# CHAPTER XXIX

## HOW PSYCHIATRY MAY HELP US TO UNDERSTAND THE PHYSIOLOGY OF THE CEREBRAL HEMISPHERES[1]

(Read before the Society of Psychiatry, Petrograd, and published in the *Russian Physiological Journal,* 1919.)

PAVLOV STUDIES TWO INSANE PATIENTS FROM THE PHYSIOLOGICAL OBJECTIVE POINT OF VIEW—BOTH ARE CASES OF CATALEPSY WHICH PAVLOV ANALYSES AS INHIBITION OF THE MOTOR REGION OF THE BRAIN—DISAPPEARANCE OF THE CHRONIC INHIBITION IN SENILITY.

My earlier researches on the circulation of the blood and on digestion convinced me that the physiological mode of thinking may derive great help from the study of clinical cases, *i.e.,* from the unlimited number of pathological variations and combinations of the functions of the human organism. For this reason during many years of work on the physiology of the cerebral hemispheres I often thought of making use of the world of psychiatric phenomena as an auxiliary to this study. The usual physiological method, which, as a mode of analysis, consists in destroying parts of the brain, is very crude in comparison with the delicacy of the mechanism to be investigated. In brain diseases one might expect in some cases to come across a much more obvious, permanent, and detailed decomposition of the elements participating in the complete activity of the brain, and a separation of its single functions in consequence of pathological causes, the effect of which sometimes reaches a high degree of differentiation.

In the summer of 1918 I had at last an opportunity of studying * a number of cases of insanity. My former hopes were realised. In some instances, I found excellent examples of facts concerning points more or less explained in physiology; in others, new details of the action of the brain were brought to light, new questions and problems for laboratory investigation arose.

My way of looking at the psychiatric material was however greatly different from the usual point of view adopted by specialists. Owing

[1] Being deprived, in the summer of 1918, of the possibility of taking his usual two months' vacation in the country, Pavlov rested by changing his work. He went to the Hospital for Mental Diseases to observe personally some clinical cases. This article is a discussion of the two principal cases that came under his personal observation.—*Translator.*

* I am greatly indebted to Dr. M. K. Voskresensky, director of the asylum for insane in Udelnaya, for admission to the asylum, and to Dr. V. P. Golovina, who spent a great deal of time in showing me the patients.

to many previous years of experience in the laboratory I reasoned on a purely physiological basis. As I always tried to explain to myself in physiological conceptions and terms, the psychic activity of lunatics, I did not experience great difficulty if I concentrated not on the details of the subjective state, but on the principal features and phenomena of the pathological state of the insane. How this was done will be seen in part from the following account.

I shall give in this paper a description and analysis of two cases. The first was an educated, well-bred girl, age about twenty-two. We find her in bed in the garden of the hospital lying motionless with her eyes half closed. At our approach she does not speak. The physician who accompanied me, told me that this was her usual behaviour. She refuses to eat without help, and is untidy. When questioned about her relatives and home, she appears to understand and remember everything quite well. She replies correctly but with extreme effort, and answers slowly. The cataleptic state of the patient is marked. For some years, periodically, she has been either nearly recovering, or falling ill again with various symptom-complexes. Her present state represents one of these complexes.

The second case was a man aged sixty. He has spent twenty-two years of his life in the hospital, lying like a living corpse without making the least voluntary motion, without pronouncing a single word; he is very untidy, having to be fed through a tube. During the last few years, as he approached sixty, he began more and more to make voluntary movements. At present he gets out of bed without help, goes to the lavatory, talks freely and quite reasonably, and eats without assistance. Referring to his former state, he declares that he understood everything around him, but experienced such an extreme and insuperable heaviness in his muscles that he could hardly breathe. This was the reason why he neither moved, ate, nor spoke. He suffered the first attack of the disease at the age of about thirty-five. The history of the case records tonic reflexes.

How are the described conditions of these two cases to be characterised from the physiological point of view?

In order to answer this question let us consider one prominent motor symptom, occurring in both cases. I refer to the catalepsy of the first patient and to the tonic reflexes of the second. When do these symptoms manifest themselves in the most striking manner in animals? Schiff observed long ago that cataleptic phenomena appear in rabbits after the removal of the cerebral hemispheres. Decerebration, introduced by Sherrington, is also a simple method by which there may be obtained tonic reflexes in cats. Poisoning by some anæsthetics, as urethane, also produces cataleptic phenomena. In all these cases there is an elimination of the activity of the cerebral hemispheres *without suppression of the lower parts of the brain.* The last circumstance is due either, as in the case of rabbits and cats, to a specific property of the cerebral tissue of these animals and to the absence of further reactive phenomena, because of the recentness of the operation; or, as in the case of poisoning by urethane, to the presence in the latter of the ammonium radical, which stimulates the lower motor centres. Such an isolated elimination of the cerebral hemispheres, the central organs of so-called voluntary motions, leads to a manifestation of the normal activity of the lower parts of the nervous apparatus for motion. This activity is first of all designed for equilibrating the organism and its parts in space, and represents the reflex of equilibration, which in normal conditions always functions, but is always masked at the same time by voluntary motions. Catalepsy is thus a normal and habitual reflex which in the above-mentioned conditions manifests itself distinctly by virtue only of the inhibition of the action of the cerebral hemispheres. The tonic reflexes are the elements of that compound reflex (plastic tonus of Sherrington, and labyrinthine and neck reflexes of Magnus).

In these patients the presence of the same kind of mechanism may be supposed to exist, *i.e.,* exclusion of the activity of the cerebral hemispheres. But, as seen, they are characterised by the exclusion of the activity of only the motor region of the cerebral hemispheres. In fact, our patients are not able to make any voluntary motions, or at least they suffer an extreme impairment of this function. This is clear to the observer, and is even stated by the patients themselves. But at the same time they understand what they are told, remember everything, and are conscious of their state, *i.e.,* they work quite satisfactorily with the other parts of the cerebral hemispheres.

A strictly limited suppression of the motor area of the cortex of the cerebral hemispheres is known also in other human or animal conditions. A person in a certain state of hypnosis understands perfectly well all that he is told, remembers it, and willingly executes commands, but he has no voluntary power over his skeletal muscles, and is compelled to retain the pose assigned him, even though it is uncomfortable and undesirable for him. The essential feature of this condition obviously lies in an isolated suppression of the motor area of the cortex of the cerebral hemispheres, a suppression which does not extend either over the whole hemispheres, or deeper into the mass of the brain. Working in the laboratory with conditioned reflexes I have observed a similar state in dogs. In one of our cases, in collaboration with Dr. Voskresensky,[2] we studied the conditions most accurately and systematically. For weeks and months the dog was often left for a long while alone in

[2] See chapter xxiv.—*Translator.*

the room, in a wooden frame and without experimental influences. In consequence of such a proceeding the whole environment of the room became for the dog a soporific agent to such a degree that it was enough to bring him into the room to have all his behaviour changed immediately. By varying the duration of the action of this agent we could see the separate phases in the development of drowsiness and sleep. The following results were obtained. A conditioned reflex for sound and food (association) was formed, that is, at the production of a definite sound the dog exhibited the phenomena of the feeding reaction: he secreted saliva and made appropriate movements, licking his lips, turning his head toward the place where he was usually fed, and immediately starting to eat as soon as food was offered.

At the first signs of drowsiness the conditioned salivary reflex to the sound disappeared, but the motor reflex to the sight of food remained normal, *i.e.,* the dog started to eat the proffered food without the slightest delay. This first phase was followed by the second, which was quite unexpected and very significant. The conditioned salivary reflex to the sound was again present, and became stronger with the addition of the natural conditioned reflex to the food itself, but the motor reflex was absent—the dog did not take the food, and even turned away from it and resisted its introduction by force. In the following phase a deep sleep ensued, and all the feeding reactions, of course, disappeared. When the animal was intentionally awakened (by means of some strong stimulus) the phases described above appeared in reversed order as the drowsiness disappeared. The second phase could be explained thus: the sleep inhibition was already present in the motor area of the cortex, but the remaining portions of the hemispheres still functioned normally and exhibited their activity on an organ quite independent of the motor region—on the salivary gland. There is here a complete analogy to an awakened person who understands (and admits), that you are rousing him by his own request, but who, unable to overcome the power of sleep, begs you to leave him alone; or gets angry and even opens hostilities against you, if you persist in fulfilling his earlier request and continue to trouble his sleep.

The first phase and its substitution by the second as the sleep grows deeper can be explained in the following way. Since in our dog all the interior of the room, *i.e.,* all the stimuli going to the eyes, ears and nose, was acting as a soporific agent, the corresponding regions of the cerebral hemispheres were subjected to the inhibition of sleep, which, though superficial, was strong enough for the suppression of the conditioned action of the stimuli. At the same time the soporific influence was not sufficient to inhibit the predominant region—the motor cortex. But when the monotonous skin and motor stimuli, resulting from the limitation of the motion in the frame, were added to the soporific action of the room, then the sleep inhibition spread over the motor portion of the brain. Now this portion being the strongest, attracted to it the sleep inhibition from all the other regions according to the law of concentration of the nervous process, thus releasing them temporarily from inhibition, until with the development of the action of other soporific agents, the inhibition invaded with an equal and sufficient intensity all the portions of the cerebral hemispheres.

In the patients described above we have enough evidence to affirm the existence of a concentrated and isolated inhibition of the motor cortex of the cerebrum, as a result of the cause which brought about the disease.

What objections from the clinical point of view may be raised against our explanation of the symptoms in these two cases? Here I shall give the apparent inconsistencies with clinical reasoning, which were pointed out by the psychiatrists when I reported to them these results of our analysis. Some of them saw in the cases cited by us a stupor-like state as a consequence of emotion. But first, this concerns not the mechanism but only the cause of the symptoms. Apparently instances of stuporousness, or of a kind of cataleptic state, may occur under the influence of strong, unusual agitation, brought about by extraordinary sounds, by strange pictures, etc. A strong irritation of certain regions of the hemispheres may bring about inhibition of the motor cortex, and thus create conditions favourable for a manifestation of the equilibrating reflex. Secondly, there are not indications in the patients of such a mechanism—the presence of extraordinary stimuli could not be detected, while one of the patients plainly refers only to the difficulty, indeed the impossibility, of voluntary motions.

Further, it was pointed out that destruction of the cerebral hemispheres in progressive paralysis is proved on pathological anatomical grounds, although catalepsy is absent. But even then there is no complete exclusion of the motor activity of the hemispheres. The patients make many voluntary motions though badly co-ordinated; and on the other hand, in the form of convulsions they often show phenomena of an abnormal motor irritation of the cortex. Therefore in progressive paralysis the chief condition for the development of the pure equilibrating reflex is lacking.

It was also pointed out that thromboses and extravasations in the cerebral hemispheres are followed by paralysis and not by catalepsy. But the conditions necessary for the production of catalepsy are absent. In these cases one observes the disappearance of even spinal reflexes. The inhibition, resulting from the destruction, spreads and reaches even the spinal cord. Inhibition should manifest itself to an even greater degree in the regions of the brain nearest to the cerebral hemispheres.

Thus in the clinical diseases of the cerebral hemispheres one does not meet with facts inconsistent with our analysis of the pathological condition of the patients. Therefore, in certain cases, one is forced to acknowledge the existence of the mechanism of pathological functioning of the cerebral hemispheres as here proposed. In the second of the cases described above the following fact also leads one to consider the symptoms as an inhibition of the motor cortex. After more than twenty years of illness the patient has begun to return to his normal state. It means that all the time his condition was of functional rather than of organic nature.

Proceeding further in the analysis of the states of the two patients it is necessary to call attention to yet another circumstance. Although the motor elements of the cortex corresponding to different movements (for instance, of the skeleton, eye-ball, organs of speech, etc.), are localised, according to physiology, in different portions of the hemispheres, and are scattered, so to speak, nevertheless in both the patients these elements are all united by a common inhibitory process, in strong contrast to the other elements of the hemispheres, which remain at the same time more or less free. This leads to the important conclusion, that *all the motor elements resemble one another* in structure or chemical constitution, or, most probably, in both. This is why the motor elements all respond in a similar way to the cause producing the symptoms of the illness, thus differing from the other elements of the cortex, such as those of sight, hearing, etc. This difference between the elements of the cortex appears most sharply in the phases of hypnosis and sleep, when some elements are in one state, and others in another,* though the actual cause is the same.

Let us now answer the question, What, in effect, is the determining cause of the given symptoms? One may think of several things. There may be a definite toxic action, whose sphere of influence is limited by the individual peculiarities of the separate cortical elements. One may also suppose that there is present an exhaustion of the elements of the cortex, resulting either from the general condition of the organism, or from overfatigue of the brain. The exhaustion might be concentrated in some definite elements of the cerebrum either on account of

* This difference between the cellular elements of the cerebral cortex should be considered unquestionable and indisputable. In the physiology of the peripheral nerves, we constantly meet with a distinct individuality (in irritability, relative strength, etc.) of the nerve fibres and of their peripheral ends of different functions. This individuality affords us a fundamental means of differentiating these different fibres in a mixed anatomic trunk, as, for example, the method of separating vasoconstrictor from vasodilator fibres.

the particular part which these elements have taken in the work producing the exhaustion, or as the result of their specific nature. Finally there is the possibility of direct or indirect (the last resulting from local changes in the blood circulation or in the general nutrition) reflex influences which may affect injuriously the different elements of the cortex. Therefore, in different cases, in spite of the similarity of the mechanism of the given complex of symptoms, the causes producing them may not be the same.

It will not be altogether amiss to put one more question: What is the explanation of the case of the second patient, in whom the inhibition of the motor region of the cortex was at last disappearing after having remained during twenty-two years nearly on the same unchanging level. This may depend only on the age of the patient. He was returning to a normal condition at the approach of the age of sixty, at which age a sharp decline in the activity of the organism is usually pronounced. How is this relation to be interpreted? If in this case, some toxic agent had been active, then one might think of a quantitative diminution of the agent which had produced the condition, a lessening of its action as the result of the senile changes in the body metabolism. If the principal cause of the disease was a chronic exhaustion of the nerve mass, then in the presence of changes in the brain accompanying old age and manifesting themselves in restricted activity and less functional disturbance of the brain (the sharp weakening of the memory for current events), the exhaustion would be less pronounced. If it is granted that sleep and hypnosis are a kind of special inhibition, then the second patient would present an example of chronic partial sleep or hypnosis. In senile talkativeness, eccentricity, and in extreme cases imbecility, one sees a more considerable decline of the processes of inhibition. From this point of view I take it that the recovery of the patient was due in reality to the senile decline of the inhibitory processes.

The physiological analysis of the above cases suggests, I think, many new problems for the laboratory investigation of the physiology of the brain.

# CHAPTER XXX

## HYPNOTISM IN ANIMALS

**(Read before the Russian Academy of Sciences, November 9, 1921.)**

MODE OF PRODUCTION OF HYPNOTISM—AN ANALYSIS SHOWS IT TO BE MOTOR INHIBITION THROUGH FEAR, A SELF-GUARDING INHIBITORY REFLEX.

THE so-called hypnotism of animals (the *experimentum mirabile* of Kircher) is produced by some energetic influence which suppresses every resistance; for example, the animal is brought into some unusual position (laid upon the back), and thus held for some time, etc. Then when the restriction is removed, the animal remains motionless for many minutes or hours. Different authors, noticing now one, now another, detail of the phenomenon, have given varying explanations. Thanks to the systematic study of the normal activity of the brain which has been conducted in my laboratory I can at present indicate the biological significance of the phenomenon and exactly explain its physiological mechanism, thus combining all the separate facts of the several investigators.

This reaction represents a self-guarding reflex of an inhibitory character. In the presence of the overwhelming power which the animal meets, there is no escape in struggle or in flight, and the only chance to save himself consists in remaining immobile in order not to be noticed (for moving objects attract especial attention), and in order not to provoke in this annihilating agent an aggressive reaction. The fixed position is brought about in the following manner. Extraordinary, extremely intensive (or unusual), external stimuli quickly bring about a reflex inhibition of all the motor region of the cortex, which governs the so-called voluntary movements. This inhibition is either limited only to the motor region, not passing into other areas of the cerebral hemispheres or to the mid-brain, or, on the other hand, it may irradiate over all these parts, depending upon the duration and strength of the stimulus. In the case of limitation of the inhibition to the motor region, there are present reflexes from the eye muscles (the animal follows with his eyes the movements of the experimenter), from the glands (saliva begins to flow when food is given, although no skeletal movements are made in the direction of the food), and finally also tonic reflexes from the mid-brain to the skeletal musculature for the retention of that position into which the animal has been put (catalepsy). In the second event, with wide spreading of the inhibition, all the above-mentioned reflexes gradually disappear, and the animal passes into a completely passive state, the state of sleep, with general relaxation of the musculature. The described course of events confirms the conclusions to which I came in my previous laboratory work, *viz.*, that the so-called inhibition is nothing more than sleep, but partial and localised. Our rigidity and stupor in the face of great fear is nothing else than the reflex which I have just described.*

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* I must add that as I could get no physiological literature until 1922, when I obtained it in Helsingfors, this lecture was written in ignorance of the fact that concerning hypnosis in animals some authors had come to this same conclusion.

# CHAPTER XXXI

## THE NORMAL ACTIVITY AND GENERAL CONSTITUTION OF THE CEREBRAL HEMISPHERES

(Read before the Society of Physicians of Finland, Helsingfors, April, 1922.)

THE SIX PRINCIPAL NERVOUS PHENOMENA—REFLEXES, INSTINCTS, ASSOCIATIONS—ROLE OF THE CONDITIONED REFLEX IN ESTABLISHING AN EQUILIBRATION—EXTINCTION, RETARDATION, CONDITIONED INHIBITION, DIFFERENTATION ARE FORMS OF INTERNAL INHIBITION—EXTERNAL INHIBITION IS ANALOGOUS TO THE INHIBITION OF SPINAL REFLEXES—DREAMS—THE WAKING STATE AND SLEEP—THE MOTOR AREA OF THE CORTEX IS ALSO A SENSORY (RECEPTOR) REGION—LOCALISATION IN THE CORTEX STUDIED BY SURGICAL OPERATION AND CONDITIONED REFLEXES—EACH SENSE ORGAN HAS A CENTRAL CORTICAL AREA AND A DIFFUSE AREA—POST-OPERATIVE COMPENSATION—CONTRASTING EFFECTS OF THE ANIMAL'S BEHAVIOUR AFTER REMOVAL OF (a) FRONTAL LOBES (b) POSTERIOR LOBES—SLEEP INHIBITION AND FATIGUE.

IN order to analyse successfully the function of any organ it is necessary to know first of all its normal activity. This holds true also for the cerebral cortex. For the last twenty years I and my co-workers have busied ourselves mainly with this problem, using the dog as an experimental animal.

All the nervous activity and all the behaviour of the higher animals may be included in a scheme containing six principal nervous phenomena: (1) excitation; (2) inhibition; (3) the wandering or spreading of both excitation and inhibition; (4) reciprocal induction—inhibition by the excitation process (negative phase), and excitation by the inhibition process (positive phase); (5) the opening and closing of paths between different points of the system, and finally; (6) analysis—the decomposition by the organism of the external *milieu* and its own internal world (everything which proceeds within it) into their units. Here I can give only a brief outline of this activity, in more or less dogmatic form, and then a brief discussion of the general functional construction of the cortex, with a description of some of our experiments.

