary to name the American Magoun and the Italian Moruzzi, have undertaken a comprehensive study of the functions of the special brain formation (called the reticular formation) that regulates the efficiency of the various sections of the central nervous system and the sense organs. This formation is supervised by the cortex. Through the sympathetic nervous system and the reticular formation, the cortex is also able to exert an indirect influence upon the nerve structures that take part in repairing damage inflicted by increasing (or, at first, possibly decreasing) the activity of these structures, improving metabolism in them, and influencing the blood supply expediently. This influence is represented in Fig. 30 by the dash line shading.

Finally—and this seems to us especially important—the cortical centres of the motor functions make it possible to incorporate them in the system of new temporary connections, new conditioned reflexes that constitute the physiological mechanism of learning, habit-formation, and production experience. The conditioned reflex mechanisms of the restoration of impaired functions are shown in Fig. 30 in square shading. It is the combined action of all three mechanisms mentioned that brings into play the "reserve", "roundabout" pathways and readjusts the relationships between the nerve centres with the ultimate result that the impaired functions are restored (shaded in dots).

The possibilities of higher conditioned reflex compensation are truly colossal. Let us amputate

all four paws of a rat. Obviously in these conditions no readjustment of the motor centres of the limbs can restore the functions of locomotion. Nevertheless, when a certain period has elapsed after the operation, the rat will roll head over heels to its food trough, and will avoid stimulation by an electric current. What has happened? The conditioned reflex mechanisms of the cortex have substantially altered the activities of the nerve centres connected with the muscles of the torso, head, and neck. These centres have been drawn into systems of new temporary connections that did not exist in the brain of the healthy animal; new locomotion habits have arisen, new experience has been acquired individually. The process of compensation has thus had as its biological effect the restoration of complex motor functions.

It must be mentioned that the new, recently-acquired nervous connections are very vulnerable and fragile. Any harmful influence upon the organism (infectious disease, overexhaustion, emotional shock) can produce a new disturbance (decompensation) of the restored functions. More than once we have observed cases of such decompensation among our animals under the influence of infection, anaesthesia, or faulty care and feeding. Similar facts are observed not infrequently in clinical practice. That is why people who have suffered a trauma of the central or peripheral nervous system should be carefully protected from all kinds of harmful influences that, at first glance, have no bearing upon their principal ailment.

Up to now we have been speaking of the

restoration of motor functions impaired by organic (i.e., destroying the nerve tissue itself) injuries of various parts of the nervous system. The question may now be asked: what is the role of the cortex in the restoration of so-called functional disturbances of the central nervous system, in which there is no direct destruction of the nerve tissues? What is its role in the restoration of impaired vegetative functions: the cardiovascular system, respiration, digestion, etc.? The findings of our laboratory, as well as the data of other investigators (for example, S. I. Frankstein), indicate that the cortex plays a smaller role in restoring the functions of damaged internal organs than it does in compensating motor disturbances. This is quite understandable, for the activities of the internal organs are less dependent upon the cortex than are the functions of locomotion. Nevertheless, there is more to this question than meets the eye at first glance.

Consider just one example. One of the reactions we studied in rabbits was the emergency rise of the number of white blood corpuscles (leukocytes) in the circulating blood. Moreover, the leukocytic picture was deliberately upset: in one case it was the organs producing and accumulating leukocytes that were primarily affected (radiation sickness), while in another it was the neuro-humoral mechanisms, which regulate the number of leukocytes in the blood (experimental neurosis, induced by a conflict of the food and defensive reflexes, resulting from the painful stimulation of the animals during meals). When the upset leukocyte picture

became quite normal again, the animals were decorticated. It was found that the decortication of previously irradiated rabbits did not upset the leukocyte picture again. But in the case of the rabbits that had experienced an experimental neurosis, the leukocyte count became distorted immediately after decortication (Fig. 31). It may therefore be assumed that the cortex plays a relatively small part in restoring impaired functions of internal organs if the organ itself—the heart, stomach, or a gland—is damaged. At the same time the cortex plays an important role in compensating disturbances in the *nervous regulation* of these organs, in eliminating pathological conditions of subcortical nerve centres. This in turn suggests that the conclusions drawn with respect to organic lesions of the central and peripheral nervous system are also valid for the so-called functional pathology of subcortical brain and spinal centres.

