I. P. PAVLOV

SELECTED WORKS

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IVAN PETROVICH PAVLOV
AND THE SIGNIFICANCE OF HIS WORKS

"Yes, I am glad that, together with Ivan Mikhailovich [Sechenov], a group of my dear colleagues and I have won for the mighty realm of physiological research the animal organism, complete and undivided, instead of a vague half. And this, indisputably, is our Russian contribution to world science and generally to human thought"

IVAN PAVLOV

A new era in one of the major branches of human knowledge—physiology—is linked with the name of the great physiologist Ivan Petrovich Pavlov.

The wise saying of the ancients "know thyself" has assumed in present-day physiology the form of strictly scientific generalizations of the physiological laws governing the activity of separate organs, systems, and of the organism as a whole in its unity with the environment. The part played by the Russian school of physiologists in advancing physiology, in assuring the tremendous benefit that it brings to vital branches of human practical activity, is truly exceptional.

The names of the great Russian physiologists I. M. Sechenov and I. P Pavlov stand out like beacons of tremendous power and faithful orientation, lighting up the pathways of scientific progress.

I. P. Pavlov reconstructed on new foundations such essential branches of physiology as digestion and blood circulation, the theory of the trophic influence of the nervous system, science is indebted to his genius for the founding of the theory of higher nervous activity.

Pavlov followed to the very end—completing a definite phase in the development of Russian science—the toilsome but glorious pathway of searching, blazed with such persistence by the splendid Russian physiologists that preceded him, the path taken by his ideological inspirer and teacher, I. M. Sechenov.

At the same time, stepping out along this pathway, Pavlov, by his investigations and by his passionately irreconcilable attitude towards idealism, carried forward the splendid traditions of the advanced Russian materialistic philosophy—the philosophy which inspired Russian naturalists and above all physiologists in disclosing the secrets of nature and in the bitter conflict with those who admitted the existence of some kind of non-material forces in nature beyond the scope of investigation.

The Soviet country is rightly proud of the Russian physiologists who have made a big contribution to the development of physiology as a whole, and of its related branches. No other country has produced so many ardent and uncompromising fighters against idealism in physiology, so many profound and penetrating theorists of this complex science, so many physiologists devoted to the interests of medicine, this noble branch of human practical activity.

The year in which Pavlov was born was the year in which the eminent founder of experimental physiology in Russia, A. M. Filomafitsky (1807-49), died. The work and writings of Filomafitsky, Professor at Moscow University, strikingly illustrate the high level reached by Russian physiology already in the forties of the 19th century. It was in Filomafitsky's laboratory that another remarkable surgeon, V. A. Basov, first performed a stomach fistula operation This operation was of immense significance for the further study of the physiology of digestion and formed the bedrock for the classical works of Pavlov in this field. At the end of the forties, and the beginning of the fifties, A. N. Orlovsky, a neglected Moscow physiologist and comparative anatomist—a contemporary of A. M. Filomafitsky—carried out experiments jointly with the famous surgeon F. Inozemtsev for the purpose of studying the influence exerted by the nervous system on the nutrition of organisms, i.e., to disclose the so-called trophic influence of the nervous system, to which Pavlov subsequently devoted a number of brilliant works. In his student days at Moscow University I. M. Sechenov was also drawn to the study of the influence exerted by the nervous system on the nutrition of tissues that was carried out by Inozemtsev and Orlovsky; among his early works there is an article on the influence of the nervous system on the nutrition of organs. S. P. Botkin was also a student in the Moscow University at that time; later on, Botkin introduced into clinical medicine the profound physiological theory of the trophic influence of the nervous system.

In his conclusions relating to the trophic influence of the nervous activity Pavlov originally proceeded from his classical works on the nervous regulation of the heart and the cardiac vessels, on the functions of the centrifugal cardiac nerves.

It should be pointed out that the work carried out by Russian physiologists along these lines had already made a big contribution to physiology. On the basis of a special article published by I. T. Glebov, an authoritative Russian physiologist of the fifties of the 19th century, it can be affirmed that the first proof of the existence of a nerve accelerating the work of the heart was adduced by A. N. Orlovsky way back in the early fifties of the last century. Shortly after this discovery by Orlovsky (who was unable to get his works published) two other Russian physiologists, the Cyon brothers, confirmed the existence of this nerve, and this time it won general recognition. One of the brothers, I. F. Cyon, was Pavlov's teacher in the field of experimental technique.

To F. V. Ovsyannikov, another of Pavlov's teachers, belongs the honour of discovering (1871) the so-called vaso-motor centre in the central nervous system. Ovsyannikov's laboratory investigated the trophic influence of the nervous system at the outset of Pavlov's experimental work. Finally, it should be mentioned that influence was also exerted on Pavlov by S. P. Botkin, one of the outstanding representatives of medicine of the 19th century, in whose clinic Pavlov worked. It was in this clinic that his basic idea of the leading role of the nervous system in all physiological processes (the idea of nervism) came into being and matured; and it was here that his views on the connection between physiology and medicine took shape.

Even these fragmentary data relating to the history of Russian physiology testify that the source of the main lines of Pavlov's experimental research can be traced to the works of the Russian physiologists of the period between the forties and seventies of the 19th century, that they are historically connected with them.

Pavlov's theory of conditioned reflexes was a landmark in the development of advanced philosophical thought and natural science in our country, where, as in no other country, the question had been resolutely raised of overcoming the dualism of matter and consciousness, of substantiating the material foundation of the psychical processes on the basis of the unity of matter and spirit, while the idealists affirmed the non-material nature and immortality of the spirit in contradistinction to the material nature and mortality of the body.

In the sixties of the last century D. I. Pisarev, an ardent popularizer of natural science and materialism, carrying forward the materialism and revolutionary democratism of A. I. Herzen, V. G. Belinsky, N. A. Dobrolyubov, and especially of N. G. Chernyshevsky, did much to publicize the highest achievements of the biological science of the time—Darwinism, physiology, etc. Pisarev summoned the young people to a crusade for science, especially natural science, he advanced the profoundly popular revolutionary-democratic task—to use science for the purpose of contributing in every way to the spiritual and social emancipation of the people.

Pisarev's ideas greatly influenced the development of Russian science. K. A. Timiryazev, A. N Bakh, N. A. Morozov and other outstanding naturalists emphasized its beneficial influence. Pavlov, too, was influenced by it.

In an autobiographical note Pavlov stated: "Influenced by the literature of the sixties, and particularly by Pisarev, our intellectual interests turned to natural science, and many, myself included, decided to take this subject at the University "*

The militant materialistic spirit in Pavlov's works, manifested in raising and solving the problems of higher nervous activity, can be properly appreciated only in its historical association with the traditions of the uncompromising struggle for materialism waged on this crucial sector of the ideological front by the Russian philosophers-materialists, and by their pupil I. M. Sechenov, Pavlov's predecessor and ideological inspirer.

The philosophical writings of Herzen, Pisarev and Chernyshevsky were of enormous significance in moulding the advanced, materialistic traditions of the Russian school of physiology in the fifties and sixties of the 19th century. The ideas of the great Russian physiologists I. M. Sechenov and I. P. Pavlov were also influenced by these works.

The fundamental similarity and the historical and logical link connecting the works of Sechenov and Pavlov consist in that the two men attributed a leading role in the shaping of the highly complex processes of psychical activity to environment, or, as Sechenov expressed it, to the conditions of existence. Pavlov's theory of conditioned reflexes showed that all the diverse manifestations of higher nervous activity are caused by constant interrelations between the organism and its environment, that they arise under certain conditions of the organism's existence. Sechenov's basic postulate that the organism cannot exist without it supporting external environment, is experimentally proved and, in a way, rounded off by Pavlov's theory of conditioned reflexes.

Also typical both of Sechenov and Pavlov is the application of objective physiological methods in studying complex psychical phenomena. Prior to Sechenov and Pavlov all the outstanding explorers of nature proved helpless when it came to the investigation of the so-called spiritual activity; unable to find the way to objective study of it they remained prisoners of philosophical dualism. Sechenov and

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* See present edition, p. 41.

Pavlov were the first to escape from this captivity, adducing convincing proof of the unity and interdependence of psychical and physical phenomena.

Pavlov's theory of the higher nervous activity rounded off the long searching by Russian philosophers and naturalists who had persevered in their efforts to overcome the constant counterpoising of spiritual and physical processes Their immense labours brought the Russian philosophers and naturalists to the *only true teaching of materialistic philosophy*—the dialectical unity of the physical and the spiritual; and the works of Sechenov and Pavlov furnished irrefutable proof of this teaching. This, so to speak, completed a definite stage in the development of science, the path of diligent searching which led from the philosophical concepts of Radishchev, Belinsky, Herzen and Chernyshevsky to the ideas of the Russian physiologists-materialists of the 19th and 20th centuries

The historical and logical sequence linking Sechenov's and Pavlov's works is marked by a significant date: two years before his death, in 1903—a memorable year for Russian physiology, Sechenov issued a revised edition of his famous book *Elements of Thought* This was the last word of the great reformer of the teaching on the nature of consciousness. That same year Pavlov read his first paper on conditioned reflexes at the International Medical Congress in Madrid.

Pavlov stated that Sechenov's *Reflexes of the Brain* exerted enormous influence on him in his youth (in his last years at the Ryazan Seminary), and gave an impulse to his work in the field of the physiology of higher nervous activity, which later developed into the theory of conditioned reflexes This extremely interesting fact illustrates the complexity of the problems encountered in scientific work, the history of the appearance of varied and important generalizations in science and their links with the generalizations of earlier scientists. The following remarkable excerpt taken from Pavlov's statement describes most convincingly the influence that a genuine teacher exerts on his pupils, testifying to the tremendous effect of a truly scientific book.

"When Tolochinov and I began our investigations the only thing I knew was that the extension of physiological research (in the form of comparative physiology) to the entire animal world would involve, in addition to abandoning our favourite laboratory objects (dogs, cats, rabbits and frogs), abandoning the subjective standpoint and essaying the application of objective methods of investigation and objective terminology (J. Loeb's doctrine of trophism in the animal world and the objective terminology suggested by Beer, Bethe and Uexküll). Indeed it would be difficult and unnatural to think and speak of any thoughts and desires of an amoeba or infusorian. But I believe that in our case, in the study of the dog, man's best friend since prehistoric times, the chief impetus to my decision (although I was not conscious of it at the time) came from the brilliant pamphlet by Ivan Mikhailovich Sechenov, the founder of Russian physiology. It was entitled *Reflexes of the Brain* (1863) and influenced me as a youth. And the influence of ideas which are strong by virtue of their originality and faithful reflection of reality—especially in one's youth—is profound, lasting, and, it should be added, often concealed This pamphlet was an attempt, brilliant and truly extraordinary for the time (of course only theoretically, in the form of a physiological outline) to picture our subjective world in a purely physiological aspect.