The chief fund of nervous activity consists of a mass of *reflexes*—constant, inborn connections of internal or external stimuli with certain activities of the executive organs. *Instincts,* as detailed analysis reveals, are the same as reflexes, but in their composition they are more complicated. The complete register, the detailed description, and the natural systematisation of all these complex reflexes is the next important task of the physiology of the central nervous system.

The next highest step of nervous activity is occupied by the so-called *associations* or *habits, i.e.,* connections formed during the life of the individual owing to the coupling or combining function of the cortex of the cerebrum. The formation of associations proceeds on the principle of signalling. When some indifferent stimulus accompanies once or several times an inborn definite reflex, then this indifferent stimulus acting alone later has the power of calling out that reflex with which it coincided. In the presence of definite conditions the associations are formed regularly and inevitably. Thus we have the right to consider the associations as pure reflexes, though acquired, and to investigate them exclusively from the physiological point of view. I and my collaborators call both sorts of nervous activity reflexes, and designate the inborn as *unconditioned,* and the newly formed ones as *conditioned,* and the corresponding stimuli which provoke them as, respectively, unconditioned and conditioned.

Obviously conditioned reflexes favour enormously the safety and welfare of the organism. Thanks to these temporary connections, diverse and complex agents become conditioned stimuli, which call out the conditioned reflexes. Centres become related functionally and synthesis of stimuli occurs. Probably the site of this coupling, combining activity is to be sought for in the points of union, the synapses of the neurones, especially in the cortex of the cerebrum; for after removal of this part of the brain all conditioned reflexes are destroyed and new ones can not be formed.

A further stage of nervous activity is characterised by an incessant correction of the conditioned reflexes. If a conditioned reflex does not correspond to reality—if under certain conditions the conditioned stimulus is not followed by the unconditioned stimulus, or is followed but not immediately—then the conditioned reflex is temporarily or constantly (in the case of constant circumstances) inhibited. The following example will explain these relations.

According to the described procedure we establish a conditioned reflex from an indifferent tone, *i.e.,* we make it the conditioned stimulus for the food reflex, one of the most important of all unconditioned reflexes. This means that this tone gives the same reaction as the food itself. The animal produces the corresponding movements and secretions (action of the gastric and salivary glands). This reaction can be most simply and exactly measured by the amount of the salivary secretion. Now, I apply the conditioned stimulus (tone) and get the usual salivary secretion, though I do not allow the dog to eat. In the further application of this stimulus after a pause of several minutes the effect is decreased, and if I repeat it, I finally get a zero effect. This is inhibition. The inhibition after a certain time vanishes of itself without our acting in any way on the animal. We call this *extinction* of the conditioned reflex.

Another case: that of the formation of a conditioned reflex which almost coincides with the unconditioned, *i.e.*, the unconditioned stimulus (in our laboratory, usually feeding) is applied very soon (three to five seconds) after the beginning of the conditioned stimulus. Under these conditions when we apply the conditioned stimulus alone, it begins quickly to act. Now let us alter the arrangement of the experiment; let us give the dog food only three minutes after our conditioned stimulus has begun to act, instead of after three to five seconds. Then the effect of the conditioned reflex is soon entirely lost, but it will reappear with this difference: its effect is manifest only in the second or third minute after the beginning of the conditioned stimulus. Thus only the terminal part of the conditioned stimulus is effective, but not the initial part. This is what we have called the *retardation* of the conditioned reflex, and, to all appearances this, too, is an inhibition.

In the next case we combine our conditioned stimulus (tone) with another stimulus (mechanical irritation of the skin) without accompanying the combination by feeding. Thereby the conditioned stimulus gradually loses its effect in the combination. This is also an inhibition, and we call it *conditioned inhibition.*

Now the last case: we have made a conditioned stimulus from the mechanical irritation of a certain place on the skin. At first after this conditioned reflex is established other points of the skin also show the same effect when they are stimulated, and the closer they lie to the first point, the stronger their effect. This spontaneous generalisation of the stimulus has a special biological significance, and is the expression of the irradiation of the excitation in the mass of the cortex. By repeating the stimulation of our chosen point in the skin and accompanying it with feeding, and not accompanying the stimulation of the other points by feeding, these latter become inactive; now they are differentiated, negative, conditioned stimuli. This kind of inhibition we call *differential inhibition.*

This form of inhibition gives us the ability to analyse, which is the most delicate relation of the organism to the elements of the external and internal worlds. The original basis for this analysis is given by the peripheral apparatus of the various centripetal nerves. These are transformers, by every one of which a definite form of energy is changed into a nervous process. Through isolated nerve fibres the nervous process is conducted to certain points of the central nervous system, and from here it is either sent out directly again through isolated paths to the periphery, where it produces some definite activity of the organism (for example, the investigating, orienting or focusing reflex, to use our terminology); or, as we have already shown, if it is more or less irradiated, it only gradually attains again a high degree of isolation by means of the differential inhibition.

Differential inhibition fulfils a still more complicated task; it forms the foundation of the differentiation, delimitation, or separation of the compound stimuli which have been previously extended in the cortex of the cerebrum by means of the coupling activity.

All the above cases of inhibition we put into one group, to which we give the name of *internal inhibition.* The process at first spreads over the cortex, and then again gradually contracts, as does the excitation process—irradiation and concentration. Concentration of the excitation as well as of the inhibition is effected and especially reinforced by *reciprocal induction,* which confines both the excitation and the inhibition processes within strict limits of time and space.

Now, after a long period of collecting facts, of doubting and testing our hypotheses, we have arrived at the conclusion that internal inhibition and sleep are in reality one and the same process.[1] In the first case this process is strictly localised and, as it were, partitioned, whereas in sleep it is continuous and widespread. Owing to the lack of time I regret that I can not enter into the details of this important theme. I shall point out, however, a fact of great significance. A more or less long-lasting stimulation, regardless of its vital meaning for the life of the animal, falling on a certain point of the cerebral cortex, if it is not accompanied by simultaneous stimulation of other cortical points, earlier or later inevitably leads to the inhibition of that point and then to a generalised inhibition and sleep.

Besides internal inhibition there is another kind which does not develop gradually as does internal inhibition, but acts immediately on the conditioned reflexes, weakening or suppressing them—*external inhibition.* It is called out by every new activity of the cortex which produces an automatic or reflex stimulation. It is completely analogous to the inhibitory phenomena recognised long before for the lower parts of the central nervous system. We are now investigating the relations between internal and external inhibition. It is probable that they are both parts of one and the same process.[2]

Thus we see that the cerebral hemispheres are an organ of extraordinary complexity, hardly comprehensible in all its details. Together with the spread of the excitation or inhibition processes arising in consequence now of strong stimuli, now of the establishing of new relations (corresponding to new combinations in the external or internal

1 For a more detailed discussion of this question, see the following chapters.—*Translator.*

2 The suggestion that all kinds of inhibition are based on the same process is met with for the first time at this place, but since then Pavlov has brought out many facts to strengthen this view.—*Translator.*

*milieu*) during the active waking state, there are in this organ constantly more or less formidable boundaries made up of innumerable, closely intermingled, and interchangeable (from a state of excitation to one of inhibition) points. These boundaries can quickly be effaced temporarily under the influence of the excitation or inhibition resulting from strong stimuli of a positive or depressive character. On the other hand, the boundaries disappear periodically, but only temporarily, when general and diffuse inhibition (sleep) sets in. Wherefore arises the marked discrepancy between reality and dreams, the traces of former stimulations, which now combine in the most unexpected manner.

The *waking state* is maintained by means of stimulations falling upon the cerebral hemispheres chiefly from the outside world, intermingling, and more or less quickly alternating; but also by means of that movement of the excitation in the brain mass occurring as a result of the existing connections between the traces of earlier innumerable stimulations, as well as of the establishing of new connections between the present and the old stimulations. *Normal periodic sleep* sets in as a consequence of a more and more preponderant inhibitory state in the hemispheres which is related to a growing exhaustion of the organ in its entire mass proceeding during the working day. It should be added that as Verworn in his theory of inhibition as a fatigue phenomenon brought out a number of facts showing the relation of the two states, in the same manner we in our conclusions regarding inhibition as a sleep, have met with many cases in which inhibition coincided with exhaustion.

With such a formula for the activity of the cerebral cortex, there opens before the physiological investigator an unbounded horizon, and there appear an endless series of questions which can be solved by purely physiological methods.

Now I come to the *general constitution* of the *cerebral hemispheres.*

First, how shall we explain the motor region of the cortex? Has it receptive or executive functions? We endeavoured to determine this in the following way. Conditioned reflexes were formed from the flexion of the leg of a certain joint, and also from the mechanical stimulation of the skin in the corresponding region. Then in one of the dogs the gyrus sigmoideus (motor region) was removed, and in another the gyri coronarius and ectosylvius (skin area, according to our experiments). The first animal retained the conditioned reflex from the skin stimulation, and lost the conditioned reflex from the flexion (motor act). On the contrary, in the second dog, the reflex to the skin stimulus was lost and that from the flexion was preserved. Wherefore we conclude from these and also from experiments of other investigators, that the *motor region,* like the eye and ear areas, has a *receptor* function, and that the motor effect from the stimulation of the cortex is in reality of reflex character. Thus the uniformity of the whole cortical region of the brain may be considered as established. According to this view the cortex is only a receptor apparatus, which in various ways analyses and synthesises the incoming stimulations. These stimulations reach the purely effective apparatus by means of descending connecting fibres.

The next important question confronting us is that of *localisation* in the cortex. On the basis of Munk's experiments it became evident that the projection of the retina lay in the cortex of the occipital lobe. Not long ago this was confirmed by Minkovsky in the laboratory of Monakov. We also have seen this in many dogs. Munk showed that stimulations from the ear bore a corresponding relation to the temporal region of the cortex. On the other hand, the Luciani school has for a long time advocated a more expansive area for the location of these centres.

At the present time Kalischer, using the method of conditioned reflexes, or as he calls it, the training method, shows that these reflexes from the eye and the ear can be obtained after removal of the visual and auditory areas. The clinicians possess a mass of material which also can not be reconciled with the theory of narrowly limited centres. We have endeavoured to elucidate this indefinite situation by the following experiments. The conditioned stimuli which we used consisted either of elementary or of various complex stimuli. For the ear experiments we employed at one time a series of four successive ascending tones, and another time a chord of two extreme tones and one middle tone from the third octave. The first stimulus of the ascending tones was easily differentiated from the same tones in descending order by the normal animal. After the formation of the conditioned reflex to the chord, its separate tones called out the same reflex but the reaction was weaker. Now in the animal having the reflex to the chord, one-half of the auditory area of Munk was removed. After this operation one of the extreme tones of the chord lost its effect when used alone, although a conditioned reflex could be formed anew on this separate tone. In the dog with the conditioned reflex to the series of tones, the posterior half of the cerebrum, all the part behind the gyrus sigmoideus at the level of the apex of the fissura fossæ sylvii and behind this fissure, was extirpated. Now it was impossible to differentiate this series of tones used in ascending order from the same series used in descending order. The separate tones of the series, however, employed as conditioned stimuli, could be easily differentiated by this animal.

In the experiments in which we used optical stimuli, after removal of the hinder part of the hemispheres along the line described in the preceding paragraph, the animal could differentiate not only various degrees of general illumination, but also equally lighted figures of various shapes, such as squares from circles. Complicated pictures, however, could not be distinguished one from the other. Obviously in this category belong the facts long since recognised: that after extirpation of the temporal and occipital regions of the hemispheres, the dogs lose forever their conditional reactions to objects and words, as well as to complicated auditory and visual stimuli.

From all these facts we conclude that each *peripheral receiving apparatus* (the "sense" organ) has in the cortex a *special central territory,* its own *terminus,* which represents its exact *projection in the brain.* Here—thanks to the special construction of this area (probably the more condensed distribution of cells, the more numerous connections between them, and the absence of cells with other functions)—can be effected highly complicated stimulations (the highest syntheses), and also their differentiation (the highest analyses). However, the given receptor elements *transcend this central area,* extending out over a great distance, probably throughout the entire cortex, but the farther they are from their centre, the more unfavourably they are disposed (in regard to their function). In consequence of this, the stimulations become more elementary, and the analyses less refined. In conformity with this view, the motor region, too, must be considered as a receptor one, as a projection of the whole movement apparatus; the receiving elements of this system, however, may be farther distributed from their central territory.

Before physiology looms up the immense, though promising, task of systematically investigating the state of synthesis and analysis at different distances from the nucleus of the projection area. The conception presented here concerning the cortex explains in the most natural way the mechanism of the gradual and slow restoration, to a greater or less degree, of functions lost after extirpation of parts of the brain, excepting of course those disturbances which are the direct and immediate effects of the operation, as pressure changes, derangements of the blood circulation, etc.

In conclusion, I ask your attention to the following. We have many examples of the compensating ability of the organism. It is obviously the highest perfection of the machine. It is evident that this property must be especially developed in the nervous system, which regulates and controls the whole organism. The most frequent threat from the external world comes in the form of mechanical energy. Consequently, the nervous system must be especially adapted to this danger. On this ground, it seems to me, one can account for all those decussations in the nervous system, the puzzling course of its fibres, the apparent superfluity of its elements, etc., as a factor of safety, a provision for a more or less efficacious neutralisation of menacing destruction.

Finally, the last question about the general functional construction of the cortex: do there exist besides the receptor parts of the brain which we have considered, still higher regions with general executive functions?

We have had two groups of cases classified according to which part of the brain was removed. We extirpated either the frontal and smaller half in one group, or the larger posterior half in the other. There was a marked difference between the two sets of syndromes. The dogs without the posterior sections appeared at first sight as perfectly normal. They were well oriented to the surroundings, chiefly by means of stimulations from the skin and from the nasal mucous membrane.

It was entirely otherwise with the dogs the forepart of whose hemispheres had been removed. They were completely helpless, and could not live without attention. They had to be fed by putting the food into the mouth or directly into the stomach, and they had to be protected against all sorts of injuries. They made no purposeful movement. It seemed as if nothing remained of the normal functions of the hemispheres. But this is not so. Our salivary reflex served us well here. Allow me to remind you that we observed the reactions of the animals, not through their muscular movements, but through their salivary secretions. In the given case it proved that these animals, judged by the skeletal muscles, were complete invalids, but judged by the work of the salivary glands, they were capable of a complicated nervous activity. They were able to form conditioned reflexes as are normal animals, and exactly to correct them, as mentioned in the beginning of this report. In one dog thus operated on it was possible to form conditioned reflexes only from the receptor surface of the mouth cavity upon which acted at the same time the unconditioned stimulus. In another dog the frontal lobes had been removed but the olfactory region left intact; in this animal the higher nervous activity could be studied by the influence of olfactory stimuli (odours). As a postmortem examination showed, during our operation the conducting paths of the posterior lobes of the brain had been seriously damaged; for they were markedly atrophied. This was the reason why no reflexes to the salivary glands could be formed from eye and ear stimuli. Yet from these receptor organs it was easy to form conditioned inhibition, and sleep ensued when the stimulations were continued.

This fact was constantly observed in partial destruction of various regions of the cortex. It was impossible to form positive conditioned reflexes from the body surfaces corresponding to the removed area, whereas conditioned inhibition could readily be obtained. Drowsiness and sleep developed very soon when these stimuli were applied. These phenomena as such form one of the foundations for the conclusion that *sleep and inhibition are identical* in character, and are *related in some way to fatigue.*

From the foregoing experiments it follows that in the destruction of the forepart of the hemispheres, together with great damage to the posterior parts, the remnant of the underlying cortex is capable of performing higher nervous activities. On this fact is founded *the law of equivalence of all parts of the hemispheres* in regard to the mechanism of their function. Already H. Munk had insisted on this.

In concluding, it is interesting to refer to the activity of the skeletal musculature in the above-mentioned animals. There was a great difference between the animals with hemispheres *entirely* removed and those with only a part extirpated. The former can, as is generally known, stand and walk, if only some days have elapsed since the operation. But our animals, with only the frontal lobes lacking, could not stand until some weeks had elapsed and they began to walk only after a month or more, and even then they assumed very unusual positions and often fell. And this continued during all their laboratory life. It was especially marked that these animals undertook simultaneously such movements as are inconsistent with the equilibrium of the body, in other words, they lacked the ability of combining movements efficiently.

How can we understand this condition? I think only in the following manner. We had removed by our operation the central receptor region of the skin and motor apparatus, by means of which proceeds the efficient and normal combining of movements. In the remaining part of the hemispheres there are only more disconnected and isolated receiving elements of the same functions—elements which can synthesise gradually and very slowly and in a very limited way. In those animals from which all of the hemispheres had been removed, the lower locomotor centres begin to function quickly, being unhindered by an unbalanced activity of the upper sections.

This report is based on the results of more than one hundred investigations from my laboratory and the work of seventy collaborators.[3]

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[3] **Most of these have been published separately in Russian.—*Translator.***

# CHAPTER XXXII

## INTERNAL INHIBITION AND SLEEP —ONE AND THE SAME PROCESS

(From the Anniversary Volume, dedicated to the President of the Russian Academy of Sciences, A. P. Karpinsky, 1922)

GENERAL DESCRIPTION OF EXPERIMENTATION WITH CONDITIONED REFLEXES—PRODUCTION OF SLEEP BY SPECIAL AGENTS OR BY DELAYING THE UNCONDITIONED STIMULUS; DEPENDENT ON THE TYPE OF DOG—THE LAW OF SLEEP—THE FOCUSING REFLEX—CELL EXHAUSTION AND SLEEP—RELATION OF SLEEP TO INHIBITION—ILLUSTRATIVE EXPERIMENTS SHOWING TRANSITION OF SLEEP INTO INHIBITION AND VICE VERSA—SLEEP ARISES AND VANISHES AS DOES INHIBITION—SUMMATION OF SLEEP AND INHIBITION—DISTINCTION BETWEEN SLEEP AND INHIBITION (SLEEP A WIDESPREAD INHIBITION)—LIMITATION OF INHIBITION BY EXCITATION; AN ILLUSTRATIVE EXPERIMENT—SIMILARITY BETWEEN THE MOVEMENT THROUGH THE BRAIN OF SLEEP INHIBITION AND OF ORDINARY INHIBITION—PREVENTION OF SLEEP—PROOF OF THE IDENTITY OF SLEEP AND INTERNAL INHIBITION—THE IDENTITY EXPLAINS MANY FACTS—EFFECT OF FAMINE ON SLEEP—REST.

In the beginning of our objective study of the higher nervous activity of animals by the method of conditioned reflexes (behaviour), we met with an undesired phenomenon in the experimental object—drowsiness and sleep. The animal (dog) was usually put on a stand on a table, fastened by loops suspended from a beam of the stand, and his head held up by a cord around his neck. Thus our animal had his movements restricted. The stand and the dog were confined in a special room where only the experimenter was present. In our laboratory later on the experimenter was removed to a position outside the chamber, and by a specially arranged apparatus he gave the stimuli and noted the reactions with the door closed. In the course of our experiments two different unconditioned reflexes were used; either the food reflex by feeding some more or less dry substance, or the defensive reflex by pouring acid (0.5%-1.0%) into the mouth of the dog. The reaction was studied and measured not by the motor effect, but by the secretion of saliva from the submaxillary or parotid gland. By means of a definite procedure (coincidence in time) conditioned reflexes are formed with the help of the unconditioned; various previously indifferent agents which had no relation to the unconditioned reflex, now call out the corresponding food or defence reaction both in the motor and the secretory activities of the animal.