The cerebral cortex in higher animals and man thus appears to be the supreme organ in the system of various protective-adaptive mechanisms. It plays the principal role in the restoration of impaired functions of the central and peripheral nervous system, acting as the real "organizer" and "director" of the campaign against the damage done to the organism. This, however, should not in any way be taken to mean that the cortex itself is invulnerable to harmful influences. It goes without saying that cortical activity may be upset, in which case the cortical cells will be involved in a pathological process. We must point out, however, that, while possessing a high sensitivity to changes

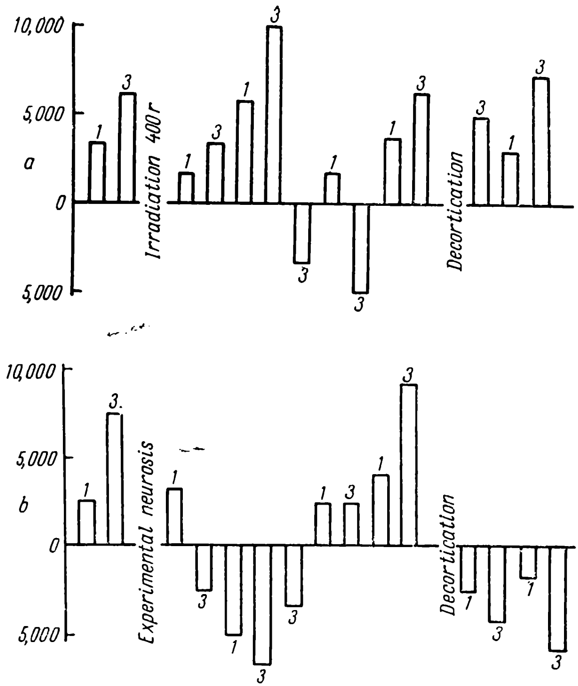


Fig. 31. Effects of decortication in rabbits that earlier experienced radiation sickness (*a*) and experimental neurosis (*b*)

The columns indicate leukocyte counts, rise or fall of number of leukocytes in blood following introduction of sodium nucleate. Figures over columns show doses of preparation in cu cm of 5 per cent solution

in the organism and in its environment, the cortex possesses diverse protective mechanisms that give reason to speak of its very high resistance to harmful influences.

Experiments carried out at our laboratory revealed an interesting regularity. If decorticated animals are given such chemical substances as insulin or adrenalin, changes in the respiration, heart rate, and blood pressure begin at doses several times greater than those that produce the same changes in normal animals. At the same time a further rise in doses, harmless in the case of normal dogs, proves fatal for the decorticated animals. Decorticated dogs are thus both *less sensitive and less resistant to chemical substances.* The adaptive potential of a decorticated organism is greatly diminished, and the ability of such an organism to "balance" fluctuations within it and in its environment are exhausted disastrously quickly.

Similar results were obtained in experiments with decorticated rabbits. Moderate doses of overall x-ray irradiation, which distinctly reduce the duration of so-called animal hypnosis, were found to have no effect on a group of decorticated rabbits. Somewhat increased doses of irradiation drastically reduced the leukocyte count in these animals and caused most of them to perish.

The biological significance of these facts will be readily understood. The high sensitivity of cortical structures to changes inside the organism and in its environment assure that various protective-adaptive mechanisms come into action in good time. At the same time the high resist-

ance of the cortex to the action of various harmful factors enables it to remain the supreme organizer and director of the "defence campaign" for a long time. This is borne out most strikingly by the action of ionizing radiation. The delicate electrophysiological investigations of M. N. Livanov and co-workers have shown convincingly that the changes in electrical activity under the influence of irradiation originate in subcortical brain centres and are immediately reflected in cortical activity. On the other hand, many investigators have been able to observe full-fledged conditioned reflexes in dogs literally on the eve of their death due to fatal doses of irradiation.