"At that time Ivan Mikhailovich made an important discovery (concerning central inhibition) which deeply impressed European physiologists and was the first Russian contribution to this essential branch of natural science which had just been greatly advanced by German and French scientists. The strain and the joy of this discovery, together, perhaps, with some other personal emotion, brought about this flowering of Sechenov's thought, which, without any exaggeration, can be described as the thought of genius"*

Thus, we see that Pavlov, the greatest physiologist-materialist of our times, developed and matured on the soil of Russian philosophical thought, and that pre-Pavlovian physiology in Russia paved the way for the tremendous contribution which the great physiologist made.

Pavlov is the outstanding representative of that brilliant galaxy of thinkers, who, in their endeavour to wrest from nature her innermost secrets, always proceeded from strictly scientific experience, from the verification of all scientific discoveries in practice. Physiological experimentation, close contact with clinical medicine, "observation and still more observation," real facts—these were the principles which guided Pavlov, the explorer of one of the most intricate domains of nature. All speculation about natural phenomena without trustworthy experimentation was alien to him.

He wrote: "The more complex the phenomenon (and what can be more complex than life?), the greater the need for experiment. Experiment alone crowns the efforts of medicine, experiment limited only by the natural range of the powers of the human mind. Observation discloses in the animal organism numerous phenomena existing side by side and interconnected now profoundly, now indirectly, or accidentally. Confronted with a multitude of different assumptions the mind must *guess* the real nature of this connection. Experiment,

* I P. Pavlov, *Complete Works*, Vol. III, Academy of Sciences of the U.S.S.R., Moscow-Leningrad, 1949, p. 18.

as it were, takes the phenomena in hand, sets in motion now one of them, now another, and thus, by means of artificial, simplified combinations, discovers the actual connection between the phenomena. To put it in another way, observation collects that which nature has to offer, whereas experiment takes from her that which it desires. And the power of biological experimentation is truly colossal. This experimentation has created in the course of some seventy or eighty years practically the entire modern, highly-developed physiology of the organs of the complex animal. The ordinary educated man, even if he is not yet familiar with biology, upon acquainting himself with the usual, but somewhat more thoroughly arranged course of demonstrative physiology of animals, designed for medical students, would undoubtedly be extremely surprised at discovering the power which the present-day physiologist wields over the complex animal organism. And his surprise would be all the greater upon discovering that this power is the result not of millenniums or centuries, but only of decades."*

The entire scientific activity of Pavlov, spread over a period of almost sixty years, is a brilliant example of experimental investigation of the laws governing the development of living organisms. In the same convincing way he demonstrated the significance of the experimental method for the study of the chemism of digestive processes, for the understanding of the mechanism of the digestive glands, for disclosing the trophic role of the nervous system and the basic laws of the nervous regulation of the work of the cardiovascular system, and finally, for elucidating the complex processes which underlie the phenomena of higher nervous activity in animals.

But Pavlov was not just a continuer of the existing traditions of a strictly scientific, experimental study of organic nature, his experimentation is distinguished for the new and original methods of investigation which he employed. The introduction of new methods of research that elevate the theory of science to a higher level is the typical feature of any classical research worker; and it is this feature that is manifested with particular force in Pavlov's work. Pavlov was a true revolutionary in science; he proclaimed and substantiated the objective, natural method of science in studying the functions of the brain and of the higher nervous activity.

In the third quarter of the last century when he began to investigate the processes of digestion in animals, he set himself the task of elucidating new methods for his investigation. He fully realized that only new methods could provide the key to new theoretical conclusions. "It is often said, and not without reason," he wrote,

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* See present edition, p 495.

"that science advances in leaps, depending on the development of experimental methods. With every advance in method, we rise, so to speak, a step higher, and a wider horizon with hitherto imperceptible objects unfolds before us Our first aim, therefore, was to develop a method"* (1897.)

And Pavlov's anticipations were realized Having found a correct solution to the problems relating to the new methodological approach, and having worked out, as we shall see later, methods of investigation most appropriate to the conditions of the intact organism, Pavlov and his colleagues made a number of major scientific discoveries.

In the eighteen years that passed between his first description of the method of the isolated "stomach-pouch operation" (1879) and the appearance of his summary work *Lectures on the Work of the Principal Digestive Glands* (1897), Pavlov and his school described a number of fundamental facts relating to the physiology of the digestive glands, thus bringing clarity into the "chaos" which prevailed in this sphere prior to the publication of Pavlov's works. As is known, these works formed the bedrock of the modern concepts of the nervous and chemical regulation of digestion; they gave a clear idea of the sequence of digestive processes in the different parts of the gastrointestinal system; they revealed certain peculiarities of the fermentative processes that take place in the intestinal tract; these works strikingly revealed the dependence of the nature of secretion of various glands on the kind of alimentary stimulus (Pavlov's classical salivation curves), they also laid the foundation for profoundly biological research into the adaptation of the glands of the digestive system to qualitatively different prolonged nutrition. The works of Pavlov and his school in the field of the physiology of digestion equipped practical medicine with a new and invaluable theoretical weapon.

The Soviet scientist, A. F. Samoilov, now deceased, one of Pavlov's closest disciples, vividly describes the circumstances in which Pavlov realized with complete success his plan for re-equipping physiological research in the sphere of the complex study of the digestive glands. In a tribute on the occasion of Pavlov's 75th birthday, he said:

"I was an eyewitness of the 'stomach-pouch' operation. I remember being fascinated by Ivan Petrovich's courage and belief in the correctness of the plan he had worked out for the operation. The first essays were unsuccessful. About thirty dogs had been sacrificed and much energy and time—almost half a year—had been spent to no purpose. The faint-hearted were already beginning to lose con-

* See present edition, p. 84.

fidence. I recall that some of the professors working in branches of science related to physiology asserted that the operation could not succeed on the grounds that the location of the blood vessels in the stomach made the operation impossible. Ivan Petrovich laughed, as only he could, at these assertions. A few more efforts and success was on the way."*

Consistency, perseverance and passion—these were the qualities which Pavlov bequeathed to the young Soviet scientists in his famous letter to the youth, and it was these qualities that brought him success.

The Pavlovian operative-surgical method of physiology, one of the major achievements of natural science at the end of the 19th century, had its origin in this searching for new methods of physiological investigation. In order to grasp the tremendous significance of this new trend, it suffices to point out that at the time Pavlov was perfecting his operative-surgical method, the so-called vivisectional method, which violated the integrity of the organism, prevailed.

Here is what Pavlov stated in this connection: "It seems to me that in modern physiology a firmer stand is to be taken by the surgical method (I counterpoise it to the purely vivisectional method), which implies performing (skilfully and creatively) more or less complex operations with the aim of either extirpating certain organs, or of ensuring access to physiological phenomena taking place in the depths of the body; of disrupting one or another connection linking the organs, or, on the contrary, establishing a new connection, and so on; it also implies ability subsequently to heal the animal and restore its state, in the measure that the nature of the operation allows, to normalcy.

"I regard the promotion of such surgical technique to be a matter of the greatest importance, because the usual method of simply vivisecting the animal in an acute experiment is, as is now becoming clearer day by day, a major source of errors, since the act of crude violation of the organism is accompanied by a mass of inhibitory influences on the functions of the different organs. The organism as a whole, the realization of the most delicate and most expedient linking of an enormous number of separate parts, cannot, in the nature of things, remain passive to destructive agents; it must, in its own interests, strengthen one part and weaken another, i.e., temporarily leaving aside, so to speak, all other aims, and concentrating on saving whatever can be saved. While this circumstance has been and still is a big obstacle in the way of analytical physiology, it appears to be an insurmountable obstacle to the development of synthetic

* A F Samoilov, *Selected Articles and Speeches*, Academy of Sciences of the U S S.R, Moscow-Leningrad, 1946, p 98

physiology where it is necessary to determine exactly the true course of one or another physiological phenomenon in an intact and normal organism."* (1897.)

It should be stressed that the results achieved by Pavlov in elaborating methods for investigating the digestive glands—methods now used in all physiological establishments—are important because they confirm the great significance of integrated study of the animal organism. This extremely important biological trend in studying the physiological processes in animals that had fully recovered from operations and behaved in a normal manner, a trend that took shape in the course of studying the physiology of the digestive glands, became more pronounced and assumed dominance during Pavlov's work on conditioned reflexes. In a paper which he read before the Ledentsov Society in Moscow in 1910, Pavlov stressed the necessity of creating better laboratory conditions for his experimental work—conditions that would permit the study of physiological processes in the organism of the animal without damaging its integrity and its normal relations with the surroundings. In this paper he stated:

"There are in addition a number of external influences which have in a greater or lesser degree a destructive effect on the organism. If the fixation of the animal on the stand is connected with very strong pressure on any part of the body, or if the thermal and mechanical apparatus attached to the skin for the purpose of its stimulation (a slight burn or excoriation) damages its integrity, if the introduction of an irritant into the mouth causes an injury of the mucous membrane, even to a minor degree, in all these and similar cases our conditioned reflex will suffer, in a greater or lesser measure, and finally disappear entirely."**

Of particular significance is the fact that the operative-surgical method worked out by Pavlov was regarded by him, in his own terminology, as a method of "physiological thinking." Precisely because of this he was able, at the end of the 19th and at the beginning of the 20th century—the period when analytical physiology reached full bloom—to become one of the few adherents of the integrated study of physiological processes. And it was not fortuitous that he linked the development of the methods of integrated study of physiological processes with the development of synthetical physiology. The subjective experience of Pavlov as a scientist at that time is vividly described by A. F. Samoilov in his reminiscences:

"On one occasion, shortly after I joined the laboratory, I was reading an article in the library of the institute. Ivan Petrovich came in and began to scan the latest magazines. I noticed that something

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* See present edition, pp. 99-100.

** I P Pavlov, *Complete Works*, Vol. III, pp 110-11.

had upset him. He read and re-read the headings of articles and then he exploded· 'We won't get very far if we waste our time on questions such as these!' He threw the magazine on to the table and leaving the room added: 'The very sight of it makes me sick!'

"Greatly puzzled, I immediately picked up the magazine that Ivan Petrovich had thrown away and began to leaf through it. It contained articles devoted to the investigation of separate cells, muscles and nerves; then articles discussed the nature of excitation and conductivity. To me at that time it seemed extremely interesting and valuable. I confess that even now, thirty years later, I am of the same opinion. The general physiology of tissue excitation is fully confirmed and is not in need of any special advocacy. But I think I know why Ivan Petrovich was so scathing and hostile towards the above-mentioned trend in physiological research.