If now, after the conditioned reflex has been elaborated, the conditioned stimulus be allowed to act alone before the unconditioned stimulus (feeding or putting acid into the mouth), even though it acts only a few seconds (15 to 30), then after some repetitions of this procedure, drowsiness and sleep begin to manifest themselves both during and after the action of the conditioned stimulus. The sleep may be so deep that it is necessary to shake the animal before he will take the proffered food, and this in spite of the fact that the dog may have had nothing to eat for 24 hours, may be very greedy, or may react very strongly to the injection of acid into the mouth.

Now the following three circumstances had been noticed at an early stage of our work. *First,* there are certain special agents out of which we form our conditioned stimuli that are particularly conducive to sleep. Of these the chief are thermal skin stimuli, warm as well as cold; mechanical skin stimuli, light scratching or pricking; and weak stimuli in general. The *second* especially noteworthy condition is the length of time during which the conditioned stimulus acts before the unconditioned stimulus. Suppose that in a certain dog we always give the conditioned stimulus 10 seconds before reinforcing it, *i.e.,* adding the food or the acid. In the course of these 10 seconds we have an extreme degree of both the motor and the secretory reaction. It is surprising how quickly the situation will change when there is apparently only a slight modification—if the unconditioned stimulus is applied not 10 seconds but 30 or 60 after the beginning of the conditioned stimulus. Drowsiness set in soon after the beginning of the conditioned stimulus, the conditioned reactions disappear, and the animal that never before slept on the stand, during every experimental séance falls asleep after the first application of the conditioned stimulus. The *third* factor: drowsiness and sleep arise under the above mentioned conditions in strict dependence upon the individuality of the dog, upon his type of nervous system. In order to avoid the obstacle of sleep, it is interesting to mention that in the beginning of our experiments with conditioned reflexes, we fell into a paradoxical error. We endeavoured to choose such dogs as would not fall asleep, as were very lively and active when outside the experimental room; but the results we obtained were exactly opposite to those we desired. These dogs under the above mentioned conditions proved especially susceptible to sleep. On the contrary, the animals we considered as stolid and inactive were particularly fit for our experiments when on the experimental stand, and even under most favourable conditions for a long time they did not sleep.

The above sleep-producing conditions finally led us to the scientific investigation of this phenomenon. What then is sleep and what is its essential relation to our experiments?

Not only practically but also theoretically my laboratory has been concerned with this question for more than ten years. We have tried and rejected five or six different hypotheses, and now at last we have come to what I think is a final conclusion, *viz.*, that the inhibition with which we had become acquainted as a recurring phenomenon in our work with the conditioned reflexes,—that this internal inhibition and sleep are fundamentally one and the same process. This conclusion conforms to the multitude of facts which we have collected during our twenty years of work with the conditioned reflexes, and also to new experiments designed to throw light on the subject.

The general law is this: a more or less enduring stimulation falling on a certain part of the hemispheres, whether or not it is of vital significance (and especially if it is without such significance), and no matter how strong it may be,—every such stimulation, if it is not accompanied by simultaneous stimulation of other points, or if it is not alternated with other stimulations, leads inevitably sooner or later to drowsiness and *sleep.* In the first place this statement is well illustrated by the fact that the conditioned stimulus which acts on a certain point of the brain, although it may be connected with the most important stimulator of the organism, food, leads, in spite of this to sleep, if it continues for a long time, or in some cases even for a few seconds if isolated and if it is not followed by the simultaneous mass of stimulations which constitute the act of eating. It must be added that there is no exception to this rule, not even in that case where the conditioned stimulus for the food reaction consists in a powerful electrical current applied to the skin of the dog. This fact is well known in its general form, though it has not been subjected to scientific investigation. *Every monotonous and continuous stimulation leads to drowsiness and sleep.* It is hardly necessary to mention every-day instances of this sort.

Once engaged in the study of this subject, we investigated the above state in other cases than those of conditioned reflexes. If there arises in the surroundings some new stimulus, *i.e.,* if there is a change in the situation, the animal responds with a general reaction during which he turns his corresponding receptor surfaces in the direction of the stimulus (looks, listens, etc.), provided the stimulus does not call out through its peculiarities some other special action. We call this general response the *orienting, investigating* or *focusing* reflex. If we repeat this stimulation at short intervals or let it last for a long time, the investigating reflex becomes gradually weaker, and finally vanishes, and afterwards, if no alternating stimulations affect the animal, he becomes drowsy and sleeps. If this is repeated several times, then the experimental sleep can be reproduced with the same exactitude as the reaction of a hungry dog to a piece of meat (experiments of S. I. Chichulin and O. S. Rosenthal). This fact is so constant that there can be no doubt regarding it. An isolated and continuous stimulation of a definite point of the cerebral hemispheres leads infallibly to drowsiness and sleep. It is most reason-able to consider the mechanism of this phenomenon as conforming with what we already know about living tissues, as a phenomenon of fatigue, and the more so because normal periodic sleep is without doubt the result of exhaustion. Thus, thanks to the continuous stimulation of the given point, it becomes fatigued and "somehow" in dependence upon this exhaustion there develops a state of inactivity, of sleep. I say "somehow" because it is not possible to understand clearly the whole phenomenon without a special insight into the series of chemical changes occurring in the given cell. The following details of the phenomenon speak in favour of this view. The inactivity, in the form of sleep, which has arisen in a given cell does not remain only at its point of origin but spreads farther and farther until it embraces not only the hemispheres but also the lower lying parts of the brain, *i.e.*, the state developing in a certain cell which has been working and has expended its energy passes over also to such cells as have not worked or been active. This is at present an obscure point in the understanding of the phenomenon. One must grant that exhaustion in the cell produces a special process or substance which stops the activity of the cell, as if to prevent an extraordinary, threatening and annihilating over-exertion. And this peculiar process or substance may be carried over to the surrounding cells which have not participated in the given work.

Now we come to the relations which exist between sleep and internal inhibition of the conditioned reflexes.

*Internal inhibition* develops when the conditioned stimulus is not attended by the unconditioned, whether this be once or always, but in the latter event, only under certain circumstances. Thus comes about extinction, retardation, conditioned inhibition, and differential inhibition. We see then that the same conditions are necessary for the occurrence of sleep as for the development of internal inhibition. It is impossible, therefore, not to consider this fact of great significance for the question as to the relation of internal inhibition to sleep, and the more so because in all our cases of internal inhibition we meet with an admixture of drowsiness and sleep. In retardation, when we delay the beginning of the unconditioned stimulus for some time after the beginning of the conditioned stimulus, in proportion to the length of this interval we have, as mentioned before, the state of sleepiness. In a dog with an elaborated conditioned reflex, if one repeats stimuli related to the conditioned stimulus (which were previously active due to irradiation of the stimulation) without accompanying them by the unconditioned stimulus, then there is a loss of their action simultaneous with the setting in of drowsiness and sleep. Exactly the same phenomenon is observed in the elaboration of the process of conditioned inhibition from a stimulus; except that the drowsiness rarely passes over into complete sleep.

Likewise, in the extinction of the conditioned reflexes, if the extinguished stimuli are repeated several times during the same experiment, drowsiness and sleep are clearly manifested. If one continues applying the extinguished stimuli during some days, then the animal that formerly had no inclination to sleep, becomes so somnolent that it is difficult to work further with him. It should be added that there are apparently some peculiarities in the various kinds of internal inhibition which affect the speed of the occurrence of sleep and its stability.

Now a further question: what special relations are observed between sleep and inhibition? We meet here with many variations. They are now the transition of inhibition into sleep and vice versa, now the alternation of sleep and inhibition, now the summation of sleep and inhibition.

We have a dog in whom the unconditioned stimulus is added to the conditioned after 30 seconds. A conditioned reflex was elaborated: the salivary secretion commences 5 to 10 seconds after the beginning of the conditioned stimulus. We repeat this experiment for weeks or months, depending upon the individual animal, always accompanying the conditioned stimulus with the unconditioned. Now we can see that the latent period of the conditioned stimulus gradually increases; 15 to 20 seconds pass, then 20 to 25 before the conditioned reflex begins; and finally the conditioned reflex does not start until the exact end of the 30 seconds or perhaps 1 or 2 seconds earlier. This is internal inhibition, *retardation,* an exact adaptation to the moment of the action of the unconditioned stimulus. Later on, the effect of the conditioned stimulus is entirely absent during the first 30 seconds of its action, but it becomes manifest if its application is continued for longer than 30 seconds. But there follows a stage, when you can not obtain any effect from your conditioned stimulus, and together with this the animal becomes drowsy and goes to sleep, or becomes quite motionless (*i.e.,* falls into a cataleptic state).

An opposite case: we have elaborated a delayed reflex in which the unconditioned stimulus followed the conditioned only three minutes after its beginning. Here the three-minute period of the conditioned stimulus is divided into two phases—the initial, inactive; and the second, active. And often during an experimental séance we observe that in the first trial of the conditioned stimulus, the animal becomes immediately sleepy, and toward the end of the three-minute period, when the conditioned reflex should begin to appear there is only a minimal, if any, effect. Further, the active effect of the conditioned stimulus increases with each repetition, fills the greater part of the stimulation period, and the state of sleep is more and more dispelled. Finally, there is no sleep and drowsiness at all, and the whole period of the application of the conditioned stimulus divides into two equal parts, or into parts having a relation of 2 : 1, the first without effect, the second with an effect which gradually increases toward the end.

Thus, we see that in the first case, inhibition passes over into sleep, and in the second, sleep changes into pure inhibition.

A similar transformation of inhibition into sleep is observed in the orienting or investigating reflex. This reflex, as has often been noted, disappears during a long duration or constant repetition of the stimulus. It is interesting that, as the experiments of Prof. G. P. Zeliony show, such a reflex provoked by a sound, in a dog having the hemispheres removed, is not lost even though it be repeated many times. Hence the reason for thinking that the cells of the hemispheres and of the lower parts of the brain bear a very different relation to their stimulations. In what way is the destruction of the investigating reflex attained in the normal animal? The experiments of N. A. Popov proved that the process lying at the foundation of the suppression of the investigating reflex is in all its details similar to the extinction of the conditioned reflexes, and is a manifestation of inhibition. Later this inhibition passes over into sleep.

Sometimes, for example in the experiment with delay of the unconditioned stimulus for about 30 seconds after the beginning of the conditioned, it happens that an animal which is usually wide awake when on the stand begins to fall asleep immediately at the commencement of each separate conditioned stimulus, going into a passive state, hanging his head, and even snoring; but after the conditioned stimulus has continued for 25 seconds, the dog awakes and gives a markedly positive reflex. This state of affairs may last for a considerable length of time. It is evident in the given case that sleep replaces inhibition, arising and vanishing exactly as does pure inhibition.

There is further the constant fact of simultaneous disappearance of sleep and internal inhibition. We have a well elaborated delayed (three-minute) reflex which in the waking state of the animal becomes effective only after one and a half to two minutes. If we now apply our conditioned stimulus after the animal has fallen asleep, the stimulus awakens it, dispelling the sleep and together with it the internal inhibition; the conditioned stimulus gives its effect immediately, and the inactive phase disappears.

Here is a case of *summation* of sleep and inhibition. We have again a well elaborated delayed reflex (three-minute). The effect begins only after one and a half minutes and attains a maximum at the end of the third minute. Now, together with the conditioned stimulus, we apply some new, rather weak, indifferent stimulus such as a hissing sound. During its first application it dis-inhibits, allows the conditioned stimulus to manifest its effect in the inactive phase, and we see the orienting reaction at the start of this new stimulus; on the second application there is no orienting reaction, the conditioned stimulus is not manifested during all three minutes, and drowsiness can be observed. The conditioned stimulus applied alone continues to give a pure, delayed reflex (experiments of D. S. Fursikov). Thus two inhibitions summated produced the state of sleep.

The same phenomenon is to be seen in the following modification of the experiment. The reflex is delayed for 30 seconds. The effect begins 3 to 5 seconds after the start of the conditioned stimulus. Now we introduce a new, additional stimulus, and repeat it until it ceases to produce the orienting reaction, but provokes drowsiness. If we apply it now together with the conditioned stimulus, we get a more delayed reflex, its action beginning after 15 to 20 seconds (experiments of S. I. Chichulin). Thus in the first case two kinds of inhibition gave drowsiness. In this second case the state of drowsiness arising from one stimulation reinforces the inhibition of the other.

All the foregoing facts strengthen our conviction that internal inhibition and sleep are one and the same process. But what is the difference between the two states and how does this difference come about? At first sight these two states seem to differ widely. Internal inhibition always takes place in the waking state of the animal, and particularly in his most exact adaptation to his surroundings, while sleep is a state of inactivity, the repose of the hemispheres. The distinction is as follows: *inhibition* is a partial, fragmentary, narrowly limited, strictly localised sleep, confined within definite boundaries under the influence of the opposing process—that of excitation; sleep on the contrary is an inhibition which has spread over a great section of the cerebrum, over the entire hemispheres and even into the lower lying midbrain. From this point of view the above cases can be easily understood: either the inhibition spreads and sleep sets in, or the inhibition is limited and sleep disappears. Let us take, for instance, the case in which during an experimental séance the formerly predominating sleep becomes gradually replaced by the appearance of pure inhibition. Here under the influence of repetition of the unconditioned stimulus, little by little the stimulation limits the inhibition process, confining it within narrower boundaries and to a shorter period: together with this, sleep disappears, and there actually occurs an equilibration of the excitatory and inhibitory processes.

From this point of view in order to limit inhibition and to prevent its change into sleep, or, vice versa, to transform sleep into pure inhibition, it is essential to form in the hemispheres points of excitation which can resist the spread of the inhibition. For a long time we applied such a procedure, although empirically. When, from a more or less delayed conditioned reflex drowsiness developed and sleep set in, we formed new conditioned reflexes out of stronger agents and made them more strictly coinciding reflexes, *i.e.*, reflexes in which the unconditioned stimulus was joined after a shorter interval to the conditioned. This often helped. Sleep was removed, and the formerly delayed reflex restored.

Recently Dr. Petrova performed experiments extending over a long period as follows. Conditioned reflexes were elaborated in two dogs: the first a very lively animal, and the second phlegmatic. In the first the conditioned stimulus was begun 15 seconds before the unconditioned, and in the second, three minutes. But soon after the formation of the conditioned reflexes both dogs became sleepy on the stand, and later to such an extent that no further experiments could be performed. The following changes were at this time made in the procedure. The unconditioned stimulus was added to the conditioned 2 to 3 seconds after the beginning of the latter, and besides the earlier reflex, which had been elaborated from the ticking of a metronome, conditioned reflexes were formed out of five new agents—a bell, a tone, the sound of air bubbling through water, the flashing of a light before the eyes of the animal, and mechanical stimulation of the skin. The reflexes formed very quickly and sleep disappeared; in the experimental séances each stimulus was applied only once, whereas formerly the metronome was repeated six times. Afterwards all the coinciding reflexes were delayed by removing the unconditioned stimulus every day five seconds further from the beginning of the conditioned. Correspondingly the effect of the conditioned stimulation was little by little retarded. When this interval between the conditioned and the unconditioned stimuli reached three minutes, a striking difference was noted between the two dogs. The experiments with the phlegmatic dog proceeded smoothly, good delayed reflexes were elaborated from all stimuli, and were retained as such though all the stimuli except the original metronome were discontinued, and the interval between the stimulus of the metronome and its unconditioned stimulus, food, was lengthened to five minutes. In the lively dog it was quite otherwise. When the unconditioned stimulus was delayed to three minutes, the excitement of the dog reached a high degree; during the stimulation the dog barked desperately, struggled energetically, developed dyspnœa, and the salivary secretion did not stop, *i.e.*, in the intervals between the separate stimulation, as is usual in dogs which display a state of strong excitation. Then all stimuli were discontinued except the metronome, which remained as a delayed stimulus. The animal slowly became quiet, but at the same time drowsy, and fell asleep,—and the reflex disappeared. In order to keep the dog awake it was necessary to apply all the stimuli again and coincidentally, *i.e.,* to follow the conditioned stimulus quickly by the unconditioned. This we did. Afterwards the unconditioned stimuli were delayed. Now the delayed conditioned reflex developed without excitation, and the reflex to the metronome, when it was again alone, did not pass into sleep, but retained its delayed character.

This experiment is of interest in many respects: here I ask you to observe that the application of many excitatory points without frequent repetition of the stimulation of one and the same point during the experimental séance caused the disappearance of sleep and the limitation of the inhibition and its inclusion within definite boundaries. The following experiment of Fursikov leads to the same conclusion. From mechanical stimulation of the skin at one end of the body a delayed conditioned reflex was elaborated, the unconditioned stimulus being retarded for three minutes. Then drowsiness set in, and the reflex disappeared. Afterwards a coincident conditioned reflex from the mechanical stimulation of the skin at the other end of the body was formed. The delayed reflex was restored, but it still showed retardation. Thus it happened that the stimulation of a new point in the skin region of the hemispheres caused a delimiting of the inhibition issuing from the first point, and simultaneously sleep disappeared.

The same thing occurs in every differentiation. If those stimuli which are closely related to the conditioned stimulus are applied repeatedly, without accompanying them by the unconditioned stimulus, then the borrowed effect of the original irradiation gradually decreases; they are inhibited, and deep sleep supervenes during the effect of these differentiated (negative) conditioned stimuli and extends beyond the period of stimulation. But through the application of such (negative) stimuli alternating with the well elaborated conditioned (positive) stimulus, which latter is always accompanied by the unconditioned stimulus, for example, food, it comes about that sleep passes off and the negative conditioned stimuli are entirely ineffective, inhibited. Consequently the stimulation of a certain point limits the spread of the inhibitory process from the neighbouring points, concentrates it, and in that way banishes sleep.

The same phenomenon that is seen in differentiation may be seen in conditioned inhibition, if the inhibiting combination is constantly alternated with positive stimuli.

A similar process is observed in extinction. If the extinction is repeated on many successive days or many times during the same séance, the affair ends in drowsiness and sleep. If the extinction is not done every day, and not often, only once or twice during a single experiment, then it proceeds quickly and there is no drowsiness. Apparently the oft-repeated stimulations which are reinforced (*i.e.,* followed by the unconditioned stimulus) do not permit the spread of the inhibition: this is the concentration of inhibition.

The foregoing explanations and conclusions embody the idea that inhibition and sleep are processes which move through the mass of the cerebrum. And it is so in fact. Many experiments in my laboratory have made it clear that the internal inhibition which is called out at a given moment persists in the nervous system for some time after the cessation of the provocative agent, and only later gradually concentrates in time and adapts itself more and more closely to the given moment. The same holds for concentration in space. In the skin one can follow exactly how far and with what speed the inhibition at first irradiates and later concentrates about its point of origin.