Physiologists and neurosurgeons noted long ago that damage to very small sections of subcortical brain formations causes serious disturbances in the organism's functions and often proves fatal to the animal. At the same time the removal of vast areas of the cortex is endured with relative ease. This fact shows that the cortex to a greater extent than subcortical formations possesses the property of plasticity, of providing functional substitution for brain centres that have been put out of action. It is in the cortex too that the protective-curative function of inhibition, basically common to the entire central nervous system, has attained the highest degree of perfection.

The cortex is—to use a figure of speech—the "headquarters" of a living organism. It is only natural that in the process of evolution there have arisen mechanisms protecting these headquarters very effectively from harmful in-

fluences. It is all too easy to imagine how disastrous it would be for the organism if various harmful influences were first of all to put out of action the cortex, which ensures the timely and all-round defence against them and, at a later stage, the restoration of the impaired functions.

In the context of these fundamental principles, it no longer appears surprising that even people whose health has been undermined disastrously sometimes retain remarkable intelligence and creative powers to the last, witness the writer Nikolai Ostrovsky, who heroically continued his work in a state of complete blindness and paralysis.

Here we consider it necessary to make a few important observations about the role of the nervous system in animal and human diseases. On this point there are two opposite views. A. D. Speransky has formulated the notion of the nervous system as the "organizer" of the disease, a notion that in many respects is in harmony with the theory of corticovisceral pathology. In the view of the sponsors of this theory, several human diseases (hypertension and gastric ulcer, endarteritis and others) are based on initial disturbances of corresponding brain centres, which lead to severe dislocations in the functions of internal organs (K. M. Bykov and I. T. Kurtsin). In opposition to this view, D. A. Biryukov put forward the concept of the nervous system acting as the "organizer of health". Both concepts, from our point of view, are somewhat one-sided.

It would be a profound mistake to assume that all the reactions without exception of higher

living organisms are biologically expedient and beneficial to the organism. Biological expedience is the result of a long process of evolutionary development, of thousands of millions of years of the adaptation of animals to their environment. It is an infinite process, as infinite as development from the lower to the higher, from the simple to the complex. It would be absurd to think that the inexpedient existed side by side with the expedient for centuries, whereas at the present stage everything has become expedient. This would imply the end of development. The very fact that useful reactions arise presupposes the selection of the biologically expedient from a multitude of less expedient variants. The useful is dialectically inconceivable without its opposite, the harmful.

We have spoken above of the extremely narrow specialization of the nerve centres in the brain and the spinal cord. This specialization has given the organism tremendous advantages in the precision, speed, and refinement of its responses. At the same time, with specialization developed to such an extent, damage to the nerve centres can have dangerous consequences for the organism. Facts show that partial disturbances of the central nervous system are the more difficult for a living being to endure, the higher its level of development.

As evolution progresses, the nervous system and the brain subordinate the activities of the internal organs to an ever greater degree, since nervous regulation is the best possible way of merging their functions in unified adaptive activity. The centralization of functions is thus a

biologically advantageous and progressive phenomenon. Yet at the same time it also has a negative feature, since the dislocation of nervous regulators in these conditions has widespread "repercussions" in all parts of the organism, even the most remote.

Defensive mechanisms have a certain sluggishness, an addiction to stereotype, that may make them detrimental to the organism (L. I. Fogelson). Coughing and vomiting are useful reactions by which the air passages and the alimentary canal eliminate foreign bodies, bad food, etc. In certain diseases, however, these reflexes become senseless and have a harmful effect on the organism. Coughing is useless when there is no expectoration in the air passages, while uncontrollable vomiting in toxaemia of pregnancy may even prove fatal. Similarly, an enlargement of the heart muscle (hypertrophy of the heart), which is an adaptive phenomenon in certain circulatory disturbances, subsequently causes degeneration of the muscle fibres. An increased heart rate in the case of an inadequate blood supply to the tissues is rightly regarded as an act of compensation, although such a reaction loses its purpose completely in the event of stenosis of the mitral valve.