"In his view all investigations devoted to separate parts of the body were divorced from the animal mechanism as a whole, from the entire organism; he considered them too abstract and too distracting; in his view, they were not of an urgent character. His talent took him in an altogether different direction, and, fortunately for science, he had the skill and the audacity to brush aside those trends in physiology which were out of his way. This approach enabled him to devote himself more fully to the lines that attracted him most. The sphere in which he was in his element was the animal as a whole and its interrelation with the environment influencing it; and this preoccupation reveals the pronounced biological inclination of Pavlov's talent. Above all he preferred experimentation with intact, non-narcotized animals, which react normally to stimulation and are gay and cheerful "*

Thus we see that Pavlov's work was a striking example of experimental investigation of vital phenomena. He blazed new paths in this direction and equipped physiologists with the method of integrated study of physiological processes. But Pavlov's significance as an experimenter is not confined to this; a distinguishing feature is that he closely connected theoretical analysis of the problems with practice, the problems of physiology with those of medicine The hours spent with his pupils observing the work of the digestive glands and disclosing the truly majestic picture of the law-governed development of this process, gave Pavlov the naturalist the greatest satisfaction. He wrote· "Indeed, the course of secretion under similar conditions has now become truly stereotyped. The deep impression produced by such, almost physical, precision in a complex vital process, is a pleasant entertainment enjoyed during many hours of

* A. F. Samoilov, *Selected Articles and Speeches*, pp. 94-95.

observation of the working glands"* In 1899, in a speech dedicated to the memory of S P Botkin, Pavlov again pointed to the "strikingly majestic picture" which opens up before the research worker observing the normal course of the digestive process. Pavlov said·

"But should we, as experimenters, be satisfied with this? I think not. When we see deviations from the normal and delve deeply into their mechanism, is it not natural to want to restore them to normal? This and this alone is the only final criterion of the completeness of our physiological knowledge and of our mastery of the subject"** And as if concentrating his thought on the necessity of establishing the closest contact between theory and practice, of verifying any physiological theory by its practical application in medicine, Pavlov went on to say: "The mechanic completes his apprenticeship by passing a test which consists in assembling the mixed-up parts of the dismantled machine. This should hold for the physiologist too. Only he who is able to restore the disordered course of life to normal can say that he has acquired real knowledge of life."***

This manifest clarity of purpose, characteristic of Pavlov the experimenter, helped him scientifically to ground experimental therapy and lay the foundations for the Pavlovian tradition in physiology—to study so as to be able to control the process. According to Pavlov, experimental therapy is "in essence the verification of physiology."

Here we come to an essential feature of the teaching of Pavlov, who developed physiology in close connection with practice. Convinced of the great significance of experimentation for the study of the processes developing in a normal organism, Pavlov became a true champion of the experimental method in medicine. "Only by passing through the fire of experiment will medicine as a whole become what it should be, namely, a conscious and, hence, always purposefully acting science.... Therefore, I make so bold as to predict that the progress of medicine in this or any other country, in this or any other scientific or educational medical establishment, depends on the attention and care which the experimental branch of medicine enjoys there."**** Consequently, it is not accidental that Pavlov's laboratory became an educational centre for the more advanced representatives of medical science who came there to prepare their dissertations. The hundreds of dissertations written in Pavlov's laboratory became valuable contributions to physiology and to experimental pathology and therapy. Pavlov's school produced

* I. P. Pavlov, *Complete Works*, Vol. II, p 37.
** *Ibid.*, p. 354.
*** *Ibid*
**** *Ibid.*, pp. 360, 364.

many leading scientists not only in theoretical physiology, but also in the clinical field. His dream of creating an experimental base for medicine which would satisfy the "craving of men for health and life" (*Pavlov*) has been realized now, in the Soviet period, thanks to the founding of the Institute of Experimental Medicine of the U.S.S.R. Later, there developed out of this Institute, in which Pavlov worked right up until his death, the present U.S.S.R. Academy of Medical Sciences.

Pavlov regarded the correlation between physiological theory and clinical practice as an organic connection of two supplementary aspects: not only physiological experimentation and the conclusions drawn therefrom help to understand the pathological process and the ways of influencing it, but the pathological process, in its turn, is essential for understanding the physiological processes. It was but natural that physiological experimentation brought Pavlov to experimental therapy. Summing up his experimental work in the sphere of studying the digestive glands, Pavlov plainly stated: "This, naturally, brings us to experimental therapy. Discard the practical aim of experimental therapy and there remains a new and fruitful method of studying life, because you approach it from a new aspect, and in any case you will be always filling the gaps in the theory of modern physiology."* These conclusions were the result of Pavlov's profound biological comprehension of the normal course and pathology of physiological processes. The pathological process and the normal process are, in Pavlov's view, not dissociated phenomena, they are phenomena of one and the same order.

Throughout Pavlov's scientific activity, observations not only on normal animals, but also on sick human beings and animals, served as an inexhaustible source for his strictly scientific conclusions in physiology. The enormous significance of his observation of diseased organisms in forming the theory of conditioned reflexes, and particularly in achieving comprehension of psychopathological states, is well known. At first Pavlov carried out his observations on casual patients, and then, systematically, in hospital conditions; and he did this with the same consistency and perseverance which characterized his work in the physiological laboratory. Clinical cases stimulated and directed his work of elaborating methods of investigation of physiological processes in the normal organism—methods now regarded as being classical.

For Pavlov a diseased organism was first of all an organism with new relations established between its organs and systems as a result of the illness; and from this point of view he appraised the significance of pathological cases for physiological observations. The

* *Ibid.*, p. 354.

organic essence of his entire work was based on the premise clearly expressed in the following proposition: "The domain of pathological phenomena is an infinite series of all kinds of specific—i.e., such as do not occur in the normal course of life—combinations of physiological phenomena. This, undoubtedly, is something like a series of physiological experiments carried out by nature and life, frequently it is a combination of phenomena of a kind that would not have entered the minds of modern physiologists for a long time to come and which sometimes could not even be reproduced deliberately by the technical means of modern physiology. Hence, clinical cases will always be a rich source of new and unexpected physiological facts. It is, therefore, natural for the physiologist to desire a closer union between physiology and medicine."

Pavlov's views on the essence of the profound biological law of development—adaptation—took shape in the course of his work in the sphere of the physiology of blood circulation and digestion.

Already in his early works devoted to the nervous regulation of blood circulation, Pavlov advanced for the first time the idea of the reflex adaptation of cardiovascular activity. His work on this subject was published in 1877 under the significant title: "Experimental Data Relating to the Accommodative (adaptive—*Kh. K.*) Mechanism of the Blood Vessels." In our time the vast scientific and practical problem of the reflex regulation of blood circulation under diverse conditions of the vital activity of organisms and of their organs has been elaborated in great detail; the sources of this elaboration can be traced in the works of the Russian physiologists I. F. Cyon, N. O. Kovalevsky, A. S. Dogel, and especially in Pavlov's works.

With the utmost thoroughness Pavlov developed the idea of the adaptive character of physiological phenomena; in doing so he took as his starting-point the numerous observations on the law-governed responses of the glandular cells of the digestive tract to certain natural stimuli acting on the digestive glands (bread, meat, milk), the so-called alimentary stimuli; he also based himself on his research on the adaptation of the fermentative composition of the digestive juices to one or another kind of prolonged diet. Pavlov first approached these problems when he analysed the rich experimental data obtained by his co-worker Yablonsky who proved that the protein ferment units in the pancreatic juice sharply increase under protracted meat feeding—a diet rich in protein—and then gradually diminish when the animal is switched to milk and bread—a diet poor in protein. In this connection Pavlov wrote:

"A more or less stable state of the gland, constantly intensified by prolonging the given diet, could be changed repeatedly in one and the same dog, in one or another direction by means of changing the diet. This circumstance completely precluded the suspicion that in our experiments there took place a certain spontaneous and irrevocable change of the gland as a result of performing an operation or of some other pathological cause."*

But this was not the only thing that interested Pavlov, in appraising the experimental data obtained by his colleagues, he, as a biologist, came to broader conclusions of a general biological character. He stated: "If the diet acts so sharply and powerfully on the chemical nature of the gland, then probably, in the usual natural conditions or under the influence of prolonged (lifetime) domestic routine (as, for example, is often the case with various breeds of dogs), firm and definite types of the pancreatic gland were to be developed Our experimental data, as we see it, really furnish us with certain indications to this effect. In absolutely identical conditions of feeding, the pancreatic juice of different dogs in our laboratory often differs in respect to content of ferments"**

We meet with these fundamental ideas of a general biological character, expressed by Pavlov on the basis of the above-mentioned research, in the subsequent long years of his work in the sphere of the physiology of the higher nervous activity. Pavlov chiefly devoted his attention to analysis of the processes which reveal a strict correlation between definite conditions of the environment and definite forms of the organism's reflex activity; at the same time he posed the question of the possibility of developing new, so-called conditioned reflexes in the individual lives of animals, underlying the historical formation of complex phenomena of the animal's adaptation to the surrounding world. Here we come to the definition of the profound theoretical essence of his teaching on conditioned reflexes.

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The history of the theory of conditioned reflexes testifies to the highly intricate and interesting path travelled by Pavlov and his school in the course of shaping this great achievement of natural science of the 20th century.

In a preface to the 5th edition (1932) of his book *Twenty Years of Objective Study of the Higher Nervous Activity (Behaviour) of Animals* Pavlov stated: "The present book is the living history of this vast branch of human knowledge, and, I make bold to say, deals with one of the urgent subjects in the elaboration of which this branch is engaged. Here, as in the history of all things, many mistakes have been made, inaccurate observations, wrongly arranged experiments and ill-founded conclusions; but there have also been

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* I P. Pavlov, *Complete Works*, Vol II, p. 54
** *Ibid*

many edifying instances when much of this was avoided or corrected, and, all in all, there has been a steady accumulation of scientific truth."

Indeed, when we read the *Twenty Years of Objective Study*. . article after article and paper after paper, we can clearly picture the conditions of Pavlov's work, the enthusiasm and loyalty of his colleagues, the brilliant manifestations of his thought, his painstaking work on the contradictions which emerged during the elaboration of this complex problem, and the errors and doubts engendered in the process of this work.

The beginning of this great scientific feat was the paper read by Pavlov at the International Medical Congress in Madrid in April 1903 The paper was entitled "Experimental Psychology and Psychopathology in Animals." Typical of the man are the simple and clear opening words of his paper: "Regarding the language of facts as most eloquent, I shall take the liberty of proceeding directly to the experimental material, which gives me the right to speak on the subject of my present communication." The audience assembled at the congress probably anticipated that a paper with the afore-mentioned title would abound in psychological and psychopathological terminology, as well as in logical propositions, that it would describe cases of pathological activity of the nervous systems of animals under experimental conditions. But Pavlov's paper dealt with altogether different questions, namely, with the results of observations on the work of the salivary glands in the different conditions of physiological experiments. Of course, this paper both in regard to its formulation of the problem and its factual material substantiating highly complex psychological problems, struck the congress as something completely new, and it can be said without any exaggeration that it was like a bolt from the blue.