The same facts are known from ordinary observations on sleep. Falling to sleep as well as awaking, the overwhelming of the brain by sleep and its release from sleep, proceed more or less gradually. I have noted this process (with L. N. Voskresensky [1]) in a dog that fell asleep as a result of the action of the whole environment of all the objects in the experimental room. One can easily distinguish between some of the successive stages of sleep manifested in various parts of the brain. It is interesting that the velocities of the spread of inhibition and sleep are of the same order. Falling asleep and awaking can be measured in minutes, few or many, and the same is true of irradiation and concentration of internal inhibition. The similarity goes even further. As is well known, human beings vary widely in the quickness with which they fall asleep and awaken; some go to sleep and wake up very rapidly, others slowly. The same is true of the movement of inhibition processes. Among the dogs that have been compared up to the present (three), the difference between the extremes was as 1:10. In one dog the hither and thither movement of inhibition (irradiation and concentration) took place in one and a half minutes; in the other extreme case, in 15 minutes. From the point of view of the extent of the spread of the inhibition, one can understand the following difference, which is seldom met with in animals. In the majority of dogs it happens that the expansive irradiation of the inhibition is manifested in complete sleep and relaxation of the skeletal musculature; the inhibition reaches those parts of the brain which lie below the hemispheres and which govern the equilibration of the animal in space. In rarer cases the inhibition is confined to the hemispheres and their motor region, and does not penetrate downward; in this latter case the result is that the animal becomes stiff and immobile, but preserves his active pose.

As the above mentioned experiment of Dr. Petrova showed, the careful and gradual development of localisation of inhibition in one of her dogs,

[1] See chapter xxiv.—*Translator.*

so operated that the previous irradiation of inhibition to the extent of sleep was finally prevented and only a narrowly localised sleep, a pure inhibition, remained. In some cases the internal inhibition, *viz.*, in differential inhibition and conditioned inhibition, drowsiness and sleep, although they occur, are of shorter duration than in other sorts of inhibition (*i.e.*, the localisation of inhibition proceeds more easily and quickly). Therefore, in order to prevent the development of sleepiness, we elaborate, usually during the period of the preliminary work, not only several conditioned reflexes but also differential inhibition or conditioned inhibition. And the desired effect is generally obtained by this procedure.

In accordance with the foregoing statements is the following fact. As an agent producing internal inhibition acts more surely and quickly on repetition, so it is with sleep; for any indifferent agent, or our conditioned stimulus which causes it, also becomes more effective on repeated application.

Here is a fact from one experiment, which seems worth mentioning although it has not yet been repeated. Sleep which appeared at the beginning of the development of differentiation, and later with the differentiation well established became imperceptible in the general behaviour of the animal, was again manifest when we undertook to destroy the differentiation by accompanying the negative conditioned stimulus by the unconditioned stimulus (food).* It was as if sleep had been temporarily liberated from its confines. But this is not so easy to imagine.

Finally an additional proof of the identity of sleep and internal inhibition is evident from the following fact, which we have often met before. It is the development of general excitation in some cases of inhibition. We are elaborating, for example, a conditioned inhibition, and when it commences to manifest itself, we see that our dog begins to be much excited, struggling, barking and panting. In some dogs this is only a short phase; in others it is an obstinate condition which remains for a long time. This has already been described by us in one of Dr. Petrova's dogs. In this dog, during the development of retardation arising from six simultaneous stimuli, there was an extraordinarily intense and persistent state of excitement, disappearing only on the removal of five of these stimuli. A like state of excitation is observed in some dogs under the influence of often repeated indifferent stimuli which then lead to sleep. Dogs that are not fastened in the experimental room make many movements, scratching, barking, etc., before lying down to sleep.** In dogs having a delayed conditioned reflex and manifesting

* Experiments of V. V. Stroganov.

** Experiments of I. S. Rosenthal.

the retarding inhibition as sleep during the inactive phase, the following characteristic sequence of phenomena is observed: as soon as the conditioned stimulus begins to act, the waking dog, which has until this time been quiet, executes some disorderly movements, and only later does rest return, now accompanied, however, by slumber (by which we mean passive position of the body, hanging of the head, and closing the eyes). Later at the approach of the active phase, the animal again makes indefinite movements, and only then commences to give the specific motor reaction to food.

Thus, the dissolving of excitation by inhibition as well as the transformation of the waking state into sleep, is attended by a temporary general excitement. Probably this is the positive phase of induction; *viz.,* the initial inhibition immediately provokes in the remote regions excitation, which is suppressed, however, through the continuous effect of the inhibiting or sleep producing agent.

This explanation of sleep and internal inhibition as essentially one and the same process has thrown light upon many formerly obscure facts. Here are the chief ones. After extirpation of the cortical projection of some receptor organ, it is impossible for weeks or even months to form a conditioned reflex from stimulation of the corresponding organ, although the same stimuli can readily appear as conditioned inhibitors. The possibility of external inhibition in these cases was excluded by special experiments. When some time has elapsed after the operation, it is possible to form a conditioned stimulus but only if the unconditioned stimulus is almost coincident, *i.e.,* following no later than three to five seconds after the conditioned. With a greater separation of the conditioned and unconditioned stimuli, the conditioned reflex vanishes. These facts are especially evident when part of the projection area of the skin is extirpated. On a certain part of the skin where the retardation may be 30 seconds, the dog stays awake and the reflexes are maintained, whereas on other skin areas with the same retardation the dog becomes drowsy and sleeps, and the reflexes are lost. In the first phase after this operation the stimulation of the parts of the skin which correspond to the extirpated parts of the projection area in the brain (and which have, therefore, lost their earlier positive conditioned action) inhibits from the start the reflexes simultaneously stimulated from other parts of the skin which correspond to areas of the brain not injured in the operation. Furthermore, the stimulation of these inactive places calls out no orienting reaction. Finally, stimulation of only these places, though of short duration, causes drowsiness and sleep, even in dogs that never before slept on the stand. Now we have no difficulty in understanding all the facts. When after the operation you stimulate the corresponding points of the receptor apparatus, then all the cells which remain—cells weakened by the operation or cells which during the existence of the cells now removed had never been stimulated or had been stimulated only together with the cells now removed—are quickly fatigued. They fatigue even during the latent period of the stimulation and therefore they provoke inhibition from the outset, and with the wider extension of inhibition, sleep as well.

A fact relating to this was observed in our laboratory in the hard years, 1919 and 1920, when we had to work with starving and exhausted animals. Even slightly delayed reflexes quickly disappeared, provoking sleep, so that further work was impossible.* Apparently the general exhaustion made itself especially manifest in the nerve cells of the hemispheres. One can understand in a similar manner the previously mentioned fact that under the conditions of our experiments lively dogs are especially susceptible to sleep. One may suppose that the vivacity and restlessness of these animals is such that with their ready excitability there is rapid exhaustion of the given stimulated points; this results in inhibition, and this in turn produces by induction a general excitation. This stimulation by impelling the dog to move to and fro generates new excitations in other cells, whereby in the state of freedom a more extensive development and spread of inhibition (sleep) is prevented. On account of the impossibility of such spread of excitation while the dog is on the stand, and with the unavoidable uniformity of external and internal stimulations, in these animals with their weak nervous systems, sleep quickly develops.

Probably it is possible to explain the temporary initial excitation which arises under the influence of the soporific stimuli during the waking state, as a means of avoiding sleep under unfavourable conditions of time and space. This avoidance is effected if the animal is constantly exposed to new external stimulations, or if stimulations are produced by the movements of his own body.

After we had seen that with a well developed delayed reflex the conditioned stimulus acting on a drowsy or sleeping animal gives immediately at the time of waking the conditioned effect without an inactive phase, it was natural for us to modify our view concerning what we call *dis-inhibition* of conditioned reflexes. Certainly dis-inhibition is a prominent and important phenomenon when internal inhibition, although it may be well elaborated, suddenly disappears under the influence of any unusual stimulus. If in analogy with the inhibition of conditioned stimuli by unusual stimuli (external inhibition), dis-inhibition were explained as a possible inhibition of inhibition, this would make more involved the understanding of an already very complicated nervous relation. Now we can give a simpler explanation. As in the

* Experiments of N. A. Podkopayev, I. S. Rosenthal and U. P. Frolov.

above mentioned case, where inhibition disappeared together with sleep, so also in all other cases one may suppose that a new, incoming, irradiating stimulation removed the inhibition just as it dispels sleep; for inhibition, according to our analysis, is a partial sleep.

After what we have said, if you accept the fragmentary nature of sleep in the cerebral hemispheres, the phenomena of human hypnotism are comprehensible on the basis of the partitioning and complexity of the great hemispheres.

In conclusion, I venture to make a general deduction from the cited facts and their comparison. If one agrees with us that sleep and internal inhibition are essentially one and the same process then we should have a striking instance of the economic principle of the organism, *viz.*, that the highest manifestation of life, the most exact adaptation of the organism, the constant correction of its temporary connections, the unceasing establishment of a moving equilibrium with the surrounding world, rests upon the inactive state of the most precious elements of the organism—the nerve cells of the cerebral hemispheres.

# CHAPTER XXXIII

## CHANGES IN THE EXCITABILITY OF VARIOUS POINTS OF THE CEREBRAL CORTEX AS ONE OF ITS FUNCTIONAL CHARACTERISTICS

(From the *Schweizer Archiv für Neurologie und Psychiatrie*, 1923, vol. xiii.)

THE CONDITIONED REFLEX MAY BE FORMED TO ANY INDIFFERENT AGENT—POSITIVE AND NEGATIVE CONDITIONED STIMULI—EXTERNAL INHIBITION; AN EXPERIMENTAL EXAMPLE—INDUCTION—RECIPROCAL INDUCTION, A MEANS OF STABILITY—AN EXAMPLE—MUCH REMAINS TO BE EXPLAINED.

UPON the physiologist devolves the colossal task of explaining the functions of the cortex of the cerebral hemispheres. At present only preliminary experiments can be undertaken and only an attempt to characterise some functions of this nervous mass from certain facts. On the basis of my many years of research I take the liberty of describing to you some of the characteristics of these functions.

For some time past we have occupied ourselves with the study of the reflexes formed under certain conditions during the life of the individual —the conditioned reflexes. The existence of such reflexes is dependent upon the presence of the hemispheres, which means that they are a special function of this part of the brain. In the investigation of these reflexes, material has been collected which has indicated to us one of the characteristics of the brain cortex.

Every agent of the external world which can be transformed into a nervous process by the special receiving apparatus may, if it stimulates a certain part of the cortex, call out the activity of one or another organ. This is effected by means of the conduction paths to the executive nervous elements (cells and nerve fibres) of the given organ. The essential condition for the formation of this new reflex is the temporal coincidence of the effect of this agent (conditioned stimulus) on the organism with the action of that stimulus (unconditioned stimulus) which provokes an inborn unconditioned reflex (including here what is usually called instinct), or which provokes well elaborated and stable conditioned reflexes. For example, all agents which formerly had no relation whatever to food, if they coincide one or several times with the act of eating, afterwards are capable, when they act alone, of calling out the food reaction —a series of definite movements and corresponding secretions. Conditioned stimuli elaborated in this way, are connected with certain definite points of the cortex. This gives us the possibility to trace exactly the changes to which these points are subjected during various activities of the brain. In the present account I shall refer to these changes as variations in the irritability of these points.

As has already been shown in our experiments, every well elaborated conditioned stimulus, if it is repeated temporarily or constantly (if constantly under certain conditions), without being accompanied with the unconditioned stimulus by the help of which it was formed, quickly loses its stimulating effect and may even become an inhibitory agent. Thus the point of the cortex stimulated by this agent loses its former irritability and acquires a new one. This inhibitory agent, if the conditions which produced it remain uniform, may express its effect, may call out the state of inhibition, directly and immediately, just as a positively acting stimulus provokes an excitation process. Also our inhibitory agent will occasion, according to its duration, different grades of an inhibition process, internal inhibition, as we call it. In this way one may speak empirically of positive stimuli (producing the stimulation process), and negative stimuli (producing the inhibition process). We have employed for some time the terms positive and negative reflexes (from the experiments of G. V. Volborth). The advantage of this conception of our facts is that it enables us to understand all different states of the nervous elements in any circumstances and under the influence of any stimulating agents, as a continuous uninterrupted succession of processes; and this corresponds to the facts.

The conditions which give rise to inhibition points in the cortex are as frequent as those which produce excitation points, and, consequently, the entire cortex represents an immense complex of positively and negatively excited areas intermingled and scattered in a checkered fashion. In this system of more or less fixed points there arise changes of irritability depending upon the changes in the internal or the external environment of the animal. And this occurs in various ways, as will be described.

A simple and constantly occurring case is the following: as soon as there is produced by a novel external or internal stimulus some new nervous activity, expressed in the work of one or another organ, our conditioned stimulus loses in strength or even becomes ineffective: that is to say, under the influence of the newly arising foci of stimulation in the cortex, the irritability at the point corresponding to our positive conditioned stimulus is decreased or reduced to zero—*external inhibition.*[1] This is apparently analogous to similar relations in the lower lying parts of the central nervous system.

Such a form of inhibition occurs only with stimuli of moderate strength. If the new stimulus is very strong and is accompanied by a

[1] The reader met with this phenomenon in the foregoing chapters under the name of external inhibition by extra stimuli. See chapter xi.—*Translator.*

FIG. 8: PROFESSOR PAVLOV AT THE OPERATING TABLE.

violent reaction of the animal, then our special stimulus not only does not lose its effectiveness, but on the contrary its action is enhanced, *i.e.*, the positive irritability of the point upon which the stimulus falls is increased. Here is an example: a conditioned food reflex was elaborated, having a certain definite effect, and at the same time in this dog the guarding reflex was strongly expressed. In the presence of the person who is accustomed to experimenting with him in an isolated room, the dog remains quietly in the stand permitting without resistance all the necessary manipulations. If, however, the usual experimenter is replaced by another, the dog exhibits a markedly aggressive reaction, and if during this time the newcomer applies the conditioned stimulus, he obtains a sharply augmented effect. But it is only necessary for him to sit motionless and the aggressive reaction gradually disappears, though the dog steadily watches the new experimenter; and if the conditioned stimulus is now tried, it produces an effect well below the normal. This result can be repeatedly obtained. (Experiments of M. Y. Besbokaya.)

If the conditioned inhibition points become fatigued under the influence of such strong new stimuli, they lose their inhibitory action, and are transformed into positively acting points (our dis-inhibition). With very weak, newly added stimuli, by which the positively acting points are not perceptibly influenced, only the inhibitory points suffer a transformation; they are dis-inhibited; *i.e.*, their negative irritability passes over into a positive irritability. The above described changes in irritability arise spontaneously, without elaboration. Further, however, there are also slowly developing fluctuations, which we shall now discuss.

In relation to these phenomena, I shall describe experiments with conditioned mechanical skin stimuli; for the skin is a great and easily accessible receptor surface upon which all the phenomena interesting us may be clearly manifested. If we have developed conditioned reflexes to the same kind of mechanical stimuli, of uniform strength on many spots of the skin, then we have in the cortex a region which is easily controlled in regard to its excitability. Now if in a series of mechanical skin stimulators fastened to the body of the dog, we have made positive conditioned stimuli from all except the outer one, and from that we have made a negative conditioned stimulus (*i.e.*, by not accompanying it with feeding it has become differentiated), then with every application of this negative stimulus, the inhibitory process spreads from its point of origin over the positively acting points, and then contracts around the original point; it first irradiates and later concentrates. This phenomenon was observed and described long ago by us (Krasnogorsky, Kagan, Anrep, and others).

Even at that time one of these authors (Kagan) noticed the following phenomenon, though only in a few cases and not marked; immediately after the cessation of the inhibitory stimulation, and indeed in points remote from the origin of the inhibition point, an increased excitability could be observed; in other words, the conditioned stimulus produces a greater effect than before. Recently, our attention has been especially directed to this phenomenon, and several of our collaborators have investigated it in different cases of internal, *i.e.,* elaborated inhibition. It proved to be a striking and constantly recurring fact. Let us first consider that inhibition which develops in the case of the differentiated conditioned stimulus. The more the differentiated (negative) agent is repeated without the unconditioned stimulus, the more quickly its inhibitory effect begins, and the stronger it is; finally, pure inhibition results. At the same time, this inhibition, even though it was formerly widely spread, concentrates more and more, under the influence of the stimulation of points with a positive action, *i.e.,* the positive conditioned stimuli. But now a new phenomenon appears. Immediately and very quickly, in the course of some seconds or minutes, after the cessation of the action of the inhibitory agent (negative conditioned stimulus) there is observed in the neighbouring points with the positive action a marked increase of irritability. In those points lying nearest to the point corresponding to the inhibitory agent this phenomenon appears as a phase, which is followed by a decrease of the irritability and finally by a return to normal. In the remote points there is only the phase of increased irritability which is followed directly by the normal (experiments of Bykov). In some dogs the increased irritability in all the observed points is replaced by the irradiating inhibition (experiments of Fursikov and Kreps). These variations are determined apparently by the degree and velocity of the irradiation as well as of the concentration of the inhibition process, and by the strength of the positively acting points. In conformity with Sherrington's term, we designate these phenomena as *induction.* Induction of the excitatory process by the inhibitory process appeared, in the case described, not in those elements * in which the inhibition occurred, but in the neighbouring elements. This is induction from a distance.

It was interesting to trace the state of excitability in the neighbouring and distant points during the action of the inhibiting stimulus. This has been done for another kind of internal inhibition in the experiments of N. A. Podkopayev. If the positive conditioned stimulus without being accompanied by the unconditioned stimulus is repeated several times in succession at intervals of some minutes, it quickly loses its stimulating effect. The conditioned reflex sinks, as we express it, to zero. This occurs in consequence of the development of an inhibition process

* Induction may now, however, be stated to exist also in the same elements where inhibition originated.

at the stimulated point. As we have seen in the process of differential inhibition after the cessation of the stimulus, this process, too, spreads—it irradiates. If through the development of extinguishing inhibition, the stimulating effect from a certain place on the skin has fallen to zero, and this zero effect is maintained by continuous stimulation (of course, without the unconditioned stimulus), Podkopayev has seen that the stimulation of other points of the skin is manifested in a very particular manner. The stimulation of all other points of the skin, neighbouring as well as distant, acts positively, but with certain peculiarities. The latent period is clearly shortened (1 to 3 seconds instead of 4 to 5), but the general effect is less in comparison with the normal. The most simple explanation of this fact is that the sharp decrease of the latent period is a sign of an increase of the irritability of the stimulated points; but as both the inhibitory and the positive impulses fall simultaneously on the effector centre, the resultant action is their algebraic sum.

We have reason to believe, however, that the opposite conditions also exist—that the excitation process can induce and reinforce the inhibition. This also results when both processes are well elaborated. We arrive at such a conclusion from the following experiments. Some years ago K. N. Krzhishkovsky had studied the rate of extinction of that kind of inhibition which we call conditioned,* in the case where the inhibited combination was followed by the unconditioned stimulus and so converted into a positive one. It proved that the extinction of this inhibitory stimulation is peculiar and that its speed depends upon whether the extinction (application of the inhibited combination followed by the unconditioned stimulus) has continued uninterruptedly or has alternated regularly with the application of one of the positive conditioned stimuli accompanying the unconditioned stimulus. If the combination followed by the unconditioned stimulus, *i.e.*, the procedure for the extinction of the conditioned inhibition, is alone tried, the annihilation of the inhibition effect appears during the first or second trials; if it has alternated with the conditioned stimulus, then the annihilation is not evident for a long time. This phenomenon can be explained by saying that the positive stimulus induces the inhibitory process, and prevents in this way its destruction. The experiment of Krzhishkovsky has recently been repeated by V. V. Stroganov and the differential inhibition studied in greater detail. A certain frequency of the metronome was made a positive conditioned stimulus, and another frequency a differen-

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* Conditioned inhibition results from a combination of a conditioned stimulus with an indifferent agent which has never been accompanied by the unconditioned stimulus; the conditioned stimulus in this combination is, therefore, inhibited, and the new agent becomes the conditioned inhibitor, while the conditioned stimulus taken alone has its usual action.

tiated (*i.e.*, formerly inhibiting) stimulus. Then the differentiation was extinguished by giving food together with the (formerly) negative conditioned stimulus. When this procedure was constantly alternated with the application of the positive stimulus, the disappearance of the differentiated inhibition and the formation of a positive stimulus (with the second frequency of the metronome) proceeded very slowly—after twenty or more trials. But in the case of continuous extinction, this result is obtained after the first or second trial.