By means of these examples we wanted to make it clear that the problem of the expedient or inexpedient, the useful or harmful for the organism calls for a truly dialectical approach. The notions of the "organization of disease" and of the "organization of health" are equally one-sided. The importance of the problem prompts us to attempt to elaborate upon the definition

of *disease* as applied to the organism as a whole and, above all, to its central nervous system.

In speaking of disease, it is customary to put the emphasis on an excessive influence that the organism cannot tolerate (trauma, burn, infection, etc.). At the same time we note the disability of the sick organism, its incapacitation, and, in the case of man, the reduced efficiency of his work. These very common definitions appear to us to be very relative. Consider the case of a person who has experienced too great a physical strain, say, has had to make a long trek through the forest with only a small supply of food and almost without resting. He has been subjected to extraordinary factors and is exhausted. His capacity to work is at a very low ebb, and he is scarcely fit for any activity. But is he a sick man? He may be tired and weak, but at the same time remain healthy (the person in our example may of course become ill, but this would be a special case).

Pavlov once made the penetrating remark that in pathological phenomena we are faced with a most complicated combination of the organism's defensive reactions and dislocations proper of functions. As a rule, several adaptive mechanisms, which are to be observed in normal conditions as well, function in the sick organism. This means that it is not the defensive mechanisms that determine the nature of the illness. Now what about the other aspect of the disease, the dislocations proper, as Pavlov called them? Are these the charred skin in the event of a burn, the fractured bone, or the torn nerve? But the skin of a corpse can also be

burned, and this would be a purely physical phenomenon.

Morbid, pathological, from our point of view, are *those reactions of the living organism,* those activities of its organs and systems *that, far from helping to restore impaired functions, make the impairments even more pronounced.* In the foregoing there have been sufficient examples confirming the existence of such reactions. Whenever an organism experiences harmful influences, mechanisms of a twofold type come into play, defensive and "self-destructive", but it is the latter that make disease a specific condition distinct from the healthy condition. In terms of cybernetics we can say that "dislocations" are essentially instances of *positive feedback* that does not eliminate a departure from the prescribed condition, but tends to increase, heighten that departure. The situation is further complicated by the fact that reactions originally useful to the organism can become harmful. The important thing is not the structure or nature of the mechanism (coughing, vomiting, hypertrophy of a muscle, or increased heart rate), but the role, the biological tendency of that mechanism at the moment.

Ageing and death are undoubtedly inexpedient for the individual, spelling its negation and destruction, but the replacement of one generation by another is the most important condition for evolution. It would be naive to visualize the ageing and death of higher animals as vulgar "wear and tear", such as the erosion of rocks or the corrosion of metals. We must remember that the living continuously renews its chemical

composition. Unicellular organisms multiply by fission, two new cells arising out of one old one.[1] The old cell has "died", but—there is no corpse! The succession of generations in the form in which it is observed in the higher animals arose historically in the process of evolutionary development, acting as a "lever" of gigantic progress, of the swift (compared with earlier stages) advance of living beings.

This brings us to our summing up of the role of the nervous system in pathology. In the process of evolution the nervous system has advanced to the fore as the most flexible and important regulator of all the functions of the organism. This quality is retained by the nervous system when, as the regulator of defensive-adaptive reactions, it comes up against harmful, destructive influences. It is noteworthy that in decorticated animals defensive reactions become clearly inadequate. They lose their adaptive significance, become exhausted quickly, and in some cases even heighten the effects of the trauma.