We shall first dwell on the well-known fact that Pavlov's work in the sphere of the physiology of the higher nervous activity was closely connected with his brilliant cycle of works on the physiology of the digestive glands. A distinguishing feature of the research conducted by Pavlov and his school in the sphere of physiology of digestion was that they investigated with the utmost thoroughness the highly complex problems of the nervous, reflex regulation of the digestive glands. But in the course of this extensive experimental work they came up against the fact that the forms of the nervous regulation of digestive-gland secretion are often conditioned not only by purely physiological factors, but also by factors known as "psychical." The attention of Pavlov and his school was attracted by the fact that reflex influences on the salivary glands exist not only when the alimentary stimuli are in direct contact with the various sensory zones of the animal's digestive tract, but also when the alimentary stimuli are at some distance from the animal and act upon the nervous system not by their primary but secondary properties (by means of signals, according to Pavlov) and, in addition, through the system of sensory (or receiving, according to Pavlov) elements outside the digestive apparatus (eye, ear, skin, etc.). It is interesting to recall that by the term "distant reflexes" or "signalling reflexes" Pavlov originally described the type of reaction which he later termed "conditioned reflexes."

The connection between Pavlov's work in the sphere of the physiology of digestion and his work in the sphere of conditioned reflexes is of a very broad character: they are united not only by their common ideas but also by their common methodological principles. The perfection which Pavlov attained in preparing animals for physiological experiments after well-performed operations, and which enabled him to preserve the integrity of the animal's nervous connections and its normal connections with the environment, was of great significance in disclosing the actual relations in the digestive processes and made possible a new approach to the study of the reflex relations of the organism. It goes without saying that so long as this basic fact was ignored in studying the work of the different glands of the digestive tract, including the salivary and gastric glands, it was difficult to discern and, what is still more important, to analyse the specific form of the reflexes—the distant reflexes emerging only under definite conditions of the animal's interrelations with the environment.

Pavlov approached this problem after a profound study of the specific forms of secretory activity of the digestive glands which he himself called "psychical secretion." This term was used by him also in his *Lectures on the Work of the Principal Digestive Glands*, published in 1897. In this book Pavlov details the most diverse cases of psychical secretion; however, he did not at that time pose the question of the possibility of analysing this form of secretion, too, as a specific manifestation of reflex activity.

In the second half of the nineties of the last century Pavlov started in earnest his experimental analysis of the essence of "psychical secretion." Although his observations revealed this kind of secretion both in the gastric and salivary glands, he concentrated his attention on the latter. By that time his closest colleague, D. L. Glinsky, had elaborated the splendid method of a constant salivary gland fistula—a method which made it possible to perform successive experiments on the dog's salivary glands over a period of months and even years.*

* D. L. Glinsky, *Experiments on the Work of the Salivary Glands* (I. P. Pavlov's paper on them). Proceedings of the Russian Medical Society in St. Petersburg, 1895, 61st year.

The very first experiments, carried out by Doctor S G. Wolfson in accordance with Pavlov's instructions, showed that the mere sight of food was sufficient to obtain a secretion of saliva. The most striking thing in these experiments was that the quality and quantity of saliva varied depending on what the animals were shown, whether edible or inedible substances. In other words, the salivary secretion caused by the sight of food reproduced, although on a somewhat smaller scale, the salivary secretion which takes place when the mouth is directly irritated by respective substances. Such results were obtained when natural food substances (meat, milk, dry bread, meat-powder) were placed in the mouth or shown to the animal.

Similar experiments were carried out by another of Pavlov's colleagues, Doctor A. T. Snarsky, who obtained very interesting facts. For instance, the repeated introduction into the dog's mouth of acid, which was coloured black, invariably produced profuse salivation. Afterwards, when Snarsky introduced water into the mouth, also coloured black, it produced the same abundant secretion of saliva. A similar effect was obtained when the animal was shown a bottle containing black liquid. The conclusion was quite unexpected for that time: "The black water began to stimulate the glands from a distance only when coloured (black) acid had been preliminarily introduced into the dog's mouth."

Another experiment consisted in the following: when the dog with constant salivary gland fistulae smelled for the first time in its life the odour of anise oil or of any other odorous substance, it did not react with a salivary secretion. But when, simultaneously with the effect of the odour, the oil was brought into contact with the oral cavity, causing a strong local irritation, the odour alone began subsequently to produce a secretion of saliva.

Snarsky erroneously interpreted the results of these experiments as a manifestation of the animals' specific psychical activity, and he suggested taking into consideration the thoughts, desires and emotions of the animals undergoing the experiment. Discussing with Pavlov the results of his experiments he emphasized the great significance of the dog's inner life and declared that the animal's behaviour was a manifestation of its psychical reaction, that the salivary gland merely reflected a certain inner state of the animal which was hardly accessible to physiological investigation

These experiments date from the very beginning of the 20th century—Snarsky's dissertation was published in 1901. By then Pavlov had become firmly convinced that it was necessary to replace the concept of psychical secretion with very definite physiological concepts. Hence his heated argument with Snarsky. The latter stubbornly insisted on his subjective anthropomorphic interpretation of phenomena and finally had to leave Pavlov's laboratory.

The more than thirty years' work of Pavlov and his school clearly showed that, apart from inborn reflexes, which rest on the anatomical connection of the central nervous system and of its conductors with the peripheral organs (muscles, glands), there are additional reflexes; the latter may arise in the individual life of the animal as a result of the coincidence of the action of various, to a certain moment indifferent, stimuli coming from the environment, with stimuli that are unconditioned agents of one or another reaction (secretory, motor, etc.). This is the principal theoretical premise for the elaboration of the methods underlying Pavlov's theory of conditioned reflexes, according to which such indifferent agents of alimentary reaction, as light, sound, pricking, etc., become conditioned stimuli of the digestive glands if they coincide in time with the action of the unconditioned alimentary stimulus of the food itself.

From the general biological point of view the experiments carried out by Pavlov's pupil Tsitovich are of special interest. The results obtained by him were published in his dissertation entitled "The Origin and Development of Natural Conditioned Reflexes" and supplied, for the first time, the clearest experimental corroboration of Pavlov's views on the existence of two types of reflexes—inborn, or unconditioned, and individually acquired, or conditioned. Tsitovich proved that pups with constant salivary gland fistulae, kept on a milk diet for a long period, acquired complex forms of conditioned reflex connections with everything that had a bearing on milk. But the appearance, colour and sounds connected with other foods and the conditions of their feeding, in particular such strong alimentary stimuli as meat and bread, did not evoke conditioned salivary secretion in the animals until they were given a meal of meat or bread. After their first meal of these substances the odour of meat or bread sufficed to evoke a profuse conditioned secretion of saliva.

Pavlov's discovery of conditioned reflexes, his description of new types of the animal's nervous connections with the conditions of life (conditioned reflex connections), represents a great step forward in the development of the theory of reflexes in physiology. Whereas throughout the more than two and a half centuries since Descartes introduced into physiology the concept of reflexes, the reflex had been regarded as the reaction of the animal's organs or of its entire organism to certain stimuli, the Russian physiologists Sechenov and Pavlov, on the basis of anatomically fixed nervous paths, raised and experimentally solved a problem of exceptional significance—the reflex connections of animal organisms bearing an adaptive character and emerging and vanishing during the individual development of the organisms in complete unison with the conditions of existence. Pavlov proved that the reflexes discovered by him are, according to the mechanism of their formation, of a coupling nature, being the result of the coupling of connections between two foci of excitation in the brain, and that they are also temporary, because they vanish under definite conditions.

That the problem could be formulated in this way is due to the Russian school of physiology the founder of which, I. M. Sechenov, as early as 1861, advanced the thesis that "the organism cannot exist without the external environment which supports it, hence, the scientific definition of the organism must also include the environment by which it is influenced."*

Proceeding from this thesis and from the Darwinist interpretation of the laws of development of life, Sechenov asserted that there are in the first place inborn reflexes (effected on the basis of anatomical reflex paths which exist at the moment of birth) and acquired reflexes, elaborated in the course of the individual life experience, and that, in the second place, all the more complex forms of nervous activity are, by the nature of their origin, reflexes.

Sechenov waged a bitter struggle against those physiologists who, unable to comprehend the unity of the organism and the environment, as well as the evolution of the nervous activity, were inclined to endow even the spinal cord with a soul, since they were unable to explain the origin, development and action of the spinal cord reflexes co-ordinated for the given conditions of existence.

That which I. M. Sechenov theoretically substantiated and which he began to elaborate experimentally, was completed by I. P. Pavlov in his theory of conditioned reflexes and in his works on the reflex nature of the cerebral activity.

The reflex theory is, above all, a biological theory. According to Pavlov, the development of a conditioned reflex is first of all a biological process which creates the prerequisite for proper metabolism and exchange of energy between the organism and the external environment. Abundant experimental data revealed to Pavlov the tremendous role played by the nervous system in the basic biological process—in the process of metabolism. Pavlov and his school demonstrated much more convincingly and with greater completeness than anybody before them, that the nervous system plays a leading part in the processes of reception and digestion of food, in its procurement, as well as in the delicate processes of the chemical transformation of the nutritious substances in the organism. The brilliant discovery made by Pavlov is that this continuous process of metabolism and exchange of energy between the organism and the external environment is effected not only by means of a complex of

* I. M. Sechenov, *Vegetatives Processes in Animal Life*, "Medical Herald," No. 26, 1861.

inborn nervous-reflex acts: in the course of the animal's individual development, in each concrete case and situation, there arise new, acquired nervous connections conditioned by the environment (temporary connections, conditioned reflexes) which, in the given conditions, make the interrelations of the animal and the external environment most optimal. In his paper "Natural Science and the Brain" Pavlov defined with the utmost clarity the biological significance of the conditioned reflexes discovered by him. He wrote: "The most essential connection between the animal organism and the surrounding world is that brought about by certain chemical substances which constantly enter into the composition of the given organism, i.e., the food connection. In the lower forms of the animal world it is the direct contact between food and the animal organism or vice versa, which chiefly leads to alimentary metabolism. In the higher forms these relations become more numerous and remote. Now odours, sounds and pictures attract the animals to food substances already in wide regions of the surrounding world.... Along with this variety and remoteness, there takes place a substitution of the temporary for the constant connection between the external agents and the organism; first, because, essentially, the remote connections are of a temporary and changeable nature, and, secondly, because, due to their variety and number, they cannot be covered as constant connections, even by the most capacious apparatus. The given food object may be now in one place, now in another, it may, consequently, be accompanied at one time by certain phenomena, at another time by quite different ones; it may be part of one or another system of the external world, and therefore now these now other natural phenomena must temporarily serve as stimulating agents producing in the organism a positive motor (in the broad sense of this word) reaction to this object."*

Pavlov regarded the conditioned, or temporary, acquired reflexes as an organ of the animal organism especially adapted constantly to effect a more and more perfect equilibration of the organism with the environment—an organ for the appropriate and immediate reaction to most diverse combinations and fluctuations of phenomena in the surrounding world, and to a degree, a special organ for the continuous development of the animal organism. Pavlov said: "The basic functions of the higher part of the central nervous system are the coupling of new and temporary connections between the external phenomena and the work of the different organs, and the decomposing by the organism of the complex of the external environment into its separate elements, that is, functions of coupling and analysing mechanisms.