Thus we have a negative of *induction;* an inhibitory process is called out by the process of excitation.

The process of induction develops in our case under the influence of the persistent action of the corresponding stimuli; it does not exist from the outset. The whole matter may be summed up thus—*for the formation of the isolated foci of stimulation and inhibition in the cortex there is necessary, first of all, the presence of the corresponding stimuli; but once these foci have been formed, induction appears in the rôle of a supporting mechanism for their maintenance and stability.*

In our present experiments with the conditioned reflexes induction manifests itself almost exclusively in the neighbouring cortical regions, but not at the points where the primary processes occur. We happened to see this last fact only in another form and during accidental observations. It will not be superfluous, I think, to mention the most marked case of this kind. The dog concerned showed a highly developed reflex of slavery (servility or obedience); it was investigated and described by U. P. Frolov. The animal had an isolated stomach pouch for study of the activity of the gastric glands. When he was put on the stand he remained wide awake and also became motionless, not even changing the position of his feet. If, however, he had been on the stand for some time and we now proceeded to free him from his harness in order to remove him from the stand, the dog fell into a state of marked excitation; he barked furiously and tried by every possible means to break away. Now it was absolutely impossible to make him return to the stand, either by calling him, whipping him, or placing a chair on which he could jump up to the stand as he always had done on entering the experimental room. When, however, the dog is taken out of the experimental room for a rest and brought again into the laboratory, he immediately rushes to his own place and springs into his stand. It is not difficult to explain this mechanism. The stand and its harness act in this very submissive animal as a strong conditioned inhibiting agent for his motor system, even though the uncomfortable position and fatigue of his limbs demand movement. And now when there is liberation from this inhibiting agent, an extreme excitement sets in through induction in that part of the motor cortex which has been for a long time inhibited. This phenomenon is observed to some extent in many dogs, but in this case it was especially prominent.

The existence of a positive and negative induction phase favours the fine and exact delimitation of those positively and negatively excitable points formed in the cortex during the life of the individual. This in the main is accomplished in the interest of preserving the organism as a separate system in its environment, by a constant and efficacious activity of that organ which maintains the finest connections of the animal with the external world—the activity of the cerebral hemispheres.

So much for the actual relations. Concerning their interpretation, the possible representation of their internal mechanism, nothing definite can be said other than that these are the general and special properties of the cortex of the cerebral hemispheres. And we do not even consider the question as to the elements of the central nervous system that are concerned. Obviously more facts are needed. For the present all remains in darkness—the spread of the inhibition process, as well as the phenomenon of the elaborated reciprocal induction, and many other of the above mentioned phenomena, above all the fact of the transformation of a positive excitation into the opposite negative process, and vice versa.

# CHAPTER XXXIV

## ANOTHER PROBLEM IN CEREBRAL PHYSIOLOGY

(From the *Reports of the State Medical Institute,* Moscow, vol. i, Part I.)

DUPLICITY OF THE CEREBRAL HEMISPHERES—THE DIFFERENTIATION OF SYMMETRICAL POINTS OF THE SKIN.

A NEW question in the objective study of the brain is that of the two cerebral hemispheres, their existence as a pair. What does this duplication signify? How is the simultaneous activity of the hemispheres to be understood and explained? What sort of compensating action is there here, and what is the advantage of a united activity of both hemispheres? On the basis of the existing scientific knowledge we know that there is a certain division of labour between the two. But also it is known from extirpation experiments on animals that the absence of one hemisphere can be compensated for after some time, either partly or in full, by the activity of the remaining one. In the physiology of the conditioned reflexes there is a series of experiments which categorically raises the question of the duplex activity of the hemispheres. In this short report allow me to discuss a few experiments pertaining to this question.

It was shown in our laboratory that the positive conditioned reflexes, as well as the negative ones, which had been elaborated on the skin surface of one half of the body are obtainable to exactly the same degree from the stimulation of corresponding symmetrical points of the other half of the body. This was first brought out by N. I. Krasnogorsky in his brilliant dissertation, "The Process of Inhibition and the Localisation of the Skin and Movement Analysers in the Cortex of the Brain" (St. Petersburg, 1911). It has been shown to be a constant and exact occurrence, and has been confirmed in detail by one of our later collaborators, G. V. Anrep. This author established for the first time the so-called stationary irradiation of the conditioned excitation, which consists in the following: if we have elaborated a conditioned reflex from mechanical stimulation of a certain point of the skin at one end of the body, then on the first tests of mechanical stimulation of other points of the skin we also note a conditioned effect, whose strength is proportional to its distance from the original point. Exactly the same relations hold for the symmetrical points of the other side of the body, though they have never been experimented with before. The experiments of Krasnogorsky and Anrep were confirmed by our co-workers, I. S. Rosenthal and D. S. Fursikov.

K. M. Bykov has made highly interesting and remarkable supplements to these experiments. He has not succeeded at the present writing, in spite of persistent attempts, in differentiating two symmetrically placed skin points. It had been previously proved in our laboratory that with mechanical and thermal agents, used as positive and negative conditioned stimuli, the differentiation of various points of the skin on the same side of the body proceeded easily; nevertheless, Bykov found it impossible to obtain the slightest differentiation between two symmetrical points on opposite sides of the body. On one side of the body positive conditioned reflexes were elaborated from the mechanical stimulation of certain points of the skin, which we shall designate by the Arabic figures 1, 2, 3, 4, 5, etc. One of the extreme points (point 1) was differentiated, *i.e.,* its earlier positive effect, which existed thanks to irradiation, was transformed into a negative effect, into inhibition, by repeatedly stimulating it without accompanying it with the unconditioned stimulus (food). The same relations between the corresponding points on the other side of the body were produced spontaneously. We shall represent the points on the other side of the body corresponding to 1, 2, etc., by the Roman numerals I, II, III, IV, V, etc.; thus if point 1 is on the knee of the right leg of the dog, point I will be situated at the same place on the left leg. On this side it came about that point I, like its corresponding point 1 of the other side, became negative (gave no saliva on stimulation), while points II, III, etc., remained positive, like their corresponding points 2, 3, etc. Now we began to differentiate one of the positive points (for example, point III) on the new side of the body, *i.e.,* we repeatedly stimulated this point without accompanying it by feeding. The following came to pass. As this point III gradually changed from positive to negative, *i.e.,* gave a constantly decreasing salivary secretion on stimulation, its corresponding point on the other side of the body (point 3) showed a parallel transformation. If now point 3 were restored to its normal positive condition by combining stimulation of it with feeding, then the positive action of point III also became restored in like manner. And this condition remained, notwithstanding that the symmetrical point III was repeatedly stimulated a hundred times without feeding; it continued to give a positive effect because point 3 continued positive. There was no sign of its becoming negative, *i.e.,* differentiated, and it was obvious that further trials would be unavailing. The same relation held between point 1 and its symmetrical point I on the other side of the body; it was impossible to differentiate them, keeping the one positive and the other negative. How is this enigma to be understood? We know from our own experience as well as from observation on animals how easily and exactly symmetrical points on the two sides of the body can be distinguished.

We have projects for further experiments by which we hope to solve this problem. Probably experiments on animals after destroying the commisural connections between the two hemispheres of the brain will help us toward an explanation.

# CHAPTER XXXV

## THE LATEST SUCCESSES OF THE OBJECTIVE STUDY OF THE HIGHEST NERVOUS ACTIVITY

**(Read at the Anniversary Celebration of the Lesgaft Scientific Institute, Petrograd, December 12, 1923.)**

**NO NECESSITY FOR AN ANIMAL PSYCHOLOGY—THE ORIGIN OF A PHYSIOLOGY OF THE BRAIN—THE CONDITIONED REFLEX AND THE CEREBRAL HEMISPHERES—SYNTHESIS AND ANALYSIS (BEHAVIOUR) FOUNDED ON EXCITATION AND INHIBITION—IRRADIATION AND CONCENTRATION—EXAMPLES OF IRRADIATED EXCITATION (EMOTION) AND INHIBITION (SLEEP)—LIMITATION BY RECIPROCAL INDUCTION—BEHAVIOUR DEPENDENT UPON A BALANCING OF THE PROCESSES OF INHIBITION AND EXCITATION—THE CONFLICT AND THE FAILURE TO BALANCE MAY EVENTUATE IN A PREDOMINANCE OF EITHER EXCITATION (NEURASTHENIA) OR OF INHIBITION (HYSTERIA)—AN EXPERIMENTAL STUDY OF SENILITY AND OF THYROID INSUFFICIENCY—MEMORY—A CERTAIN CEREBRAL IRRITABILITY IS NECESSARY FOR THE FORMATION OF CONDITIONED REFLEXES—SENILE GARRULITY AND SENILE DEMENTIA—ASSOCIATION AND HIGHER ORDER REFLEXES—THE FUTURE OF BRAIN PHYSIOLOGY.**

Why is it that physiology is just beginning to master the secrets of the animal organism? Because the most complicated and important part of the animal, the highest section of the nervous system, the hemispheres of the brain, were, in spite of their great interest, considered beyond the scope of physiology.

Why is this?

The answer is that the rôle of physiology in this domain was contested by psychology—a branch of philosophy which does not even belong to the group of natural sciences. Certainly psychology, in so far as it concerns the subjective state of man, has a natural right to existence; for our subjective world is the first reality with which we are confronted. But though the right of existence of human psychology be granted, there is no reason why we should not question the necessity of an animal psychology. What means indeed have we to enter into the inner world of the animal! What facts give us the basis for speaking of what and how an animal feels? The word "zoöpsychology" is, it seems to me, a misnomer, the result of a misunderstanding. That this is so is exemplified by the following: In a 300-page book by an American author the analogies between the imagined internal worlds of various animals and that of man are discussed, and there constantly recurs the conditional phrase "if they have consciousness". But what kind of discipline is this for a science? Suppose the animal has no consciousness, then all this is only empty babbling, a flow of words.

But though zoöpsychology as a science is to be condemned, the data which zoöpsychologists collect is worth while. These data are derived from a study of the influence of the external world on animals and of their responding reactions. The facts obtained are of course valuable, and will be of service in the future. As long as we have no definite knowledge of the internal world of the animal, zoöpsychology, I repeat, has no right to existence. And all this material must fall to the lot of the physiology of the higher sections of the nervous system, a physiology which, as I have said, has just begun to develop. Only a quarter of a century ago did investigators in Europe and America assume a true scientific attitude in this regard.

Although physiology of the brain had an energetic beginning in 1870, it has not even yet developed, and it remains fragmentary. The obtained facts have borne almost no relation to the manifestation of the highest nervous activity (*behaviour*) of animals. For example, movements of various groups of muscles were seen to result from the stimulation of the corresponding areas of the brain, but what explanation did this give of the highest nervous activity of the animal, how was it to be applied to the reaction of the organism to the outer world?

At last, a quarter of a century ago, a pure physiology of the brain appeared which on the one hand, treated the matter scientifically and objectively, and, on the other hand, considered the behaviour of the animal toward his surroundings. In spite of the newness of this physiology its borders are so extensive that it affords us the possibility of understanding the mechanism of the general conduct of the animal.

The central conception of this physiology is the so-called *conditioned reflex.* Besides the word, conditioned, an adjective describing other of its properties may be used to designate it, such as temporary, individual, etc. The phenomena of the conditioned reflex consist in the following: The basis of the higher nervous activity rests upon the inborn connections of the animal with the external world. A *destructive* stimulus calls out a defence reaction; *food,* a positive reaction—grasping the substance and chewing it. In this group of inborn connections of the animal are included all the reactions which usually are termed *reflexes,* or if they are complicated, *instincts.* Such reflexes are the function of the lower parts of the nervous system.

The cerebral hemispheres, on the other hand, have to do with the formation of the conditioned, *temporary reflexes;* their function is to combine certain external agents, which formerly were isolated, with some physiological activity. All these new unions are formed on the basis of the inborn reflexes. If some agent—which, thanks to an inherited connection, calls forth a definite response—acts on the animal, and if simultaneously with this, a new agent acts, then, after several such coincidences, the new agent begins to call out the same reaction as the original agent did (*i.e.*, the agent calling out the inborn reflexes). Thus, food, for example, is an agent which has an *inborn* connection with a certain reaction of the organism; the dog tries to get to the food, to seize it, and to eat it. There is also an accompanying glandular reaction—saliva and other secretions begin to flow. And now if with this unconditioned agent, food, some other stimulus influences the animal—for example, a picture, sound, odour, etc.—this last stimulus becomes an exciter *per se* of the food reaction. The same law applies to all other unconditioned connections—the defensive reflex, sexual reflex, etc.

Thanks to this fundamental phenomenon of the higher nervous activity, there is a favourable, or even unlimited, opportunity to study the entire activity of the cerebral hemispheres, to investigate the analyses and syntheses which the animal makes of both the external and the internal worlds. However, the whole *behaviour* of the animal is included in this *synthesis* and *analysis*. In order to maintain an equilibrium with the surroundings, it is essential, on the one hand, to analyse as well as to synthesise the external world, because not only simple separate agents act on the animal but also their combinations: and, on the other hand, to analyse and synthesise the corresponding activity of the organism.

The basic processes upon which this synthesis and this analysis are founded, are, on the one hand, the excitatory, and on the other hand, the inhibitory process,—this latter a kind of opposite to the excitatory process. I say "a kind of opposite," because we do not know exactly the nature of either of these processes. We have only hypotheses concerning them, which have not led to definite results. The formation of conditioned reflexes rests upon the process of excitation, but the matter is not settled by this statement. In order to attain to a proper relation of the organism to the surroundings, there is required not only the elaboration of the temporary connections, but also a continual and rapid adjustment of them. For if they do not correspond to reality under the given circumstances, then they are suppressed. And this abolition of the temporary connections comes about as a result of the inhibitory process.

Thus both processes, that of excitation as well as of inhibition, participate in this incessant maintenance of equilibration with the surroundings. And a multitude of reactions of the animal become comprehensible once we are acquainted with the characteristics of the two processes. Arising under the influence of definite stimulations, these two processes move through the mass of the hemispheres with a speed which is measured not only in seconds but also in minutes. At present we have no accurate information of the inter-relations of the velocities of these reciprocal processes. It is possible that the inhibitory process moves the more slowly.

We know that this movement proceeds in two directions. Both excitation and inhibition first spread out over the cortex of the hemispheres—they *irradiate*. During the next phase, they collect around a definite point—they *concentrate*.

The processes of excitation and of inhibition with these their properties condition all the activity of the hemispheres. The chief function—the formation of temporary connections—is based on the ability of the process of excitation *to concentrate*. The mechanism of the elaboration of the conditioned reflexes, the mechanism of association, may be considered to proceed as follows. If a strong stimulation, for example, that proceeding from food, occurs, then all other stimuli falling simultaneously on other parts of the brain, are drawn to this point of intense excitation (food center), *i.e.*, they concentrate here.

The process of inhibition concentrates in a similar way, giving rise to the formation of conditioned inhibitory reflexes.

*Irradiation* may be seen in a very important manifestation of the higher nervous activity. Let us take some strong stimulation: the resulting excitation spreads far and wide in the hemispheres, and this is expressed in the immediate heightened activity of many functions of the organism. We have such an occurrence in the case of the *emotions*. I recall the instance of a dog which had an intensely developed aggressive reflex toward strangers. He recognised only one master, the experimenter, and guarded only him, reacting to the appearance of every other person in the experimental room by fierce barking. When I myself took the place of the usual experimenter and tried the conditioned food reflexes, I obtained, not a decrease, but an extraordinary reinforcement of these reactions. The food which I offered was eaten with extreme greed. So we are compelled to conclude that the original excitation in the aggressive center irradiated, and also charged the food center.

I shall now show you, on the other hand, a striking case of *irradiation of inhibition*. Detailed investigations have proved that the inhibition which exists always simultaneously with excitation and controls it, is, in essence, the same process as sleep. Sleep is no more than an extreme irradiation of the inhibitory process. In order to prevent sleep, it is necessary to limit the inhibition by opposed stimulations. If the inhibitory process does not meet with resistance (from an excitatory process) it irradiates and overflows the cerebral hemispheres, even passing over to the lower parts of the brain, producing a completely passive state—the *sleeping* state of the animal.

In this way, the reciprocal limitation of both processes gives rise to an enormous *mosaic* in the cerebrum, consisting of excited points and inhibited or temporarily sleeping points. And by the presence of these closely intermingled, now excited, now sleeping points, the entire behaviour of the animal becomes determined. To some stimulations the animal reacts by activity, to others by inhibition.

This delimitation of the processes is greatly favored by another phenomenon, that of *reciprocal induction.* There exists such a relation—an excitation arising in a certain place causes an inhibitory process around this region and owing to this the spread of the original excitation becomes limited. On the other hand, the inhibitory process induces an excitatory process, and this in turn checks the spread of the inhibition. Thus the whole cortical area is partitioned off into excited and inhibited points.

The above is a hasty account of our earlier work. Passing over now to our recent investigations, I feel constrained to say that it is not my personal work, but for the most part that of my collaborators. I have not only made use of the hands of others, but I have also amalgamated our ideas together.

The entire *behaviour* of the animal, as is evident from what I have said, is dependent upon the balancing of the excitatory and the inhibitory processes, and upon the adaptation of these two processes to the various agents of the external world.[1] However, this balancing is no light task for the animal, and is often accomplished at the cost of great fatigue and strain. This can be clearly seen in our laboratory animals.

If I have produced a process of excitation and now limit it with one of inhibition, this is trying on the animal; it begins to whine and bark and attempts to free itself from the stand. The only reason for this is that I have brought about a difficult *balancing* of the processes of excitation and inhibition. Let any one of us consider his own personal life and experiences and he will find many similar examples. If, for example, I am occupied with something,—*i.e.,* I am under the influence of a definite process of excitation—and if some one suddenly proposes to me to do another thing, it is unpleasant for me. For it means that I must inhibit the strong excitatory process in which I was engaged, and only after this can I start a new one. "Perverse" children are classical examples belonging here. You order such a child to do something, *i.e.,* you wish to inhibit the excitatory process present and to start another. And a scene often follows, the child throwing himself on the floor, stamping his feet, etc.

And even more. A stress of such nature, this difficult conflict between the two processes, can, as we have already seen in many of our dogs, produce painful results, *i.e.,* marked disturbances in the normal nervous activity. In all probability these cases explain the genesis of the illnesses which we often see in actual life as a result of very strong processes of excitation or of inhibition, *e.g.,* as when you experience a powerful

[1] See chapter xxviii.—*Translator.*

stimulation, but are compelled by the circumstances of your life to suppress, to inhibit, it. Now there may follow a derangement in the normal activity of the nervous system.