In the course of the evolutionary process the higher centres of the brain have acquired two characteristic qualities: a high sensitivity to changes inside the organism and in its environment, as well as a high stability in comparison with other organs and systems. Accordingly, in the course of ageing the functions of the higher centres of the central nervous system are retained

[1] In view of the popular nature of this book, we shall not discuss here the complex and little-studied problem of the uneven character of cellular division.

far longer than the functions of growth, sexual activity, and certain others. As the organism ages, it loses first of all not what "wears out more quickly", but what loses its biological meaning. The function of reproduction is exercised to the extent to which it is needed in order to maintain the species; hence its loss at a relatively early stage. The organism, however, continues to exist, and an express condition for this is brain activity. The high stability of the brain is *relative,* just as is the expedience of the reactions effected by the central nervous system. It participates in both defensive and "self-destructive" reactions, but in the process of evolution the former definitely *appear to be gaining the upper hand over the latter.* Let us consider why this is so.

The more highly organized an animal is, the greater the significance of its individual experience (conditioned reflexes) compared with the inborn, inherited forms of behaviour. It is not the succession of generations and not the inheritance of acquired properties, but the accumulation of individual experience and its transmission to the rising generation that acquires the decisive significance for the progress of living beings. This fact has acquired a new quality at the human level. The structure of the human body has remained practically unchanged over the past tens of thousands of years, but the progress of human thinking, under the influence of social life, has been truly breath-taking.

It may be assumed that the period in which the succession of generations has lost its significance as the principal factor of development,

yielding it to the transmission of individual experience, has been too small to affect the life-span of the higher living beings. But this period may have been sufficient for the role of the higher brain centres in regulating the defensive functions of the organism to prevail over the participation of the nervous system in pathological proper, or "self-destructive", reactions. That is why, while not accepting the one-sided formula of the nervous system as the "organizer of health", we do consider it possible to treat the cerebral cortex as the supreme organ *primarily of restoration and defence.*

The fourth fundamental principle of the reliability of the brain is thus the utilization, in compensation processes, of the mechanism of temporary nervous (conditioned-reflex) connections, the organ of which in the higher animals and man is the cerebral cortex, as well as the combination of the high sensitivity of the cortex and its high stability.

7

LEARNING FROM NATURE

We have considered the basic principles underlying the high resistance of the central nervous system to damaging influences. To what extent can these principles be utilized in enhancing the reliability of complex automatic devices? The problem is one that confronts the authors with natural difficulties. Far removed professionally from present-day automation and remote control, they may appear to the experts to be naive, to say the least, in their recommendations. Happily, we have no intention of making such recommendations. We trust, merely, that the engineer, designer, and worker who reads our little essay will himself give thought to the problem of which of the points mentioned may be useful to him in his technical quests. That is the first point we wish to make.

Secondly, it appears appropriate to add the reminder once again that many defensive-compensatory mechanisms of the organism are bound up indissolubly with the specific qualities of living matter, with the constant renewal of its chemical composition, with the inheritance of acquired characteristics, and with the laws of organic evolution. These specific qualities are

clearly evident in the phenomena of protective inhibition, where the mechanisms of defence are literally interwoven with the processes of continuous metabolism.

It is only after making these two reservations that we venture to embark upon what might be called "a physiologists' experimental digression" into the realm of engineering simulation, the realm of the artificial reproduction of processes characteristic of brain activity.

Protective Inhibition. Perhaps we should imitate nature and make use of every moment that certain elements, certain units of a complex automatic system are idle for their repairs, adjustment, testing, and, if need be, replacement. Let us assume that in our complex system there is a special mechanism that does not participate in its basic activity. At the same time its role is not confined to locating elements that are out of order and to sounding emergency signals of a "breakdown". The mechanism "handles" elements not in operation at a given moment: it tests them, determines the degree to which they are worn out, and carries out preventive maintenance.