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* See present edition, pp 208-09

"By means of these activities there are established finer and more delicate adjustments of the animal organism to the environment, or, in other words, a more complete equilibration of the system of matter and energy which constitute the animal organism, with the matter and energy of the environment"*

The method of conditioned reflexes opened fundamentally new ways for studying the function of the brain, namely, the cerebral cortex and its different functional parts. Pavlov radically revised the views then prevailing on the physiology of the cerebral cortex and based this important branch of physiology on new principles. The old static concepts of the localization of functions in definite, strictly confined sections of the brain were superseded by Pavlov's absolutely original concept of the functions of the cerebral cortex. Of particular significance in this concept is the theory of the so-called analysers. By analysers of the cerebral cortex Pavlov implied the "head end" of the receiving, sensory nerve elements. Pavlov's theory of analysers threw new light on the aims and methods of the physiology of the sense organs as the physiology of the central and peripheral receiving mechanisms, as the physiology of analysers.

The peculiarities of the processes of excitation and inhibition in the cerebral cortex were disclosed and elucidated on an absolutely new basis; Pavlov and his school experimentally proved the applicability to the cortex of the remarkable proposition advanced by N. E. Wedensky, one of I. M. Sechenov's disciples, concerning excitation and inhibition as stages of one and the same process.

Pavlov founded the biological theory of sleep and the remarkable theory of protective inhibition as a physiological method of mobilizing the defensive reactions by means of regulating the processes of excitation and inhibition in the cerebral cortex. In Pavlov's lifetime highly valuable data were obtained on the methods of therapeutic regulation of the processes of excitation and inhibition in the cerebral cortex (by means of bromide and caffeine).

The last fifteen years of Pavlov's life (i.e., from the early twenties) were the best and most fruitful years of his school. By that time the number of his followers had grown considerably; they were able to establish their own, independent laboratories; considerable funds were also allocated by the Soviet Government to the existing Pavlov laboratories for the purpose of extending them and supplying them with better equipment; in addition, the famous Koltushi Biological Station was built specially for Pavlov's research.

The turning-point in all this was the famous decree signed by Lenin in 1921 and providing for all the facilities Pavlov needed for his work. Lenin placed Maxim Gorky at the head of a special com-

* See present edition, p 220.

mission appointed to carry out a number of measures designed to secure normal conditions for Pavlov in the hard times of the early twenties. The opening lines of the decree noted the enormous historical significance of Pavlov's work for the working people of the world.

Considerable sums were allocated by the Soviet Government for the Koltushi Biological Station; this resulted in the opening of one of the finest biological institutions in the world, where every opportunity was provided for the work of Pavlov and his school. They devoted special attention to problems connected with the evolution of the higher nervous activity. Here, over a period of ten years, they conducted their well-known investigation of the higher nervous activity of anthropoids.*

In 1922 Pavlov's immortal work *Twenty Years of Objective Study of the Higher Nervous Activity (Behaviour) of Animals* was published. This was a symposium of articles, papers, lectures and speeches devoted to this important branch of natural science—a branch elaborated by Pavlov and his numerous followers. The book was soon translated into a number of foreign languages.

In the spring of 1924 Pavlov delivered a series of lectures at the Army Medical Academy before a large audience of physicians and naturalists. These lectures summed up the work carried out by Pavlov and his school over a period of almost twenty-five years in the sphere of the physiology of the cerebral hemispheres. Before sending them to the printer Pavlov spent more than one and a half years editing his lectures. In 1927 his fundamental book *Lectures on the Work of the Cerebral Hemispheres* appeared in Leningrad; together with *Twenty Years of Objective Study...* this book can be regarded as a major contribution to the development of the natural science of the 20th century.

During the Soviet period new trends have appeared in Pavlov's teaching on conditioned reflexes. A number of his followers have elaborated a new branch of the theory of the higher nervous activity—the comparative physiology of conditioned reflexes; they have disclosed the common and differing features in the formation of conditioned reflexes, and the functions of definite sections of the brain in different animals under the peculiar conditions of their existence (oecological peculiarities).

According to Pavlov's designs, the major problems of the development of conditioned reflexes, in the light of the problems relating to the evolution of functions of the nervous system, were to be elaborated at the biological station founded by him in Koltushi.

* Prior to this work and parallel with it the problems of conditioned reflex activity of apes were thoroughly studied in the Sukhumi Subtropical branch of the All-Union Institute of Experimental Medicine.

There has been opened a new vast field of conditioned reflex connections, which are established on the basis of reflex connections between the internal organs and the cerebral cortex (the work of K M. Bykov and his colleagues). The extensive application by Soviet physiologists of modern delicate electro-physiological methods in investigating the cerebral cortex must be regarded as a considerable achievement of the objective study of the laws governing the formation of temporary connections

The theory of conditioned reflexes has been theoretically advanced by Pavlov's followers; it has found wide practical application in analysing the various disturbances of the nervous activity and in elaborating ways and means of restoring it to normal.

The development of the theory of higher nervous activity in the Soviet period is seen in the big contribution made by Pavlov himself, for instance, his broad biological generalizations of the role of conditioned reflexes, his elucidation of the specific properties of the human conditioned-reflex activity, his new principles in the experimental therapy of nervous disturbances, and his vigorous struggle against idealism.

In appraising the significance of conditioned reflexes Pavlov, as a naturalist, invariably took up major problems of general biological significance. For example, when classifying the reflexes, he stated that the inborn reflexes are the reflexes of species, whereas the acquired reflexes are those of the individual. "From the purely practical point of view, we call the first reflex unconditioned and the second—conditioned. It is highly probable (and there are indications to this effect) that newly formed reflexes, given the same conditions of life in the course of successive generations, invariably become constant reflexes. Consequently, this must be one of the acting mechanisms in the evolution of the animal organism."*

In his last, summary article "The Conditioned Reflex" written for the Big Medical Encyclopaedia in 1935, Pavlov touched on the general biological significance of conditioned reflexes; he pointed out that conditioned reflexes provide all that is required for the well-being of the organism, as well as the species.

In the speech which he delivered at the International Physiological Congress in 1913, Pavlov resolutely stated: "It can be accepted that at a later stage some of the newly formed conditioned reflexes are transformed into unconditioned reflexes by heredity."**

In the early twenties N. P. Studentsov initiated a special investigation in Pavlov's laboratory with the aim of verifying the correct-

* See present edition, pp. 220-21
** I P Pavlov, *Complete Works*, Vol. III, p. 217.

ness of this idea. In 1924 the American geneticist Morgan came out against these experiments and their interpretation.

However, Pavlov did not relinquish his elaboration of the problem in this biological direction, on the contrary, he continued it, adhering to his fundamental principle that the conditioned reflex is one of the "acting mechanisms in the evolution of the animal organism," the transforming of individually acquired conditioned reflexes into unconditioned, hereditary ones.

Here begins a new stage in Pavlov's activity—study of the genetics of the higher nervous activity. This new field of research, the bedrock of the work of the Koltushi Biological Station, was designed to give final shape to Pavlov's complex concepts of the biological significance of conditioned reflexes as the basis for the development of inborn (unconditioned) reflexes.

Pavlov and his school elaborated with the utmost thoroughness the typology of the behaviour of different dogs and utilized these observations as a biological base for experiments with different animals and for eventual conclusions in each particular case. In the above-mentioned summary article "The Conditioned Reflex," he pointed out that "the study of conditioned reflexes in numerous dogs gradually led to the idea of different nervous systems in different animals, until, finally, sufficient data were obtained to systematize the nervous systems according to some of their basic properties."

"Thus," wrote Pavlov, "type is a congenital, constitutional form of the nervous activity of the animal—the genotype. But since the animal is exposed from the very day of its birth to the most varied influences of the environment, to which it must inevitably respond by definite actions which often become more and more fixed and, finally, established for life, the ultimate nervous activity of the animal (phenotype, character) is an alloy of the characteristics of type and the changes produced by the external environment."*

These Pavlovian ideas laid the foundation for a grand plan for the further investigation of the animal's higher nervous activity by the methods of genetics and physiology and opened up new prospects for this sphere of research. Death prevented Pavlov from accomplishing this task as fully as he had elaborated a number of other branches of physiology—digestion, blood circulation, conditioned reflexes and the trophic role of the nervous system.

Pavlov's theoretical generalizations disclosing the nature of the higher nervous activity culminated in his concept of the first and second signalling systems, of which the latter was regarded by him as inherent only in the human brain.

He said: "When the developing animal world reached the stage

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* See present edition, pp. 260-61.

of man, an extremely important addition was made to the mechanisms of the nervous activity. In the animal, reality is signalized almost exclusively by stimulations and by the traces they leave in the cerebral hemispheres, which come directly to the special cells of the visual, auditory or other receptors of the organism. This is what we, too, possess as impressions, sensations and notions of the world around us, both the natural and the social—with the exception of the words heard or seen. This is the first system of signals of reality common to man and animals. But speech constitutes a second signalling system of reality which is peculiarly ours, being the signal of the first signals. On the one hand, numerous speech stimulations have removed us from reality, and we must always remember this in order not to distort our attitude to reality. On the other hand, it is precisely speech which has made us human, a subject on which I need not dwell in detail here. However, it cannot be doubted that the fundamental laws governing the activity of the first signalling system must also govern that of the second, because it, too, is activity of the same nervous tissue."*

These exceptionally important ideas were brilliantly expressed by Pavlov in the article "The Conditioned Reflex," written for the Big Medical Encyclopaedia. Before sending the article to the Encyclopaedia Pavlov read it at one of his regular "Wednesdays." According to one of his closest colleagues, those present at the gathering were struck by the depth and originality of the problems raised by Pavlov. Most striking, of course, were his ideas concerning the second signalling system; they opened before his followers new avenues of research in the sphere of the physiology of the higher nervous activity, the way indicated to future generations of physiologists by their great teacher. Pavlov's ideas concerning the second signalling system were historically related to the remarkable psychophysiological views of I. M. Sechenov who advanced the profound problem of object thinking. Sechenov stressed at the same time that abstract thought arises in the course of human interrelations with surrounding objects, and although their verbal expression is sometimes far removed from the original object reality, it is, nevertheless, profoundly connected with it.

The problem raised by Pavlov of the second signalling system and the highly important question of the interrelation between the first and second signalling systems are of exceptional significance for the physiology of the higher nervous activity, as well as for psychology, linguistics, pedagogics and clinical medicine.

Disclosing the actual laws governing the activity of the brain and the evolution of the higher nervous activity, Pavlov formulated a

* See present edition, p. 262.

number of dialectical propositions. This dialectical interpretation of processes was the result of his entire experimental work.