We are now engaged in the more detailed investigation of the above phenomena. The deviations from the normal may be in either one of two directions, depending upon the type of dog; in one, the processes of excitation suffer, in the other, those of inhibition. Dogs in which the latter processes are affected show it very plainly. The animal that was usually quiet becomes extremely nervous and restless. We see from our experiments, moreover, that the inhibitory processes have disappeared; the animal gives the impression of having lost his ability to inhibit. In the conflict between the two processes, we see the excitatory one has taken the upper hand. I recall such an animal that had to be removed from experimental work for three to four months before there was a return of the normal relations. Only then could we, by exercising great care and proceeding gradually, re-establish the process of inhibition.

So much for the deviation from the normal activity toward the predominance of the excitatory process. There are other cases, however, in which the disturbances are characterised by an excess of the processes of inhibition. In these one can see a decrease in general, positive activity of the dog, a tendency toward sleep and inhibition out of all proportion to the circumstances.

If we turn our attention now to human pathology we find here analogous conditions. There are, on the one hand, *neurasthenics,* who are incapable of even weak inhibitions, and, on the other hand, the various kinds of *hysteria,* where inhibition takes the form of anæsthesias, paralyses, increased suggestibility, etc. I now believe that these pathological conditions correspond to the deviations from the normal which we have observed in our experimental animals.

Here, in the investigation of these deviations (in the direction of the preponderance of the inhibitory processes and the weakening of the excitatory) I am constrained to mention one of the discoveries of our distinguished, though deceased, physiologist, N. E. Vvedensky.[2] Vvedensky did much to advance the physiology of the nervous system, and although he succeeded in bringing to light obscure facts, for some reason he has not received recognition in the foreign scientific literature. In one of his books, entitled *Excitation, Inhibition and Narcosis,* he described the changes in the nerve fibres caused by strong stimulation and he distinguished several phases. It now seems that these peculiar phases are entirely reproduced by the nerve cells if there is an intense collision be-

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[2] Compare with next to last paragraph of chapter xxxvi. The pathological states are discussed in detail in the chapters, "Normal and Pathological States," etc., of *Activity of the Cerebral Hemispheres,* I. P. Pavlov, 1926.—*Translator.*

tween the processes of excitation and inhibition. I have no doubt that Vvedensky's researches will finally receive the recognition they merit.

Besides the observations which I have just described, we have recently been able to study the functional changes in the highest parts of the brain in *senility* and during disturbances in the metabolism of the given organism. Simultaneous experiments were carried on by two of our collaborators: in the one case on a very old dog, and in another on a thyroid ectomised animal. It is known that a complete removal of the thyroid gland in man impairs the function of the cerebral hemispheres and causes cretinism.

What happened in our cases? In order to form conditioned reactions we generally use the food reflex. But with this we were totally unable to form a definite temporary connection. Months passed, and still there was no temporary connection. In the old dog there was not the slightest sign of a conditioned food reflex. In the animal that had been deprived of the thyroid, the reflex appeared but only toward the end of every séance, and on the next day we had to begin all over. This indicated that there was a great deficiency in the activity of the hemispheres of the animal.

What is the significance of this? Upon what changes in the brain does it depend? Our conclusion is that in both cases we have to do with a very lowered irritability of the hemispheres. We old people know all this very well; for with increasing years memory [3] for present events falls sharply, and in order to remember a thing we must keep the attention on it for a longer time, and only then is the excitatory process retained. Thus in the case of our dog, the normal cortical activity can be restored by some method which increases the irritability of the hemispheres. Therefore we replaced the food stimulus by a stronger one. As a rule, during the experiment we give only small portions of food, and the main feeding comes only when the work is ended and the dog is returned to his kennel. It seems that the feedings during the séance were too little to produce a sufficient excitation, and we substituted for them the defence reflex by putting acid into the dog's mouth. The motor reaction of the animal had taught us that this reflex was connected with a stronger excitation in the brain. Our supposition proved to be true. After we had thus increased the irritability of the brain, it was possible to form the conditioned acid reflex. An important fact comes to light; in the state of decreased irritability there was an insufficient activity of the hemispheres, but to restore this activity it was only necessary to increase the irritability.

We went still further. Having obtained the conditioned reflex to acid we decided to see how the inhibitory process was affected. We began

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[3] **For an account of Pavlov's memory, see biographical sketch.—*Translator*.**

to elaborate a differentiation, which, as you know, depends upon inhibition.

The conditioned reflex had been formed to a metronome of 100 beats per minute; the differentiation was formed to one of 50 beats. In the other dog we used two tones one octave apart. It turned out that for both animals the elaboration was an impossibility. In the dog without the thyroid the negative conditioned stimulus was applied 600 times, and still there was no differentiation. The old dog died during the course of the experiments, but the other one survived. We come to the conclusion that these animals are incapable of differentiation, *i.e.*, of inhibition. For a normal animal such differentiations are easily accomplished.

Then we thought that perhaps the inhibitory process might be dependent upon the excitatory, and that it was possible that we had not increased the irritability, the tonus of the hemispheres, sufficiently. Thereupon, instead of the acid stimulus we used a strong destructive one, *viz.*, induction shocks of the electric current applied to the skin. A strong reaction ensued, which continued for some time after the cessation of the current. The animal repeatedly jerked up the foot which had been shocked. Now the tone we had used quickly became a *conditioned destructive stimulus*. No sooner was it applied than the animal began to scuffle and whine, etc.

And now the differentiation could be formed easily. If we applied the higher pitched tone without accompanying it by the unconditioned stimulus, the dog readily distinguished it from the lower tones; to the latter he reacted by a violent defence reflex, while to the higher tone there was no reaction.

Thus we had increased the irritability of the brain by the application of electric shocks, and what was impossible for the dog became possible. Evidently there is some kind of relation between the processes of excitation and of inhibition; if the former is diminished, then the latter becomes weaker or even fails altogether.

From this point of view we can understand the *garrulity or dementia of senility*. Whence comes this talkativeness? Normally a person speaks only what is sensible and appropriate. If he commences to talk without any special reason he is obviously unable to restrain himself, to inhibit. Dementia is to be understood in the same way except here the thoughts have no correspondence to reality. In the normal person all such mental processes are suppressed or rejected. In cases where inhibition is seriously interfered with everything comes out together in a confused mass without discrimination.

After these experiments a case which I saw five years ago in the asylum for the insane is now clear to me. There was an old man who had lain like a corpse for twenty years. From the age of thirty-five or forty to sixty he did not make a single movement or speak a word. After the age of sixty he gradually began to make ordinary movements, to speak and to walk. In conversation with him we found that during the whole time he had been completely conscious, seeing, hearing and understanding everything, but he had been unable to respond—to move or speak. Thus for all this time his nervous system, especially the motor region of the cortex, had been inhibited, and only in old age, when these negative processes weakened, did the inhibition at all give way or diminish.

Now you can see some of the facts in the normal and pathological behaviour of the human which become clear from the point of view of this new pure physiology of the nervous system.

I shall add another instructive example. Our ability to understand is based chiefly upon a long chain of excitations, upon *association.* And in our experiments we had to deal with this phenomenon too. It was interesting for us to see whether we could form a new conditioned reflex not with the help of an unconditioned reflex (ordinarily the food reflex), but with the help of another conditioned reflex (although one which had been well elaborated). For example, if we have formed a conditioned food reflex to a metronome of 100 beats per minute, then the sound of the metronome will regularly call out the food reaction; the metronome is a positive conditioned stimulus, *i.e.,* it has always been accompanied by feeding. Should it not be possible to form a new conditioned reflex not directly to the food reflex, but to the metronome of 100 beats unaccompanied by feeding? Such would be a reflex of the *second order,* or a *secondary* reflex. Now it happened, if we applied a new stimulus, for example a slight mechanical irritation of the skin, simultaneously with the formerly used metronome of 100 beats, that the skin stimulation alone finally became able to evoke the food reaction. Furthermore, the following happened: for a long time we were unable to form a reflex of the third order; we could never go beyond a reflex of the second order. Upon what does its formation depend? It appears that you have only to augment the general irritability of the brain, and that then you can form conditioned reflexes of the third order. When we used a stronger unconditioned stimulus (the electric current, a destructive agent) than the unconditioned food stimulus, it was easy to elaborate a *tertiary* conditioned reflex.

This short report about our latest experimental results, will, I think, show you how the behaviour of man and his most complicated reactions to the outer world can be included, analysed, explained by physiology. Along this path of research it is my belief that great achievements and conquests await the human mind. Even at my age I hope to see something of this, but it is beyond doubt that many of the younger generation will be witnesses to these extraordinary attainments.

Such is the value of the objective and scientific method when it attempts to enter into the most complicated of all regions, which until now has been studied only from the subjective point of view.

# CHAPTER XXXVI

## RELATION BETWEEN EXCITATION AND INHIBITION AND THEIR DELIMITATIONS; EXPERIMENTAL NEUROSES IN DOGS

(Dedicated to the memory of my revered friend, Robert Tigerstedt, to whom physiology owes so much, not only for his investigations, but for his promotion of physiological knowledge and research.)

INTRODUCTION—FIRST LAW OF RELATIONSHIP BETWEEN EXCITATION AND INHIBITION—SECOND LAW (DELIMITATION)—THE CONFLICT, AND THE DESTRUCTION OF NORMAL NERVOUS ACTIVITY—TWO EXPERIMENTAL EXAMPLES (DIFFICULT DIFFERENTIATIONS)—THE RESULTING NERVOUS DISORDER CAUSED BY THE COLLISION OF EXCITATORY AND INHIBITORY PROCESSES—AN EXPERIMENT SHOWING FOUR STAGES IN THE ABNORMAL RELATIONS BETWEEN THE EFFECT OF STRONG AND WEAK STIMULI RESULTING FROM A COLLISION OF EXCITATION AND INHIBITION—NERVOUS DISORDERS WERE PRODUCED IN THE EXPERIMENTAL ANIMALS BY THE LENINGRAD FLOOD—LESIONS OF THE CORTEX FOLLOWING EXTIRPATION—SENILITY—THYROID INSUFFICIENCY—CLASSIFICATION OF THE CORTICAL STATES—EXAMPLES OF PARTIAL SLEEP OR ISOLATED INHIBITION (SLEEP WALKERS, THE MILLER AND THE MILL, ETC., CATALEPSY, SUGGESTIBILITY)—PHYSICO-CHEMISTRY OF THE NERVE FIBRE IS NECESSARY.

ALL the following facts have to do with the functions of the cerebral hemispheres and have been obtained by the method of conditioned reflexes, *i.e.,* reflexes formed during the individual life of the animal. As the significance of conditioned reflexes even now has not become well known and recognised among physiologists, to avoid repetition, I refer the reader to my recent lecture on this subject (see chapters xxxi and xxxii).

By the great difference in facts we were compelled to assume in the work on the cerebral hemispheres two different kinds of inhibition, and we called them *external*[1] and *internal.*[2] The former appears in our conditioned reflex at once; the second develops in time and is gradually elaborated. The first is an exact repetition of inhibition, well known for many years in the physiology of the lower parts of the central nervous system when stimuli, acting on various nervous centres and provoking various nervous activities, meet; the second may relate only to the cerebral hemispheres. Probably, however, the difference between these two inhibitions has to do only with the conditions of their origin, but not necessarily with the process itself. We are still investigating this question. Here I shall speak only of internal inhibition, referring to it, however, without its adjective, simply as inhibition.

[1] See especially chapter xxxii.—*Translator.*

[2] See especially paragraph 7, *et seq.,* chapter xxxii.—*Translator.*

There are two conditions, or better one condition, the presence or absence of which determines whether the impulse brought from the outside into the cells of the cerebral hemispheres will excite in them a process of stimulation or a process of inhibition; in other words, whether this impulse will become positive or negative. This fundamental condition consists in the following: if a stimulus entering into a cerebral cell coincides with some other extensive stimulation of the hemispheres or some lower parts of the brain, then this stimulus is a positive one; under the opposite conditions (*i.e.,* when it acts alone), it becomes sooner or later a negative, an inhibitory stimulus. Relating to this indisputable fact there arose the question, Why is this so? But until now there has been no answer.[3] Therefore we must begin with this fact without having analysed it. Such is the *first basic relation between excitation and inhibition.*

Physiologists have for many years been familiar with the spreading of excitation processes. The study of the higher nervous activity led us to a conclusion concerning the spreading also of the inhibitory process from the point where it first originates. The facts from which this conclusion is drawn are simple and obvious.[4] Now, if from one point an excitatory process spreads, and from another an inhibitory, then they limit each other, each confining the other to a definite space and within definite borders. In this way it is possible to obtain a very delicate functional delimitation of the separate points in the cerebral cortex. If we have to do with such separate points in the cortex which under corresponding conditions are subjected to stimulation, then this result can be easily explained by the plan of the cellular construction. This interpretation meets with difficulties when we have to deal with an excitatory or an inhibitory process corresponding to various intensities or other similar variations (for example the different frequencies of the strokes of a metronome) of one and the same external stimulating agent. In order to explain this according to the simple cellular scheme, it is necessary to presuppose as a point of application of this agent not a single cell, but a group of cells. In every case, as a matter of fact, it is possible to associate with a certain intensity of a known elementary agent the excitatory process, and with another intensity of the same agent the inhibitory one. Therefore, the second general relation between stimulation and inhibition in the cortex is their mutual limitation in space, their *delimitation.* The most evident demonstration of this is obtained in the experiments with mechanical stimulation of various points on the surface of the skin.

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[3] Some suggestions concerning this point will be found in chapter xxxix, paragraph 13.—*Translator.*

[4] See chapter xxi, paragraph 27.—*Translator.*

From this we are forced to presuppose some struggle between two opposing processes, ending normally in a certain equilibrium between them, in a certain balance. This conflict and this balancing are not too easy for the nervous system. We have seen this from the very beginning of our work and we see it constantly even until now. The animal often expresses this difficulty by motor disquietude, by whining and dyspnœa. But in the majority of cases the equilibrium is at last established, each process is allotted its proper place and time, and the animal, after becoming perfectly quiet, reacts to the corresponding stimuli by the process of excitation or of inhibition.

Only under special conditions does this conflict of the two processes lead to destruction of the normal nervous activity and then there originates a pathological state which may last for days, weeks, months, and perhaps even years. This may of itself gradually return to the normal when the experiments are interrupted and the animal is given a considerable rest, but if the conflict is too violent, it can only be removed by definite means, and the animal must be given regular treatment.

These special cases at first arose accidentally and unexpectedly, but afterwards we reproduced them intentionally in order to study them. Their description follows in chronological order.

The first of these cases we came upon many years ago (in the experiments of M. N. Yerofeyeva). The conditioned food reflex was elaborated not from an indifferent agent but from a destructive one, evoking an inborn defensive reflex. The skin was irritated by an electric current and at the same time the dog was fed, although at first the feeding had to be forced. A weak current was applied which was later increased to the maximum. The experiment ended thus: with the strongest current, as well as with burning and mechanical destruction of the skin, there could be provoked only the food reaction (the corresponding motor reaction and the salivary secretion) and there was no trace of any interference by the defensive reaction, there were no changes in breathing or heart beat, characteristic of this last reaction. It is clear that this result was attained by the transference of the external excitation to the food center and that simultaneously with this an inhibition of the centre for defensive reactions must occur. This special conditioned reflex persisted for some months and probably might have remained stable under the given conditions had we not changed them so that the electric irritation was systematically transferred at every excitation to another new point on the skin. And when the number of these points became considerable, then in one of our dogs the condition suddenly changed. Everywhere, beginning with the first location of the skin stimulus and even with the weakest current there was manifested only the strongest defensive reaction, and not a single trace of the food reaction.

By no means were we now able to reproduce the former results. The dog which in the former experiments had been quiet became very excited. In another dog this result came about only when—in addition to the considerable number of places on the skin from which we evoked only the food reaction in spite of the very strong current—during one and the same experiment the irritation was often and quickly moved from one place to another. Both dogs had to be rested for some months, and only in one of them were we able by proceeding slowly and cautiously, to restore the conditioned food reflex to the irritating agent.

The second case of the same sort was observed a little later (experiments of N. R. Shenger-Krestovnikova). A conditioned food reflex was elaborated in a dog to a circle of light projected on a screen in front of it. Differentiation of the circle from an ellipse of the same size and intensity was afterwards tried, *i.e.,* the circle was always accompanied by feeding; the ellipse, never. Differentiation was thus elaborated. The circle called forth the food reaction, but the ellipse remained without effect, which is, as we know, a result of the development of inhibition. The first ellipse applied was markedly different in shape from the circle (the proportion of its axes was as 2:1). Afterwards as the form of the ellipse was brought closer and closer to that of the circle, we obtained more or less quickly an increasingly delicate differentiation. But when we used an ellipse whose two axes were as 9:8, *i.e.,* an ellipse which was nearly circular, all this was changed. We obtained a new delicate differentiation, which always remained imperfect, lasted two or three weeks, and afterwards not only disappeared spontaneously, but caused the loss of all earlier differentiations, including even the less delicate ones. The dog which formerly stood quietly on his bench, now was constantly struggling and howling. It was necessary to elaborate anew all the differentiations and the most unrefined now demanded much more time than at first. On attempting to obtain the final differentiation the old story was repeated, *i.e.,* all the differentiations disappeared and the dog fell again into a state of excitation.

After these observations and experiments we recently undertook the investigation of the described phenomena more systematically and in more detail (experiments of M. K. Petrova). As it is possible to assume from the above facts that the destruction of the normal relations occurred as a result of the collision between the excitatory and the inhibitory processes in certain difficult circumstances, we performed in two dogs of different types—the one very lively, the other inactive and quiet—special experiments with various inhibitory agents and their combinations. Together with the conditioned reflexes which had been retarded for three minutes, *i.e.,* when the unconditioned stimulus was followed by the conditioned only three minutes after the beginning of the latter, as a consequence of which the positive effect appeared only after a preliminary period of inhibition of one to two minutes, there were applied other kinds of inhibition (differentiations, etc.). But this problem was solved by these different nervous systems, although with varying facility, yet without damaging the normal relations. Then we began to elaborate the conditioned food reflex with a destructive agent. Now it was sufficient, having formed this reflex, to repeat it several times on the same spot on the skin, in order that the pathological state might appear. This deviation from the normal proceeded in the two dogs in opposite directions. In the lively dog the elaborated inhibitions suffered to a considerable degree or even disappeared entirely and changed into positively acting stimuli; in the quiet dog, on the contrary, the positive conditioned salivary reflexes markedly decreased in strength and disappeared. And in both cases these changes were very stable, they lasted for months and did not alter or vanish without special treatment. In the lively dog with the weakened inhibitory process, there was in the course of a few days a permanent return to the normal, brought about by means of rectal injections of potassium bromide. It is interesting to observe that together with the appearance of normal inhibition, the strength of the positive conditioned action not only was not decreased, but was even somewhat augmented. On the basis of these experiments we are, therefore, compelled to think not of a decrease of one nervous excitability under the influence of bromide, but of a true regulation of the nervous activity. In another dog we failed to restore a permanent and measurable salivary reflex, in spite of various means which we employed for this purpose.