Modern engineering has many protective devices in its arsenal for safeguarding complex systems from excessive fluctuations of various physical factors: electric current intensity and voltage, gas or vapour pressure, a rise of the temperature or level of radiation. But does engineering always and to a sufficient extent provide against "futile energy expenditure", against the reaction of mechanisms to weak signals of little consequence for their basic activity? Or

what about the selection of signals? Is this dynamic, does it involve an assessment of the signal's significance in a given, specific situation? All this provides food for thought. It may well be that a designer will take an interest in the mechanisms of inhibition in the central nervous system: the exclusion of pathways (and not of receiving or effecting instruments), the "interception" of signals in initial links of a communication line (recall the suppression of the initial elements of a reflex arc), or the existence of mechanisms regulating the state of all the main units of an operating system (reticular formation of the brain).

Latent Reserves. The most important factor behind the high reliability of the central nervous system is the superfluous number of functional units, the presence of reserve elements. What if an automatic device were to have three types of elements: (1) the permanently-operating elements with rigidly prescribed functions, which operate with particular speed and precision; (2) similar elements that do not function in normal conditions, but that take over whenever elements of the first type go out of action, and (3) multipurpose elements with a wide range of functional variability. The elements of the third type will evidently be inferior to the first two categories in the speed, precision, and perfection of their work, but on the other hand they will ensure the continuous operation of a complex system until it is possible to replace or repair the basic structural units concerned. In general, the principle of the dynamic readjustment, flexibility, and plasticity of the ele-

ments of a complex automatic system appears to hold out great promise for technical progress. It is not for us to judge about the concrete designs in which this principle may be embodied, but the example of the living brain has shown us its extraordinary effectiveness.

Independence and Centralism. Without a certain independence of the units of a complex system, without "technical encouragement of separatist tendencies", it is difficult to visualize a highly reliable automatic device. If all the units, all the elements of the system are interconnected to such an extent that a fault in one element puts the whole system out of action, there is little hope of the system operating uninterruptedly. At the same time the relative independence of the individual units must constantly be united and directed by higher regulative systems. It is important to point out here that multistoreyed regulation does not imply primitive duplication. Every new level imparts new properties, a new quality to the activity regulated. Such a principle has at least two corollaries. The subordinate regulators are capable of functioning even if the "master" mechanisms are put out of action. The higher integrators, for their part, are relieved of elementary functions so that they can engage in more complicated activity.

This principle too must be dynamic. The higher regulator may not interfere in the normal, uninterrupted work of subordinate units. If the threat of a malfunction arises somewhere, the supreme organs of defence are informed of the "dislocation" and mobilize the mechanisms

for repairing the damage. The higher regulators should, in all probability, possess two qualities: (1) a high degree of sensitivity to changes in various parts of the complex system, since intervention in its work can be effective only provided it is timely, and (2) maximum protection from possible "dislocations", since any malfunction in the regulators has widespread repercussions in subordinate units.

Finally, no small role in enhancing the reliability of automatic devices could be played by utilization of the *principle of temporary connections,* temporary couplings to a certain extent simulating the conditioned reflex. We have in mind in this case not the creation of "learning automata" to achieve industrial effects (this is a topic in itself), but the application of the principle of temporary connections to the elimination of faults. What we have in mind could therefore be called "automata learning to restore impaired functions". The possibility of such devices being created does not belong to the realm of science fiction; "learning" automata exist, but their activities are, as a rule, centred on external objects. Apart from "self-regulation", it is desirable to provide for the "self-compensation" of impaired activity and to embody this in the design of the machines.

We repeat that the purpose of this brief digression is above all to demonstrate that it is possible to borrow from nature her remarkable achievements. At the same time far be it from our intention to suggest any solution in terms of design, prompted by a study of the work of the brain. We would merely like to emphasize that

what has been attained by living beings in the course of their evolution is not only instructive in dealing with the problem of reliability in modern engineering, but goes a long way towards providing the key to a more rational utilization of the "man-automaton" system.

The fact is that the control of huge automatic devices, working at high speeds, imposes exacting requirements upon the operator. The need to keep a large number of instruments under observation and to respond to their readings quickly and exactly taxes the powers of the human brain to the utmost, if not requiring the impossible of them at times. After all, the human operator functions as a single channel information system, for at any given moment he can receive only one signal (the interval between consecutive signals must not be less than 250-500 msec).