Pavlov's theory of the higher nervous activity is of enormous significance also for philosophy.

S. I. Vavilov, the late President of the U.S.S.R. Academy of Sciences, said: "At all the stages of his scientific work Pavlov unswervingly adhered to the strictly materialistic path and his astonishing results are recognized as a permanent and basic part of the natural-scientific foundations of dialectical materialism."

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V. I. Lenin highly appraised Pavlov's work. The decree signed by V. I. Lenin in January 1921, designed to ensure favourable conditions for Pavlov's work, stressed the enormous significance of his activity for the working people of the world.

That high appraisal testified first of all to the great importance which the Soviet State and the Communist Party attach to advanced science, and in particular, to the branch in which, thanks to Pavlov's genius, it proved possible for the first time in the history of science to apply the precise method of investigation of natural science to the highly complex phenomena of the so-called psychical activity in man and animals. The facts obtained by Pavlov and the generalizations made by him in the sphere of conditioned reflexes which he had discovered, appeared at the beginning of the 20th century as a new and powerful corroboration of the materialistic view of the unity of mental and physical manifestations, of the physiological foundation of the complex manifestations of behaviour and consciousness. This explains why the teaching was so ardently supported and developed in the young Soviet State which set itself the aim of battling for a new, progressive social system; and this explains why it encountered the animosity of a number of scientists and idealist philosophers.

Among the critics of Pavlov's teaching was Charles Sherrington, leading British physiologist. In London, in a conversation with Pavlov, he said: "You know, your conditioned reflexes would hardly be popular in Britain because of their materialistic flavour."

In connection with Sherrington's attitude towards Pavlov's conditioned reflexes a certain interest attaches to the "historical research" of his pupil, the American physiologist John Fulton, who seeks to persuade physiologists all over the world that priority in founding the theory of conditioned reflexes belonged to none other than ... Charles Sherrington! In one of his books on problems of the physiology of the nervous system, Fulton even adduces excerpts and drawings taken from an early work by Sherrington, in an attempt to "substantiate" the priority of the latter in the discovery of conditioned reflexes In one of my other works I show in detail that the facts refute Fulton's viewpoint.*

It would be interesting to know what Sherrington himself would have thought of this gift from the pupil who depicts his teacher as the "founder" of a materialist teaching! At the same time, however, Fulton tries to prove that the theory of conditioned reflexes is merely of historical interest.

It is clear that the above-mentioned statement by Charles Sherrington stems from a definite source—from non-recognition of Pavlov's teaching which "has a materialistic flavour." It is equally clear that Pavlov's teaching is highly appraised by the Soviet Government and the Soviet people precisely because it contributes to the liberation of mankind from the age-old prejudice concerning the dissociation and counterpoising of matter and spirit, of the mental and the physical, a prejudice from which the leading British physiologist could not free himself.

In the second quarter of the 20th century Charles Sherrington again proclaimed that thought, emotions, etc., are not subordinated to matter and to the concept of energy, that they are beyond it, and, consequently, beyond the confines of natural sciences. He also stated that matter and energy are granular, and probably, life too, according to its structure, but not consciousness. The latter, he said, is conceived as a specific phenomenon, which undoubtedly cannot be related to physical energy, etc.

The attack launched by Sherrington on Pavlov's materialist theory of conditioned reflexes, his fundamental idealistic concept of the dissociation of matter and spirit, of the physical and the mental, and his slogan of the unknowableness of psychics—all met with a crushing rebuff from Pavlov. Brought up on the traditions of Russian materialist philosophy and in the spirit of irreconcilability to idealism, and being a true follower of the great thinker I. M. Sechenov, Pavlov, criticizing Sherrington's book *The Brain and Its Mechanism*, at one of his "Wednesdays" in September 1934, said:

"It appears that up to now he is not at all sure whether the brain bears any relation to our mind. A neurologist who has spent his whole life studying the subject is still not sure whether the brain has anything to do with the mind. . . .

"How can it be that at the present time a physiologist should doubt the relation between nervous activity and the mind? This is the result of a purely dualistic concept. . . . Sherrington is a dualist who resolutely divides his being in two halves: the sinful body and the eternal, immortal soul."**

* Kh. S. Koshtoyants, *Essays on the History of Physiology in Russia*, Moscow-Leningrad, 1946, Academy of Sciences of the U.S.S.R., pp. 300-01.
** See present edition, pp. 569-70.

The same spirit of militant irreconcilability is revealed in Pavlov's struggle against those who tried to prevent science from accomplishing its great aim of getting to know the laws governing the activity of the brain on the basis of natural science He entered into heated polemics on this subject with scientists in many countries. Highly appraising Pierre Janet as a neuropathologist, Pavlov at the same time criticized him for his erroneous psychological views: "Of course he is an animist, i e., he believes in a specific substance which is not subject to any laws and which is unknowable."* For over twenty years Pavlov polemized with Claparède, the Swiss psychoneurologist Denouncing the decorative verbiage of Claparède's psychological reasoning in the sphere of associations and conditioned reflexes, Pavlov called it "sheer twaddle" and added: "Undoubtedly, this is a special breed of people, a special sphere in which there is no place for genuine thought, where it is always buried in the devil knows what."**

For years Pavlov carried on a heated discussion with the American Lashley. He sharply criticized the so-called Gestalt-psychologists—Woodworth and others.

About Koehler, professor of Berlin University, then investigating the behaviour of animals (apes, in particular), he said the following.

"...Koehler is a confirmed animist, he simply cannot become reconciled to the fact that this soul can be grasped by hand, brought to the laboratory, and that the laws of its functioning can be ascertained on dogs He does not want to admit this"*** Ridiculing the vague descriptions given by Dunker, one of Koehler's pupils, Pavlov called his judgement on the principles of education "thought convulsions"

Thus Pavlov waged a systematic and fierce struggle against those who endeavoured to deflect the solving of a fundamental scientific problem—the essence of consciousness—from the exact path of natural science and to direct it on to the idealistic path (as Pavlov put it, the path of "dualism" and "animism").

Deeply conscious of the tremendous power of the theory of conditioned reflexes as an effective weapon for this decisive sector of the ideological front, the great Soviet physiologist, only three months before his death, addressed his colleagues with the following words (at the "Wednesday" gathering on November 6, 1935):

"We must understand that the conditioned reflexes occupy an exceptional place in the world of physiology because there is a dislike for them on the part of many who have a dualistic world outlook. This is quite obvious. The conditioned reflexes force their

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* *Ibid*, p. 617.
** *Ibid.*, p. 623.
*** *Ibid*, p. 565.

way to the forefront They wage a continuous fight against this dualism which, of course, does not surrender"*

At the Fifteenth International Physiological Congress Pavlov was recognized as the "princeps physiologorum mundi." But among the world physiologists he was also the first tribune, the ardent fighter against idealism. Pavlov never lost confidence in the victory of materialism over idealism. In 1932, in Rome, where reaction and clericalism had long been entrenched, the great Russian materialist-physiologist declared from the rostrum of the International Congress:

"I am convinced that an important stage in the development of human thought is approaching, a stage when the physiological and the psychological, the objective and the subjective, will really merge, when the painful contradiction between our mind and our body and their contraposition will either *actually* be solved or disappear in a natural way."**

Pavlov passionately combated idealism, which maintained that the immortal soul and the mortal soma (body) are disunited and fundamentally opposed. Carrying on the traditions of his teacher I. M. Sechenov—the first to proclaim the unity of the organism and conditions of existence—Pavlov founded the theory of conditioned reflex connections, which in his view were indispensable for the maintenance of individual life and for the development of the species. In the course of more than fifty years' work in the sphere of physiology, which enriched this important branch of knowledge with a multitude of new facts and theoretical conclusions, Pavlov took as his starting-point the principle of active intervention in physiological processes. According to him, the aim of the scientist is to "control" physiological phenomena; the physiologist must always bear in mind the interests of practical medicine and experimentally elaborate means for restoring to normal the vital processes deranged by illness.

Pavlov ardently loved his native land, its history, culture, art and science. He was a true patriot of the great Soviet country.

It is these features of scientist and patriot, of the fighter against idealism and obscurantism, innovator and persevering worker, whose life's work was directly linked with urgent practical tasks, and, what is most important, who blazed new trails and opened absolutely new paths in science—it is these qualities that endear Ivan Petrovich Pavlov to Soviet scientists and to the Soviet people as a whole.

Kh. S. Koshtoyants

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* See present edition, p. 625.

** *Ibid.*, p. 286.

IVAN PETROVICH PAVLOV

AUTOBIOGRAPHY

I was born in the town of Ryazan in the year 1849 into the family of a priest. I received my secondary education at the local theological seminary, which I recall with gratitude. We had a number of excellent teachers. One of them was the priest Feofilakt Antonovich Orlov, a man of lofty ideals. In general, in the seminary at that time (I do not know how it was afterwards) one could follow one's own intellectual inclinations, which was not the case, regrettably so, in the notorious Tolstoy gymnasiums* (and, I think, also in the present ones). One could lag in a given subject and get on in another, but this did not threaten one with trouble, including expulsion; in point of fact it focused attention on one, and gave rise to speculation about the talents and abilities of the student in question.

Influenced by the literature of the sixties, and particularly by Pisarev, our intellectual interests turned to natural science, and many, myself included, decided to take this subject at the University.

In 1870 I entered the Petersburg University and studied in the natural history section of the physics and mathematics faculty. The faculty was in its heyday at the time.

* Named after D. Tolstoy, tsarist Minister of Public Education, who converted the gymnasiums into scholastic schools with barrack-like discipline.—*Ed.*

We had a number of professors with great names in science, men who were outstanding as lecturers. I chose animal physiology for my major course and took chemistry as a minor. We physiologists were tremendously impressed by Cyon. We were fascinated by his ingeniously simple exposition of the most complex physiological questions and his skill in conducting experiments. One can never forget such a teacher. I did my first physiological work under his tuition.

In 1875, after obtaining the degree of Candidate of Natural Sciences, I enrolled in the third-year course of the Medico-Chirurgical Academy. I did so not for the purpose of becoming a physician, but with the idea that after getting the degree of doctor of medicine, I would qualify for a chair in physiology. I must say, however, that at the time this plan seemed a vain dream because a professorship appeared as something unattainable, incredible.

When I entered the Academy I was to become assistant to Prof. Cyon (he read lectures on physiology at this Academy too) in place of S. I. Chernov, who had to go abroad. But an incredible thing happened: the brilliant physiologist was expelled from the Academy. After some time I obtained a position as assistant to Professor K. N. Ustimovich, lecturer on physiology at the Veterinary Institute. When Professor Ustimovich left the Institute—in 1878 I think—I entered the laboratory attached to Professor S. P. Botkin's clinic, where I worked for many years after taking a course at the Institute for the Perfection of Physicians, and after my subsequent two years' sojourn abroad; I remained there up to the time I obtained a chair. Despite certain unfavourable circumstances in this laboratory, the chief of which were, of course, its scanty means, I consider that the time I spent there was most beneficial for my future in science. First of all I had complete independence and the opportunity to devote myself entirely to laboratory work (I had no duties in the clinic itself). I worked without distinguishing what came within the range of my duties and what within the range of others. For months and years I participated with my entire laboratory work in the researches of my colleagues.