The following experiments done on a third dog for another purpose, however, gave similar results but more instructive details (experiments of I. P. Razenkov). Many positive conditional reflexes were elaborated on the animal, from various receptors or from the same receptor with varying intensities of one and the same agent. Among others a reflex was obtained to a definite frequency of a mechanical stimulus of a certain place on the skin. After this we began to elaborate differentiations from the same place on the skin, but with a mechanical stimulation of another frequency. This differentiation was attained also without great difficulty, and without noticeable changes in the general nervous activity of the animal. But when immediately after the application of completely inhibited rhythm of the mechanical skin stimulus, there was tried without delay stimulation by a positively acting rhythm, the dog manifested a peculiar disturbance, lasting five weeks, and only gradually disappearing. Restoration to normal was perhaps aided by our special measures. For the first days after the experiments in which there was a collision of the nervous processes, all positive conditioned reflexes disappeared. This state lasted for ten days. Afterwards these reflexes began to reappear, but in a peculiar order; contrary to normal, strong stimuli were without effect, or acted minimally, and considerable effect was obtained only from the weak stimuli. This state continued for fourteen days. Again ensued a special phase. All stimuli now acted equally, and with about the same force as strong stimuli in the normal animal. This extended over a period of seven days. Finally came the last period before the normal, characterised in that the stimuli of moderate strength were greater than in the normal state, strong stimuli were less than in the normal, and weak ones had lost their action entirely. This too lasted for seven days, and then there was a return to normal. With the repetition of the foregoing procedure which evoked the disturbance described above, *i.e.,* the repetition of an immediate transition from the inhibitory-acting mechanical stimulation of the skin to the positive-acting stimulation, there occurred the same disturbance with the same phases, but running a shorter course. With further repetitions the derangements became more and more fleeting, until finally the same application provoked no disturbance. The decrease of the pathological state was expressed not only in the shortening of the duration of the abnormal condition but also in the reduction of the number of phases, and the disappearance of the more abnormal phases.

Thus with the collision of the excitatory and the inhibitory processes, there appears either a predominance of the stimulating process, disturbing the inhibition (it is possible to say, a lingering increase of the tonus of the excitation); or in other cases a predominance of the inhibitory process, with its preliminary phases, disturbing the excitatory process, *i.e.,* an increase in the tonus of the inhibition.

But we have seen the same phenomena under other conditions than the above. Under the action of exceedingly unusual directly inhibiting stimulations affecting the animal, there occurs a chronic predominance of the inhibitory process. We observed this in a high degree in some dogs after the great inundation in Leningrad of September 23, 1924, when our experimental animals were rescued with great difficulty and subjected to quite exceptional conditions.[5] The conditioned reflexes disappeared for some time and only slowly reappeared. For a considerable period after this reappearance each more or less strong stimulus, which was formerly followed by a considerable conditioned effect, as well as the application of an earlier elaborated and even well-

[5] For a detailed account of this case, see chapter xxxix, paragraph 4.—*Translator.*

concentrated inhibition, provoked again this chronic state of inhibition; either as a complete inhibition or as its preliminary phases mentioned above (experiments of A. D. Speransky and V. V. Rikman). In less degree and for a shorter time the same is often observed under more usual conditions, as the removal of a dog to a new environment, or his transference to a new experimenter, etc.

On the other hand, a slight change in the application of a well-elaborated positive conditioned reflex, *viz.,* an unconditioned stimulation following immediately the beginning of the conditioned, so increases the tonus of the stimulation that if the elaborated inhibitions are now tested, they are seen either to have entirely disappeared or to have suffered a great loss in constancy and regularity. Also a frequent interchange now of positive and negative reflexes leads, especially in lively dogs, to a high degree of general excitement (experiments of M. K. Petrova and E. M. Kreps).

The facts given above do not exhaust our material concerning the relation between excitation and inhibition. In the course of our work we have met with many quite peculiar cases of just this very same kind.

It was noticed in many instances that in certain phases of drowsiness in normal dogs there occurred a distortion of the effects of conditioned stimuli. The positive stimuli lost their effect, but the negative became positive (experiments of A. A. Shishlo). In the light of this knowledge, we can understand the frequent fact that in the drowsy state of the animal an apparently spontaneous salivary secretion sets in, which is absent in the waking state. The explanation consists in this—that at the beginning of the elaboration of the conditioned reflexes of a given animal many accessory stimuli, indeed the whole *entourage* of the laboratory, become conditionally connected with the food centre, but later all these accessory stimuli are inhibited, owing to the adaptation to which we subject the conditioned stimuli. In drowsiness these inhibited agents recover, as we are inclined to think, temporarily, their original activity.

The temporary transformation of the elaborated inhibitory stimuli into positive ones is observed also in pathological attractions of the cerebral cortex produced by post-operative cicatrisation, especially during the intervals between convulsions. It is interesting that along with these elaborated inhibitory stimulations during this time only the weakest positive stimuli act, *viz.,* light, whereas all other positive conditioned stimuli of moderate or of considerable strength remain without effect (experiments of I. P. Razenkov). Here belongs the former fact, frequently reproduced by us, that new stimuli provoking one or another reflex of moderate strength during their action convert the conditioned inhibitory reflex into a positive reflex (our so-called inhibition of inhibition—dis-inhibition).[6]

In lesions of the cortex, on the other hand, which follow extirpations, the positive conditioned stimuli belonging to the injured cortex become inhibitory. This I have already mentioned in my foregoing article on sleep. The phenomenon is especially marked in the skin region of the hemisphere, where it has been best studied (earlier experiments of N. I. Krasnogorsky and newer ones of I. P. Razenkov). If the lesion is inconsiderable, the previous positive conditioned mechanical skin stimulus produces an effect less than the normal, and if repeated during the course of one experiment soon becomes inhibitory, *i.e.,* being joined with other effective stimuli it weakens their action, and applied alone produces in the animal a state of sleepiness. If the destruction is more serious, it has, under usual circumstances no positive action, being purely inhibitory, and causes after its application a complete disappearance of all positive conditioned reflexes in other parts of the brain.

But this inhibiting agent, being now inhibitory, can nevertheless, under certain conditions manifest a positive effect. If the animal becomes sleepy, then this stimulus, as well as the elaborated inhibitory agent, as mentioned above, manifests a small positive effect. But this effect can be brought about in the animal by still another procedure. If this stimulus is repeated several times, with only this slight change, that it acts alone for 5 seconds instead of the usual 30 seconds (*i.e.,* if the unconditioned stimulus is added 5 seconds instead of 30 seconds after the beginning of the conditioned), then after displacing it to 30 seconds, we may have a positive effect, which, however, is very unstable. When it appears quickly enough after the beginning of the stimulation, it begins to fall rapidly during the continuation of the stimulation and finally entirely disappears (a markedly weakened excitability). Such a transitory effect may be obtained also by a preliminary injection of caffein, or by many other similar measures (experiments of I. P. Razenkov).

Somewhat different but still related to this theme are the following facts. With a very weak general excitability of the cortex, as is observed in senility of animals (experiments of L. A. Andreyev), and also in animals from which the thyroid has been removed (experiments of A. V. Valkov),[7] or in certain states brought about by convulsions in post-operative scarring of the cortex (experiments of Razenkov), the inhibitory process is either much weakened or becomes impossible. In these cases only by an increase of the irritability of the cortex by

[6] Discussed in detail in chapter xi, paragraph 22, and in chapter xxii.—*Translator.*
[7] See chapter xxxv, paragraph 27.—*Translator.*

the application of stronger unconditioned stimuli can we sometimes provoke an inhibitory process.

Here belongs the phenomenon of reciprocal induction, which I have mentioned in the previous chapters (experiments of D. S. Fursikov, V. V. Stroganov, E. M. Kreps, M. P. Kalmikov, *et al.*).[8] And finally the last fact consists in the following: if by a corresponding procedure, separate points of the cortex are reinforced for a long time, some always as points of excitation, some others always as points of inhibition, then they gradually become highly constant in their effects, and stubbornly resist the influence of the opposite processes. Extraordinary means are sometimes required in order to bring about a change of their function (experiments of B. N. Bierman, U. P. Frolov).

All these facts permit us, I think, to classify the various conditions to which the cortex is subjected in a certain consecutive order. At one pole of this system stands the state of excitation, an extraordinary increase of irritability, when an inhibitory process becomes very difficult or impossible. After this is the normal waking state, the state of normal equilibrium between the processes of excitation and of inhibition. Then follows a long but also consecutive series of states transitory to the inhibition, of which the following are the most characteristic: a state of equalisation, when in contradistinction to the waking state all stimuli, independent of their intensities, act exactly equally; the *paradoxical phase* when only weak stimuli act and when strong stimuli either have no action at all or have a barely noticeable effect; and finally the *ultra-paradoxical phase,* during which only the previously elaborated inhibitory agents have a positive effect. After this follows a state of complete inhibition. The explanation is not yet clear of that other state in which the excitability itself is so low that inhibition in general becomes very difficult or impossible, just as in the case of the state of extreme excitation.

At present we are occupied among other things with the experimental decision of the question: In all cases of normal transition from the active state to that of inhibition as in the state following sleep or in the process of elaboration of negative conditioned reflexes, etc., are there to be found transitory states which are so sharply expressed in pathological cases? Already we have some clues to the answer to this question. If this should prove to be so, then only as a prolongation of the transition from one state to another, a certain isolation and fixation of those transitory states which normally change quickly or almost imperceptibly, can be considered as pathological.[9]

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[8] See chapter xxiii, paragraph 12.—*Translator.*

[9] Detailed discussion of the recent work relating to this will be found in chapter xxxviii.—*Translator.*

The above facts open the way to the comprehension of many phenomena of both the normal and pathological activity of the higher nervous system. I shall give some examples. In foregoing articles I have shown how normal conduct is based on the elaborated delimitation of the points of excitation and of inhibition, on that magnificent mosaic in the cortex, and how sleep is to be considered as irradiated inhibition. Now we may add some details showing how it is easy to understand certain variations of normal sleep as well as separate symptoms of hypnosis when they are considered as different degrees of extensiveness and intensity of the inhibitory process.

Cases of sleep while walking or riding horseback are well known. In other words inhibition is limited to the confines of the cerebral hemispheres, and does not spread below over the subcortical centers established by Magnus. Further we know of sleep with partial waking in relation to special stimuli, although they may be feeble: the sleep of the miller who wakes when the noise of the mill ceases; the sleep of the mother who awakes on the faintest sound coming from her ill child, but whose rest is not disturbed by much stronger sounds from other sources, *i.e.,* sleep in which easily excitable points stand on guard.

Catalepsy in hypnosis is evidently an isolated inhibition of only the motor regions of the cortex, not spreading to the centers of equilibrium, and leaving free the remaining parts of the cortex.[10] Suggestion in hypnosis can also be considered as such a phase of inhibition, in which weak conditioned stimulation (words) acts more effectively than stronger direct external stimuli. The symptom established by Pierre Janet of the loss of the sense of reality during many years of sleep can be explained as a chronic inhibition of the cortex interrupted only for short intervals, and especially in the presence of feeble stimuli (usually at night), this inhibition concerning particularly the skin and motor regions, which are the most important for the influence of reality on the organism and for the action of the organism on the outer world. Senile talkativeness and dementia too find a simple explanation in an extraordinary weakening of inhibition resulting from the feeble excitability of the cortex. Finally our experiments on dogs give us the right to consider those changes which we produce—the chronic deviations of the higher nervous activity from the normal—as pure neuroses, and some light can be thrown on the mechanism of their origin. In this way the action of an exceedingly strong and unusual stimulation (for example the flood of 1924) on dogs with a weak nervous system, having a predominant inhibitory process, in other words, on a central nervous system with an increased tonus of inhibition, reproduces the etiology of a special traumatic neurosis.

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[10] For details of this statement see chapter xxix.—*Translator.*

It is obvious that the time has not yet come for a theory to explain all the enumerated phenomena and to assign them a common basis, although many hypotheses have been proposed, each one of which has a certain justification. In the present situation, one may use various conceptions in the work if only they permit a systematisation of the material, and suggest new and detailed problems.

Thus in our experiments we think of different phases which develop under special conditions in the cortical cells, from extreme excitation to the deepest inhibition, and which depend upon the intensity and duration of the corresponding stimulation and upon the conditions under which this stimulation occurs. The manifest analogy between the changes which we have observed in the function of the cerebral cortex and in the changes of the nerve fibre inclines us to this view. The latter changes occur under the influence of various strong influences; they are aptly described by N. E. Vvedensky, in his well known work, *Excitation, Inhibition, and Narcosis.* We do not agree with his theory, but we have grounds on which to refer all the observed transitions from excitation to inhibition to one and the same elements, the nerve cells, as Vvedensky has rightly done in the case of the nerve fibre.

One can hardly deny that only a study of the physico-chemical processes taking place in nerve tissue will give us a real theory of all nervous phenomena, and that the phases of this process will provide us with a full explanation of all the external manifestations of nervous activity, their consecutiveness and their interrelations.

# CHAPTER XXXVII

## EFFECT OF INTERRUPTING THE EXPERIMENTATION IN DOGS WITH CONDITIONED REFLEXES

(From the volume dedicated to Charles Richet, May 22, 1926.)

DESCRIPTION OF FIVE CASES.

An interruption of two months in experiments with several dogs having conditioned reflexes gave us an opportunity to observe peculiar changes in their behaviour.

Dog No. 1.—This very active animal, when experimentation with it was begun after an interruption, showed a hyper-excitability, continually wagging his tail and reacting very briskly to the slightest movement of the experimenter.

The conditioned food reflexes, however, disappeared and the animal would not take the proffered bread mixture.*

After several ineffectual attempts to provoke the conditioned reactions, we resorted to a differentiation ** which was well elaborated, *i.e.,* it represented a strong inhibitory process. After this the vanished reflexes reappeared, and the dog took the food.

The explanation of these phenomena is based on the fact that the dog possessed a pronounced reflex of freedom.[1] By the systematic use of conditioned and unconditioned stimuli for the food reflex, before the experimentation was interrupted, the reflex of freedom had been inhibited. During the interruption of the work the conditioned food reflexes were weakened, and so the reflex of freedom, formerly present, became strengthened and prepotent. But it has been established in our laboratory that internal inhibition, owing to induction, strengthens the excitation process. By applying the strong internal differential inhibition, the action of all of the positive conditioned food reflexes was reinforced; consequently the reflex of freedom vanished.

Dog No. 2.—This animal was very strong and excitable. There had been established, although with much difficulty, a differentiation of two frequencies of pricking the skin (mechanical stimulus), one frequency

* This consists of a mixture of one part of meat powder and three parts of black bread crumbs. The meat powder is prepared from finely ground roast beef (previously dried), and the mixture is moistened before feeding.

** For this one uses two stimuli, one of which is always accompanied by feeding (positive), and the other of which is never associated with food (negative). In the latter case the salivary reaction is inhibited.

[1] See chapter xxviii.—*Translator.*

was a positive stimulus, and the other frequency a negative stimulus. Then during an experiment, the negative pricking stimulus was immediately followed by the positive pricking stimulus. This change proved to be too great a strain for the nervous system of our animal. The differentiation began to weaken, and continued to weaken inversely to our efforts to maintain it. Finally not only the mechanical excitation of the skin, but also all the surroundings became conditioned stimuli of this painful state of the animal's nervous system. All other conditioned reflexes became weak or unstable, or even disappeared completely. The dog refused all food, was uneasy during the experiment, and strove to free himself from the stand.

After the interruption, the conditioned reflexes from pricking the skin disappeared, but those from visual and auditory stimuli became reestablished and were augmented. A single application, however, of the positive pricking of the skin was sufficient to throw the animal into the state which existed before the interruption of the work.

Dog No. 3.—This animal had a very strong passive defensive reflex, and it was therefore extremely timid.

After the interruption of the work the conditioned reflexes, although they were old and well formed, disappeared, and the animal, in spite of his voracity, refused food. One may suppose that the environment of the laboratory, having ceased to be familiar for this dog after two months' interruption of the experiments, had become, consequently, inhibitory. The presence, during the course of the séances, of the familiar experimenter close to the dog (ordinarily the animals and the experimenter are separated—in two rooms—during the séance), and the application of the differentiation (as in Dog No. 1) permitted the reestablishment of the conditioned reflexes little by little; and gradually the dog commenced to take his food.

Thus the social excitant (the experimenter) and the stimulation induced by the internal inhibition of differentiation overcame the external inhibition produced by the surroundings.

Dog No. 4.—This was a sluggish animal which became quickly drowsy during the employment of weak conditioned stimuli. By appropriate measures we succeeded in overcoming the state of somnolence, and the conditioned reflexes became perfectly regular.

After the interruption of the experiments all these reflexes disappeared entirely and the dog refused the feedings.

The somnolent state, it is evident, reappeared owing to the inhibitory, hypnotising surroundings of the laboratory and the application of weak conditioned stimuli. From numerous experiments it appeared that after the interruption, the positive conditioned reflexes were more affected than the negative ones.

When, by the means described above, we had again banished the drowsy state of the dog, the positive reflexes were quickly restored and the dog greedily ate the proffered food.

Dog No. 5.—This dog had a great number of positive and negative (inhibitory) conditioned reflexes which functioned regularly.

After the interruption, they were tried anew. None of them had diminished in strength. But the next day, during the experiment, the animal became very restless and dyspnœic and without any apparent external reason the positive reflexes were weakened.

Evidently the great nervous strain imposed upon this dog by the first séance after the interruption, undertaken without any preliminary training, provoked this painful state of his nervous system. This condition continued, and that constitutes an indirect proof of our hypothesis.

These observations show that the presence or the absence of such and such conditioned or unconditioned factors determines exactly and continuously the behaviour of the animal. In connection with these conditions, there were observed certain modifications of the general tonus of the nervous system, now in the direction of excitation, now in the direction of inhibition, and, on the other hand, there is a like transformation in the relations among the special reactions to the surroundings.

In other words, these facts argue in favour of the conception of a strict and absolute determinism operating in the higher nervous activity of the animal.

# CHAPTER XXXVIII

## NORMAL AND PATHOLOGICAL STATES OF THE HEMISPHERES

**(Read at the Sorbonne in Paris, December, 1925, on the occasion of the conferring of an honorary degree on Prof. Pavlov by the University of Paris.)**

DIFFERENCE BETWEEN UNCONDITIONED AND CONDITIONED REFLEXES—THE TWO FUNCTIONS OF THE CEREBRAL CORTEX—POSITIVE AND NEGATIVE CONDITIONED STIMULI—THE BRAIN AS A MOSAIC—TRANSITORY PHASES BETWEEN THE WAKING AND SLEEPING STATES—TWO EXPERIMENTAL EXAMPLES—THE PARADOXICAL PHASE AND HYPNOSIS—ANOTHER CONFIRMATION OF THE IDENTICAL NATURE OF SLEEP AND INHIBITION—TWO EXPERIMENTS SHOWING A CHANGE IN THE INHIBITORY PROCESS (ONE WITH AN ELECTRIC CURRENT AS THE CONDITIONED STIMULUS; THE OTHER WITH DIFFICULT DIFFERENTIATION)—RECOVERY WITH REST AND BROMIDE—OTHER EXPERIMENTS SHOWING PREDOMINANCE OF THE INHIBITORY PROCESS—A DIFFICULT COLLISION IS THE CAUSE OF THE PATHOLOGICAL DISTURBANCE—HYPOTHESES CONCERNING THE SEAT OF FORMATION OF CONDITIONED REFLEXES AND THE NATURE OF EXCITATION AND INHIBITION—FUNCTIONAL SENSITIVENESS OF THE CORTICAL CELLS; ILLUSTRATED BY THE RUSSIAN FAMINE—TWO TYPES OF NERVOUS SYSTEMS.

I HAVE the high honour to direct your kind attention to the recent results of the investigations in my laboratory. This report of research will, I trust, stimulate considerable interest. The experiments have been carried out on animals, *viz.*, on the dog, the friend of man since prehistoric times. For twenty-five years now we have made researches on this animal in order to understand the entire higher nervous activity of his organism from a purely physiological point of view, discarding all the while psychological explanations and terms.