When a person has before him a control panel with a large number of instruments, his glance is moving continuously from one instrument to another. Two different signals cannot be received by him simultaneously. These natural limits of a human being's potentialities lead some writers to speak of the imperfection of the human brain and its inferiority to high-speed machines. Let us consider this point briefly.

Two conflicting views are expressed on this point, as a rule, in the vast literature on cybernetics. Some writers believe that there are no limits to perfecting automatic devices. Their answer to the question whether the machine can become more clever than its creator is a firm "Yes".

Other thinkers, no less convinced in their belief, hold that it is impossible to simulate such functions of the human brain as creative thinking, as thinking in abstract terms, and, especially, as the sphere of human emotions. It should be pointed out that the arguments in support of the superiority of the brain to the machine are based on reverent awe of the human brain rather than the sound logic of irrefutable proof. Since even the most complicated activities of the brain can be boiled down to reflexes, the arguments invoking such terms as "creation", "emotion", and "imagination" have a greater lyrical than scientific appeal.

From our point of view, this controversy, which has been dragging on now for so long, is pointless, since *a machine and the human brain are incommensurable* in terms of "which is better?" An automatic device of any degree of complexity (and any machine in general, for that matter) is an integral part of an "automaton-human being" system. Torn out of that system, it becomes a mere combination of hardware. What has happened to ultrarapid machines in some ways resembles the irrational reverence of money: it is a case of man attributing to an external object the properties that he himself bestowed upon that object and that are a result of human social *relations*. If we hypothetically assume the case of an automaton getting out of control, we must remember that it will *always* be up against not an unarmed man, but a man armed with at least a similar automaton. That is why the question really deserving our attention is not the scholastic dilemma of what is

better, the brain or the machine, but the question of the *place* of man and the machine in the single complex system enabling man to advance more confidently, more easily, and along a broader front in mastering his natural environment.

Here again the study of the work of the brain can be of help to us. In a certain sense, a man controlling automatic machines has to play the part of the cerebral cortex with respect to subordinate centres of the nervous system and the organism as a whole. The operator does not have to receive information about all the particular processes taking place in an automatic system. Or, rather, he must receive that information in a generalized, integrated form. He will then be able to intervene in the most essential links of the process. Only special, extraordinary events are "entitled" to the operator's attention. But here too there is a principle of efficiency that it is important to observe. A human being may not have the time to prevent an extraordinary event, say, a breakdown. That is why, simultaneously with the alarm signal addressed to the human being, "independent" automatic mechanisms at a lower level must go into action to repair the fault. The operator, on receiving the signal, will then be able to come to their aid and swing the whole complex of restorative measures into operation.

Observations of the activity of machines helped man at one time to understand certain aspects of the functioning of his organism. Today the study of the work of the brain is proving an ever greater asset in designing and operating automatic devices. Actually, people have

been learning from their own nature for a long time. What we must put to the credit of cybernetics is the conscious application of certain principles of the operation of the nervous system to the field of engineering simulation. Such an application is only possible through a stage of mathematical analysis of the principles, a stage in which they are expressed in mathematical terms. We shall not dwell here on the significance of the reverse effect of mathematics and engineering on the physiology of the nervous system. We shall confine ourselves merely to saying that before our eyes a prophesy of Pavlov's is beginning to come true, the prophesy that the majestic formulas of mathematical analysis will one day interpret the incredible complexity of the work of the brain.

The problem of the reliability of the brain is a far bigger one than it is shown to be in our little essay. We have confined ourselves to outlining the principles governing the restoration of functions impaired by external agents; we have scarcely touched upon the mechanisms that enable the brain to operate for so long and without interruption in normal conditions. How can a more refined analysis of external signals (stimuli) be achieved? How can mistaken and retarded responses due to fatigue be prevented? What principles of training help to make new and complicated human motor habits quite automatic? These are problems that the physiologists are studying, among them the staff of several laboratories at our institute. And the problem of reliability is one of the most important commanding the interest of research workers.

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