But I constantly profited by this work: I had an ever growing practice in physiological reasoning, in the broad sense of this word, as well as in laboratory technique. Besides, there were the always interesting and instructive (though, unfortunately, very rare) conversations with Sergei Petrovich Botkin. I prepared my thesis on the cardiac nerves in this clinic, and it was there, upon returning from abroad, that I began my research into digestion, which later won me considerable fame abroad. Both these researches were conceived by me quite independently.

My journey abroad was of great importance, above all, because it enabled me to make the acquaintance of such scientists as Heidenhain and Ludwig—men who devoted their whole life, with all its pleasures and sorrows, exclusively to science.

Until 1890, when I obtained a chair, I, now married and the father of a son, had always been hard up. However, thanks to the help of friends, as well as to my passion for physiology, I cannot say that this situation caused me any undue worry.

Finally, at the age of forty-one I was given a chair, my own laboratory, and filled two posts simultaneously; I was nominated professor of pharmacology (afterwards physiology) at the Military Medical Academy, and Head of the Physiological Department at the Institute of Experimental Medicine. Thus I suddenly found myself with ample financial means and every possibility for carrying out in my own laboratory any research work I liked. Before this the constant necessity to pay for every experimental animal, at a time when there was a scarcity of financial means, told heavily on laboratory work.

Since then life has gone quite smoothly, marked with ordinary laboratory and family events. The only thing which grieved me very much for a full decade was the strained atmosphere in the Military Medical Academy caused by its late chief.

In conclusion I must say that looking back on my life I would describe it as being happy and successful. I have received all that can be demanded of life: the complete realization of the principles with which I began life. I dreamed of finding happiness in intellectual work, in science—and I found it. I wanted to have a kind person as a companion in life and I found this companion in my wife Sara Vasilievna, née Karchevskaya, who patiently endured all the hardships of our existence before my professorship, always encouraged my scientific aspirations and who devoted herself to our family just as I devoted myself to the laboratory. I have renounced practicality in life with its cunning and not always irreproachable ways, and I see no reason for regretting this; on the contrary, precisely in this I find now certain consolation.

Above all I am forever grateful to my father and mother; they taught me to live a simple, unassuming life and made it possible for me to get a higher education.

I

PUBLIC AND SCIENTIFIC SPEECHES AND ADDRESSES

[MESSAGE FROM THE CHAIRMAN OF THE ORGANIZING COMMITTEE OF THE FIRST SECHENOV PHYSIOLOGICAL CONGRESS, READ AT THE OPENING OF THE CONGRESS ON APRIL 6, 1917[1]]

Dear Comrades,

I deeply regret that I am unable to be with you. We are living in really extraordinary times.

Hitherto dispersed and separated, we are coming together now and forming a society that will have common interests and a common aim—to maintain Russian physiology at the highest possible level. And our prime concern at the moment is our journal. One can say that in the permanent international exhibition of physiology we shall, at last, have our own pavilion! Each of us must do his best to make it as rich and as interesting as possible; it will give foreigners a better idea of our activity, better than they had when we were dispersed; it will enable them to appraise us. The circumstances favour the appearance of our journal. Our new intercourse in the form of regular papers from all parts of our motherland, exchange of views, demonstration of experiments and apparatus, and even, so to speak, entire physiological establishments—our laboratories—as well as the mutual encouragement and mutal assistance they entail—all this cannot but intensify our usual work. The present extraordinary situation in Russia is bound to add in a big way to our own particular upsurge.

We have just parted with the sombre epoch of oppression. It suffices to remind you that this congress was not permitted to be held over Christmas, permission was granted for it to be held at Easter only after the members of the Organizing Committee had signed a statement saying that no political resolutions would be presented at the congress. But that was not all. Two or three days before our Revolution, final permission was obtained on the condition that the theses of the papers be submitted beforehand to the city head.

But thank God, this is already a thing of the past and, let us hope, the irrevocable past.

A grievous sin was committed by the Great French Revolution when it executed Lavoisier and when his appeal for a postponement that would enable him to complete important chemical experiments was answered by the statement that "the republic needs neither scientists nor their experiments."[2] But in this respect, too, the past century has seen a real revolution in the human mind; now we need not have any fears about a democracy disregarding the eternally majestic role of science in human life.

We cannot but anticipate, and with the new system of our life we must anticipate an exceptional growth of the means for all kinds of scientific activity.

And this being so, it should be an added incentive for us to step up our effort to the utmost.

How timely, then, in our free motherland, now being renovated and endeavouring to create the best possible conditions in all spheres of life, are the society and its journal, so happily linked with the glorious name of Ivan Mikhailovich Sechenov, the founder of Russian physiology and the embodiment of a genuinely free spirit!

Hearty greetings, comrades, and best wishes for a good beginning to our undertaking!

LETTER TO THE ACADEMY OF SCIENCES OF THE U.S.S.R.[3]

TO THE PRESIDIUM OF THE ACADEMY OF SCIENCES OF THE U.S.S.R.

I am most grateful to my own dear Academy for the greetings and good wishes. Whatever I do, I always think that I am thereby, as much as my strength allows me, serving first of all my country and our Russian science. And for me this is both a powerful incentive and a source of deep satisfaction.

Academician *Ivan Pavlov*

Leningrad, October 2, 1934

[LETTER TO THE SECHENOV PHYSIOLOGICAL SOCIETY, LENINGRAD[4]]

I express my sincere gratitude to the Sechenov Physiological Society for the celebration at a special session of my sixty years in science.

Yes, I am glad that, together with Ivan Mikhailovich, a group of my dear colleagues and I have won for the mighty realm of physiological research the animal organism, complete and undivided, instead of a vague half. And this, indisputably, is our Russian contribution to world science and generally to human thought.

Ivan Pavlov

Leningrad, October 14, 1934

[LETTER TO THE ACADEMY OF SCIENCES OF THE U.S.S.R.[5]]

TO THE ACADEMY OF SCIENCES

I am sincerely grateful for the warm comradely greetings. My dream is that our joint work in the laboratory shall leave its mark in the attainment of human happiness, and leave in the science that I love a memento worthy of the Russian mind!

Ivan Pavlov

Leningrad, December 23, [1934]

[A LETTER TO THE YOUTH[6]]

What would I wish for the young people of my motherland who dedicated themselves to science?

First of all—consistency. Of this very important condition for fruitful scientific work I cannot speak without emotion. Consistency, consistency and again consistency. Right from the very beginning inculcate in yourself the habit of strict consistency in acquiring knowledge.

Learn the ABC of science before you attempt to scale its peaks. Never embark on what comes after without having mastered what goes before. Never try to cover up the gaps in your knowledge, even by the boldest guesses and hypotheses. No matter how this bubble may delight the eye by its profusion of colours, it is bound to burst, and you will be left with nothing but confusion.

Develop in yourself restraint and patience. Never funk the hard jobs in science. Study, compare, accumulate facts.

No matter how perfect a bird's wing may be it could never make the bird air-borne without the support of the air. Facts are the air of the scientist. Without them you will never be able to take off; without them your "theories" will be barren.

But when studying, experimenting and observing, do your best to get beneath the skin of the facts. Do not become hoarders of the facts. Try to penetrate into the secrets of their origin. Search persistently for the laws governing them.

The second thing is modesty. Never think that you know everything. No matter in what high esteem you are held always have the courage to say to yourself: "I am ignorant."

Do not let pride take possession of you. It will result in you being obstinate when you should be conciliatory. It will lead you to reject useful advice and friendly help. It will deprive you of the ability to be objective.

In the team of which I am leader, everything depends on the atmosphere. All of us are harnessed to a common cause and each pulls his weight. With us it is often impossible to discern what is "mine" and what is "yours," but our common cause only gains thereby.

The third thing is—passion. Remember, science requires your whole life. And even if you had two lives to give they would not be enough. Science demands of man the utmost effort and supreme passion. Be passionate in your work and in your quests.

Our country is opening wide vistas before scientists, and—it must be owned—science in our country is being fostered with a generous hand.

What is there to say about the status of our young scientist? Here, it would seem, everything is quite clear. Much is given to him, much is expected from him. For him, as for us, it is a matter of honour to justify the great trust that our country puts in science.

I. P. Pavlov

[SPEECH AT THE OPENING OF THE FIFTEENTH INTERNATIONAL PHYSIOLOGICAL CONGRESS[7]]

I hereby declare the Fifteenth International Physiological Congress open. *(Applause and cheers. All rise.)*

On behalf of the entire Russian physiology I welcome the esteemed colleagues who have come from all parts of the world and hope that the time spent here will prove pleasant and useful to them.

For the first time an international congress of physiologists—the fifteenth—is being held in our country. This is in the order of things. Ours is a young physiology. Russia has only its second generation of physiologists, admittedly a hoary one that is living out its days. Sechenov must be regarded as the father of our physiology; he was the first to read lectures that were not lifted from the books of others, but as a specialist, illustrating them by demonstrations, and it was he who founded the first school of physiology in our country. All this, of course, was the result of his exceptional abilities. That is why we have considered it appropriate to present the members of this congress with his best works and with a medal bearing his image. Sechenov initiated physiological work on a considerable part of the earth's surface.

The manifold benefits of international congresses are so obvious and have been mentioned so often, that I shall merely draw attention to a few points of special significance at the moment.

It is high time that we, physiologists, as has been said here so many times, and as already practised at other congresses, reached a final decision on the so-called programme problems, i.e., on those problems which are the subject of particularly keen interest at the moment; at the same time, however, the papers on particular subjects should be read, too, although the number might be cut. General meetings should be arranged, and in addition to the disputants, those scientists working on the given problem invited beforehand. With such pre-arranged and stimulating conditions for discussion even off-hand remarks by colleagues not working on the given problem may assume no small importance.

The second point I would like to stress is one that is of particular significance for us, namely, the special influence of gatherings such as ours on the young generation of scientists, on the beginners. I know the effect of this influence from my own experience, from my early years in connection with the congresses of Russian naturalists and physicians of those times. Our government allocates extraordinarily large sums for scientific work, it is attracting masses of young people to science, and the spectacle of world scientific research represented here is bound to have a tremendous stimulating effect on this youth.