The chief organ of this higher nervous activity is, of course, the cerebral hemispheres.

The important phenomenon in the activity of the cerebrum, about which centres all our experimental material, is what I call the *conditioned reflex.* The conception of reflexes in physiology, the gift of Descartes' genius is a purely scientific comprehension. It is now sufficiently established, we may say, that so-called instincts[1] are the same phenomena as reflexes, though often of a more complex kind. It is preferable, therefore to use the one term reflex for all these constant and regular reactions of the organism, and for the sake of precision we add to this word the adjective unconditioned or conditioned.

Let us take one of these unconditioned reflexes, a most common one, of daily occurrence, the food reflex. A definite motor and secretory reac-

[1] See chapter xxvii, first paragraph and footnote 1, for a discussion of the relation between instinct and reflexes.—*Translator.*

tion to food as a stimulus occurs when it is placed before the dog or when it gets into his mouth. If a few seconds before the food is in the mouth of the dog, there acts, for example, on his ear, the sound of a metronome, and if such coincidence takes place one or more times, then the metronome will call out the same reaction as the food, *i.e.*, there will appear the same movements and the same salivary and other digestive secretions. This new food reaction can become as exact as if the food actually were in the mouth, and it may exist for an indefinitely long time.

These reactions are what I call *conditioned reflexes.*

Why should this not be considered a reflex? The mechanism is the same—a definite external agent, the conduction of the impulse along a certain afferent nerve, and a central connection with special efferent nerves to the muscles and glands. The *difference* is not in the mechanism of the reaction but in its perfection. The mechanism of the unconditioned reflex is ready in all its parts from the day of birth. The conditioned reflex is elaborated during the course of the individual's existence in one region of the central nervous system, *viz.*, in the cerebral hemispheres; for with their removal the conditioned reflexes disappear from the activity of the nervous system. As in the normal animal this elaboration of the reflex mechanism arises inevitably under definite physiological conditions, there is absolutely no basis for considering it other than physiologically. The establishment of the mechanism in the conditioned reflex consists evidently in a *coupling,* in the formation of a functional union in the path in which the excitatory process moves. And now we possess the facts which permit us to consider this act of coupling as a physiological process and even as an elementary one.

Conditioned reflexes may form on every conceivable agent of the surroundings if only there exists for them a receptor apparatus in the given animal, and they may form on any of the unconditioned reflexes. Their biological significance is enormous, for they alone make possible the establishment of the most delicate and exact equilibrium between the complex organism and the surroundings. The innumerable conditionally acting agents signal, as it were, for a few, near agents, directly favourable or harmful to the organism. Even very fine and distant conditioned stimuli acting on the eye, ear or other receptor organs can provoke the movement of the animal—on the one hand, *toward* food, the opposite sex, etc., or, on the other hand, *away from* all harmful and destructive agents.

From such a point of view the physiological rôle of the cerebral cortex is either (1) a connecting, combining or *coupling* function (according to the mechanism), or (2) a *signalling* function (according to its significance). And the signallisation is adaptable in strict correspondence with the external agents.

Just a few words here about our method. For the formation of conditioned reflexes we employ two unconditioned reflexes almost exclusively: the *food* reflex and the *defensive* reflex (the latter is seen upon introducing into the mouth of the animal not food but substances which the dog rejects, such as a weak solution of acid). We register not the motor component of the conditioned reflexes but the secretory, the secretion of saliva; for the reaction is easier to measure in this way.

The above described reaction is a *positive conditioned* reflex; for the conditioned stimulus calls forth in the cortex of the cerebral hemispheres a process of excitation. But along with the positive there exist *negative*, inhibitory conditioned reflexes when the conditionally acting agent calls out a process not of excitation but of inhibition. We elaborate, for example, a positive conditioned reflex to a tone of 1000 vibrations per second. Now if we try other tones we find they also have a positive conditioned action. If, however, we repeat them without supporting them by the unconditioned stimulus (food or acid), then they gradually not only lose their positive effect, but become inhibitory agents. Their inhibitory nature can be clearly demonstrated, for shortly after their application, during the next minute or even many minutes, the positively acting tones are weakened or completely inactive.

At the present time our investigations of conditioned reflexes have proceeded so far as to permit me to discuss them more or less fully. In addition to the foregoing necessary introduction, I must mention briefly two or three other details before discussing the special subject of my communication.

Both the process of excitation and that of inhibition execute a certain movement over the cerebral cortex, at first *irradiating* more or less widely from the point of origin, and then *concentrating* around this point. With the concentration of these processes there occurs a very fine definite localisation of them, and owing to this the whole cortex becomes reduced to a huge *mosaic* of points of excitation and of inhibition closely intermingled.

This mosaic is formed and reinforced partly by the reciprocal crowding in of the opposed processes of excitation and of inhibition, directly called out by the corresponding *external* agents; partly, however, by *internal* relations, in particular by *reciprocal induction*, when one process leads to the strengthening of the other.

In a recent lecture (chapter xxxii) I reported a long series of experiments, proving, I think beyond doubt, that sleep is the same inhibition which co-exists side by side with the process of excitation during the waking state, not delimited, however, but continuous and irradiated not only over both hemispheres, but over the neighbouring and lower parts of the brain.

Recently we have investigated the *transitory phases* between the waking and the sleeping state. In our experiments the dog is placed in the stand in such a way that his movements are restricted and he is alone in the experimental chamber, isolated even from the experimenter. Under the influence of these conditions, together with the definite character of the applied stimuli there developed in the central nervous system of the animal a special state, tending, so to speak, toward sleep. Partly owing to the individual peculiarities of the nervous systems of different dogs, partly as a consequence of some special procedure in our experiments, we are able to observe and investigate certain fixed, as it were, stages in the transition from the waking state to that of complete sleep. Of such phases we can clearly recognise several.

Here I shall consider only two of them.

When the conditioned reflexes are formed from different external agents with the help of one and the same unconditioned stimulus, then the effects received show a wide quantitative variation in spite of the definite elaboration of all reflexes. To the ordinary thermal and mechanical stimuli of the skin, as well as to light stimuli, the conditioned reflexes are usually smaller than are those to sound stimuli. As we have been taught by our recent experiments, this depends upon the absolute energy of each stimulus—the greater the energy of the stimulus the greater is its effect. In a special phase during the transition from the waking state in the direction toward sleep this normal relation of the effects disappears. Either all the effects become equal (the equality phase), or the relation becomes reversed, so that the effects from weak stimuli are greater than those from the strong, or the latter may even remain without any effect (*paradoxical* phase).

Here are examples. A dog formerly showing differences in the size of the conditioned reflexes corresponding to stimuli of different strength falls, in the course of prolonged experiments, into a barely perceptibly drowsy state and the conditioned reflexes, compared by the size of their effects, all become equal. It was only necessary to give a small subcutaneous injection of caffein in order to have the animal fully awake; and immediately thereafter all the reflexes, measured by the size of their effects, returned to the proper order.

In another dog, always remaining wide awake during the experiments, we often repeated and continued the application of the inhibitory stimuli for a considerable time. Thus we brought him into the drowsy state. Trying now a weak positive conditioned stimulus we found it inactive, and after this we gave the dog a little food. This, of course, lessened to a certain degree the sleeping state. On repeating the conditioned stimulus a second time we had a slight action from it. We fed the dog again. For the third time the conditioned reflex to that stimulus attained its usual size or even exceeded it. The conditioned stimulus was now accompanied by food. In a further application one of the strong conditioned stimuli showed a smaller effect than the previously applied weak stimulus. With the continuation of the experiment in this manner, we finally succeeded in establishing the normal relation between the stimuli, corresponding, as in the former case, to their strength.

It is evident that the excitation produced by repeated acts of eating gradually overcame the sleepy inhibitory state of the cerebrum which we had brought about in the beginning of the experiment and from which state it passed by the same consecutive stages back again into the fully waking state.

Here is another instance. This is a dog in which it was possible to elaborate quickly many reflexes to agents of varying strengths. In the elaboration of one more new reflex (to a weak stimulus) the stimulus was applied several times in succession in each experiment and also for several consecutive days. This led to a marked change in the general state of the animal. He gradually became less restless on the stand and stolidly remained in a given pose as if he were cut out of marble: and at the same time, of the formerly elaborated stimuli only the action of the weak ones was preserved. With weak stimuli the full secretory effect was received for the whole period of their action, and the dog began now to eat the food immediately upon its presentation. With strong stimuli only at the very beginning of their action did there flow even a small quantity of saliva, but this secretion diminished and the dog did not turn toward the offered food. If we entered the room and stimulated the dog in some way, by stroking him, calling him by name, etc., then after this all the conditioned reflexes became re-established, and the stimuli, compared by the strength of their action, had their normal effect. When, on the contrary, the dog for several days received no special stimulation on the stand, all the conditioned reflexes finally disappeared, and the animal did not take the food given him. But you had only to free the animal from the stand and to put him on the floor and he fell to eating greedily.

Almost without doubt in the experiments described we have to do with a special *hypnotic* phase. I think that this paradoxical phase is the actual analogy of a specially interesting phase of hypnosis in man, the phase of *suggestion,* in which the strong stimuli of the real world give way to weak stimuli, the words of the hypnotiser. The paradoxical phase explains many cases of *abnormal sleep,* interrupted or continued. It lasts sometimes for years. During this time the subject returns only for short intervals to the waking state, and then especially in the absence of strong stimuli, which always occur in the day. Therefore the waking intervals come oftener during the night. The case of five years' sleep observed by Pierre Janet and that of twenty years' sleep seen in St. Petersburg are examples.[2]

Thus the *transitory* phases between the waking state and sleep appear as different degrees of extensiveness and intensiveness of the inhibitory process in the hemispheres. The so-called *animal hypnotism* (known for a long time) is a real hypnosis, one of the transitory phases between the waking state and sleep, an inhibition affecting chiefly the motor area of the cortex, by virtue of the peculiarities of the procedures by which it is produced. *Catalepsy* which sets in during hypnosis evidently arises owing to the manifestation of the activity of the equilibrating centres of the brain (discovered by Magnus and Klejn), now freed from the masking influence of the motor area of the cortex. Our experiments showed that various transitory phases and sleep can be produced from weak as well as from strong stimuli, and also from unusual ones. Thus the waking state is established in general by an average strength of customary stimuli, which is especially the case for some types of nervous system.

Especially interesting is the fact that we were able to observe the paradoxical phase in other states in addition to those described above in the dog. After each single application of the inhibitory conditioned stimulus, particularly soon after the reflex had been elaborated, there was seen a long successive period of inhibition over the whole of the hemispheres. And during this period too, we could detect the characteristic paradoxical phase. Our former conclusion that sleep and inhibition are one and the same process received here another confirmation.

Let us pass over to the other series of experiments. At first we met accidentally, but later we were able to produce voluntarily, pathological functional changes in the dogs' nervous systems analogous to neuroses in the human.

In two dogs the conditioned reflexes were gradually formed not from indifferent stimuli but from a very strong electric current applied to the skin. With this shock there was no howling nor exhibition of the defensive reflex whatever, but the animals, on the contrary, turned toward the place from which they were accustomed to receive food, licked their lips, etc., in short, they responded by a lively food reaction and there was an abundant flow of saliva. The electric current could be replaced by cauterisation and wounding of the skin, but the effect remained the same.

This conditioned reflex continued for a long time without change. Then we began to move the site of the stimulation, *i.e.,* to apply the current every time to a new place on the skin. For a long time the effect remained unaltered. But in one dog, when a certain number of spots

[2] See chapter xxix.—*Translator.*

had been tried, the results underwent a sudden and radical change. The conditioned food reflex to the electric current disappeared completely, and now a much weaker current even when applied to the first elaborated spot called out only the strongest defensive reaction. In another dog the mere transference to a new skin spot did not bring about the same result; but when in one and the same experiment we stimulated these different places consecutively there was exactly the same effect as seen in the first dog. Both the animals became very excited and restless. It was necessary to let them go three months without any experimentation, and even then it was possible in only one of the dogs and by beginning very slowly and with a weak current, to re-form the old reflex. In the other dog we did not succeed in doing this.

In the next dog a conditioned reflex was formed on the projection of an illuminated circle on a screen close in front of the animal. Then an ellipse was differentiated from the circle. In the beginning it also gave a positive conditioned action, but on repetition without support by feeding it became an inhibitory agent. This first differentiated ellipse was in the same position and received the same illumination as the circle but its shape was very different (elongated). Later there were successively differentiated ellipses, each one more nearly circular. These new differentiations were well elaborated and stable. When, however, one of the most nearly circular ellipses, closest in form to the original circle, was now tried, there began a reversal; the differentiation (absence of effect owing to differential inhibition), which after some few trials had become effective, when repeated again and again failed to maintain its inhibitory character, *i.e.,* this last ellipse began anew to have a positive action, which increased with every application though it was never accompanied by feeding. And at the same time so did all the earlier and less delicately elaborated though more stable differentiations. Now we had to do the elaboration of the ellipses all over again, and to operate more carefully and slowly than the first time, beginning with the ellipse whose form was farthest removed from that of the circle. On the application of the most nearly circular ellipse which could be differentiated, the same history recurred. And in this dog too there was after the experiments a marked alteration in the general conduct; he was no longer gentle and docile, but became very excited and irritable (nervous).

It was evident that in both cases,—in the experiments with the conditioned reflexes to electric shock as well as in those with the circle and differentiated ellipses,—it was the inhibitory process which suffered permanently. In the first case, in order that the food reaction should be connected with the electric shock, it was first necessary that the defensive reflex to the current be inhibited. In the second case, as has been shown above, the differentiation was also based on the inhibitory process.

These observations were begun long ago in our work, and they remained as detached and unused facts. We could not make heads or tails out of them. Only in recent years have we been able to work out special themes with them on a larger scale and thus to fathom their relations.

In many dogs we have obtained the same results.

Under the influence of similar circumstances their nervous systems markedly lose their inhibitory functions. From a large number of different cases of inhibition there remained intact only a few of the most stable ones, and even in these there were defects. The pathological condition lasted sometimes for months and often remained stationary. It is interesting to mention that in some cases a marked improvement was quickly brought about by several daily injections of bromide.

But in other dogs, evidently of another nervous type (*see* preceding chapter), we got entirely different results. In them our experiments caused a *predominance* of the *inhibitory* process. The positive conditioned reflexes either entirely disappeared or exhibited the peculiar properties of the above described transitory phases between the waking and the sleeping state.

Here is such an experiment. There was elaborated a conditioned reflex to a rhythmical, mechanical irritation (having a definite frequency) of the skin. From this conditioned stimulus there was differentiated a stimulus almost identical with it except in the frequency of the rhythm. One frequency was made a positive conditioned stimulus and the other a negative one (a conditioned inhibitor as a differentiated stimulus). When both these reflexes had become stable, the positive conditioned stimulus was applied immediately, *i.e.,* without any interval, after the action of the conditioned inhibitor, the differentiated stimulus; in other words, one frequency of the mechanical stimulus of the skin was replaced by the other. This led to a striking pathological state of the nervous system, which only after many weeks, and then aided perhaps by some of our special procedures, returned to normal. We observed the animal every day without exception. The trouble began by the disappearance of all the conditioned reflexes. Then we observed them returning by and by, passing through those definite phases already described: but the interesting point is that they remained in each phase for several days, in some of them up to ten. Among the other phases there again appeared, and especially characteristically, the paradoxical phase and the phase of equality.

Thus there occurred in the pathological cases the same nervous phenomena as we observed in the normal. But in the latter they lasted only a short while, whereas there they were constant. This refers to the predominance of the positive (excitatory) as well as to that of the inhibitory processes.

What are the general characteristics of all the pathological instances? Upon what depends the persistent and marked deviation from the normal brought about by our procedures? We have the right to answer, I believe, that it is a *difficult collision, an unusual confronting of the two opposing processes of excitation and inhibition (be it in time or intensity relations or even in both together)*, which leads to a more or less permanent destruction of the normal balance existing between these two processes.

It is necessary to add, however, that some of our procedures by which we brought about the pathological states did not prove effective in all dogs. There are some animals which undergo them well, without damage. We can not extend this statement to the applications of the electric shocks as conditioned stimuli, as such experiments have been too few. We can describe all the above facts as characteristic of the physiological work of the cerebral hemispheres, according to the following hypothesis, which gives us a scheme for conducting further experiments. The coupling, the elaboration of new unions (new paths for the nervous processes in the hemispheres), we attribute to the function of the inter-cellular membrane, if it exists, or simply to the fine ramifications between the neurones, between the separate nerve cells. The fluctuation of the excitability and its transformation into inhibition may be attributed to the very cells themselves. This distribution of function appears to us as a probable explanation in the light of the fact that when the new connections are well elaborated they are preserved for a long period, whilst the alteration of the excitability, the change into inhibition, is a vacillating phenomenon. The processes of excitation and inhibition appear to us to be different phases in the activity of the cortical cells of the cerebrum. We are compelled to assert that these cells have a high degree of reactivity and, consequently, sensitiveness and destructibility.

This quick functional sensitiveness is the chief impulse to the origin in the cells of a special process of inhibition—an economical process, which not only limits a further extreme functional destruction, but also assists in the restoration of the depleted excitatory substances.

Thus do we explain the most constant and striking fact with which we have to deal in the work with conditioned reflexes. The fact itself is as follows: If the conditioned stimulus is applied even some ten seconds not supported by the unconditioned reflex, there inevitably sets in sooner or later, but in all cases, and in some dogs with astonishing rapidity, a state of inhibition in the cell; and beyond the cell the state spreads over the cortex and even into some of the lower-lying centres of the brain until complete sleep will ensue. That the prompt addition of the unconditioned stimulus near the beginning of the action of the conditioned stimulus prevents this occurrence is not a contradiction of our explanation of the facts. Our recent experiments show that during the action of the unconditioned stimulus the positive conditioned stimulus loses its effectiveness, becomes inhibited. The most wide-awake signal plays its responsible rôle,—and then when its part is finished and its work is no more needed, its rest is thoroughly secured and cautiously guarded.

The value of the excitatory substance of the cortical cells and the limited nature of it is clearly shown by the following experiments. A few years ago when we suffered a great food shortage our experimental animals, too, were, of course, in a starving condition. With such it was almost impossible to perform researches on conditioned reflexes. A positive conditioned stimulus, in spite of all our corrective measures, rapidly passed over into an inhibitory one. All the researches converged to one theme—the effect of the famine on conditioned reflexes. It is necessary to add that this tendency of the stimuli to go over into the state of inhibition has been manifested not only by the conditioned food reflexes but also in the same degree by the conditioned reflex to acid. This fact once more speaks for the great delicacy of the method of the conditioned reflexes in the physiological study of the cerebral hemispheres.

In the light of the facts just discussed one can readily understand the existence of different types of nervous systems which we have encountered in our dogs. Evidently it is the same with our own nervous systems. It is easy to find nervous systems which, from the day of birth, or in consequence of trying tasks during the individual's life, possess only a small store of excitatory substances in the cortical cells, and therefore easily pass over into the inhibitory state, in some one of its phases. They can, indeed, persist in one of these phases.

I have finished, and I should be very happy if any of my highly esteemed listeners would come to me for explanations or with objections. Such a vast and complex subject can hardly be discussed satisfactorily in so short a time.