And finally, a third point. Although we are profoundly different, we are now united and stirred by keen interest in our common vital cause. We are good comrades and in many cases we are even linked together in manifest friendly feeling. We are working, obviously, for the rational and final unification of mankind. But should war break out many of us would become hostile to each other, and precisely on the grounds of our science, as has been the case more than once. In such circumstances we would have no desire to meet as we do now. Even our mutual scientific appraisal would radically change. I can appreciate the grandeur of a liberation war. At the same time, however, one cannot deny that war is essentially a bestial method of settling life's difficulties (*loud applause*), a method unworthy of the human mind with its immeasurable resources. We observe now an almost world-wide desire and striving to avert war by means which are, perhaps, more reliable than hitherto. And I am glad that the government of my great country, in its fight for peace, has proclaimed for the first time in history: "Not one inch of foreign soil." (*Loud applause.*) And we, of course, must particularly sympathize with this struggle for peace and promote it. And as seekers of truth, we must add that it is necessary to be strictly just in international relations. (*Applause.*) But it is at this point we encounter the chief difficulty.

This year our truly world-wide association has lost two of its loyal members: Professor Shafer of Edinburgh University, who dedicated the whole of his long life to science, and Professor Macleod of the Aberdeen University, Nobel Prize winner, who died in his prime. Let us rise in honour of our late colleagues. (*All rise. The band plays Chopin's funeral march*)

In conclusion, we, Russian physiologists, wish to express gratitude to our government which has enabled us to receive our esteemed guests in a worthy manner. (*Applause.*)

The chairman of the committee appointed by the government to further the work of the congress has the floor. (*Applause.*)

[SPEECH AT THE RECEPTION HELD BY THE GOVERNMENT FOR THE DELEGATES TO THE FIFTEENTH INTERNATIONAL PHYSIOLOGICAL CONGRESS ON AUGUST 17, 1935, IN THE GRAND KREMLIN PALACE]

You have heard of, and you have seen (says Ivan Petrovich addressing the foreign guests), the exceptionally favourable status enjoyed by science in my country. I would like to illustrate the relations that have been established in our country between the state and science by the following fact: we, the heads of scientific establishments, are really worried and alarmed because we are not sure whether we shall be able to justify all the allocations that the government has placed at our disposal. As you know, I am an experimenter from top to toe. My whole life has been filled with experiments. Our government, too, is an experimenter but in an immeasurably higher category. I passionately want to live and to see the successful completion of this historic social experiment. (Pavlov's toast "the great social experimenters," is warmly applauded.)

[REPLY TO GREETINGS DURING A VISIT TO RYAZAN IN AUGUST 1935[8]]

I want to tell you that scientists were honoured in the past as well. But this expression of esteem took place inside a small circle, that is to say, among the same kind of people—scientists. That which I behold now has nothing in common with the restricted ceremonies of the past. At present science in our country is honoured by the whole people. I had evidence of this in the morning when I was met at the station, then in the collective farm and again on my way here. There is nothing fortuitous in this. I think I shall not be mistaken when I say that this is an achievement of the government of my country.

Formerly science was cut off from life, alienated from the people. Now I am seeing something altogether different—I see science honoured and prized by all the people. I raise my glass to the only government in the world that prizes science so highly and supports it so generously—to the government of my country.

[ON THE PROSPECTS OF WORK IN 1935[9]]

I am resting just now in my beloved Koltushi, and oh how I want to live for a long, long time. . . . At least until the age of a hundred . . . and even longer!. . .

I want to live for a long time because my laboratories are now in their heyday. The Soviet Government has allocated millions for my scientific work and for laboratory extension. I want to believe that the measures taken to encourage physiologists—and after all I remain a physiologist—will achieve their purpose, that my science will flourish on my native soil. . . .

Whatever I do, I always think that in doing it I am, as much as my strength allows me, serving first of all my country. Social reconstruction on a grand scale is now under way in my country. The enormous gulf between rich and poor has been eliminated. I want to live and see the final results of this social reconstruction. . . .

An enormous achievement of Soviet rule is the steady strengthening of the defence capacity of the country. One of the reasons why I want to live as long as possible is that I have no fears for the security of my native land.

[A MESSAGE TO THE GATHERING OF LEADING MINERS IN THE DONETS BASIN]

Dear Miners,

All my life I have loved and still love work, mental and physical, and the latter perhaps even more than the former. And I experienced the greatest satisfaction every time I succeeded in transplanting a good idea into my physical work, that is, when I was able to combine brain and hand.

You have taken the same path. My heartfelt wish is that you continue along this path, the only one that can ensure happiness for man.

With sincere greetings,

Academician *I Pavlov*

January 7, 1936, Koltushi

II

WORKS ON BLOOD CIRCULATION AND THE TROPHIC ACTION OF THE NERVOUS SYSTEM

[AN ABSTRACT OF A PAPER BY V. N. VELIKY AND I. P. PAVLOV[10]]

V. N. Veliky and I. P. Pavlov have given an exposition of their joint works: a) *The Influence of the Laryngeal Nerves on Blood Circulation*, b) *The Centripetal Accelerators of the Heart-Beat.*

On the basis of experiments they have reached conclusions that are the opposite of those drawn by Schiff; they cannot, therefore, admit that there are in the laryngeal nerves of the dog fibres accelerating the heart-beat and emanating from the n. accessorius Willissi,[11] and have confirmed the experiments of Bezold and Cyon, which showed that the accelerating nerves come from the spinal cord through the ganglion stellatum.[12] This viewpoint is confirmed not only by their first work, but also by the second, which is not yet completed; it follows from the latter that there are centripetal accelerating nerves, which can be traced as follows: one of the nerve bundles proceeding from the heart enters the lower cervical ganglion in the angle formed by the n. laryngeus inferior and the n. vagus;[13] thence it turns into the ganglion stellatum and then, judging by one observation, it goes to the brain. The irritation of the central end of this nerve causes acceleration of the heart-beat. Consequently, it can be assumed that this is a sensory nerve and that its action on the heart is of a reflex character.

EXPERIMENTAL DATA CONCERNING THE ACCOMMODATING MECHANISM OF THE BLOOD VESSELS[14]

(PHYSIOLOGICAL LABORATORY OF PROFESSOR A. O. USTIMOVICH IN ST. PETERSBURG)

In a whole number of articles received in recent years from Professor Ludwig's* laboratory in Leipzig many of the outstanding properties of blood circulation have been touched upon and experimentally elucidated.[15] Thanks to these highly valuable experiments it has become known that 1) adaptability to larger or smaller amounts of blood is inherent in the vascular tube, the average blood pressure not showing any prolonged fluctuation over a considerable period; 2) this adaptability is of a nervous origin.

Nevertheless, it must be admitted that this opens up a new field for further investigation. No matter how significant the above-mentioned research may be, the elucidation of the mechanisms governing the adaptability of the blood vessels, as well as of their immediate properties, still remains a matter for future research.

These considerations have prompted us to carry out a number of investigations of the role of certain nerves in the accommodation of the blood vessels. But with the pub-

* Collected Papers of the Leipzig Physiological Institute, 1873, 1874, 1875. (Papers by Tappeiner, Worm-Müller and Lesser.)

lication in the meantime of the results of various investigations relating to the action of the vaso-dilatory nervous system, part of our own work provided for in our original plan of investigation, had to be dropped; still, this field of research proved extensive enough for our investigations as well.

Below we shall dwell only on one of a series of experiments the results of which will be published later. But we believe that this particular case, due to its promising significance, speaks for itself.

When numberless facts convinced us that the curve of the blood pressure in a curarized animal[16] cannot be always compared with the normal curve, and that in all cases without exception the given curve in an intoxicated animal undergoes certain fluctuations evoked by known and unknown causes, we deemed it necessary to carry out our first investigations on non-intoxicated, intact dogs. The dog selected for the purpose was tamed to such a degree that when the operation was being performed and the blood pressure taken, it lay perfectly still, tied to the operation board. Because of this we obtained curves of blood pressure which, in respect of evenness, can be regarded as model.

The manometer was as a rule connected with the artery which lies almost at the surface of the inside of the knee joint. Only two or three minutes are needed to bring the artery out and the operation is absolutely painless. The pressure in the art. cruralis was taken only once. The animal was well fed and given drink twenty-four hours before the experiment; twelve hours before the operation it was given drink once more.

After the blood pressure had been taken under these conditions, we began to feed the animal with dry bread or dried meat; the blood pressure was taken at different intervals after the feeding. It was established that the maximum decline of blood pressure (including that in the art. cruralis) reached only 10 mm. Hg.

Sometimes comparative measurements of the blood pressure within twenty-four hours after the feeding, recorded no changes whatever. It should be further pointed out that the pressure remained unchanged for 20-30 minutes after feeding and only then began to decline. These results once again confirmed the data obtained by Tappeiner, Worm-Müller and Lesser, according to which, in a normal state of the organism, too, there is, apparently, a tendency towards retention of average pressure. As is known, the above-mentioned states produce conditions that should have considerably contributed to a decline of blood pressure, namely, an appreciable dilation of the visceral arteries and secretion of large quantities of digestive juices from the blood flow; meanwhile the decline was a mere 10 mm. and sometimes the pressure even remained unchanged. Hence, the question arises: what kind of mechanisms maintain this equilibrium? Proceeding from the above-mentioned observations by Ludwig's pupils on the accommodation of the vascular tube, we considered it necessary first of all to find an answer to this question: is it really the case that the constriction of the blood vessels alone is responsible for this equilibrium of the blood pressure? Everything could have been accounted for simply by stating that simultaneously with dilation of the visceral vessels, there would be constriction of the vessels of other parts of the body, for example, of the skin, muscles, etc. It is possible that in these conditions there is a two-way reflex action of food, stimulating both the vaso-dilatory visceral nerves and the vaso-constrictory nerves of other regions. As is known, stimulation of the sensory cutaneous nerve evokes dilation of the cutaneous vessels and at the same time constriction of the visceral vessels. We had also to take into account the assumption that the reverse could have taken place, namely, that to stimulation of the sensory visceral nerves of the abdomen the abdominal vessels could have reacted with dilation, and the cutaneous vessels, on the contrary, with constriction.

We considered it important first of all experimentally to elucidate whether constriction of the cutaneous vessels is really caused by stimulation of the sensory visceral nerves.

We chose the ear of a rabbit as the most suitable object for our observations. Dissection of the internal organs served as a stimulus; we gave preference to this method over the application of electric and other stimuli because, above all, we wanted to reproduce as much as possible the conditions brought on by mechanical stimulation by food. In this respect electric stimuli seemed to us least suitable.

Our expectations were soon justified by the experiment. Each time the stretching of the intestinal loops out of the abdominal cavity of a curarized rabbit under artificial respiration caused constriction of the ear vessels, and this persisted for some time even after the peritoneum had been closed. Now it was necessary to preclude any suspicion of a passive reflux of blood from the ear vessels to the abdominal cavity, since it could be said that, given active hyperaemia of the abdominal vessels as a consequence of active dilation, the rabbit's ear revealed passive anaemia. Two kinds of experiments were carried out in order to refute this objection. In one case the cervical sympathicus was sectioned on one side and the effect of the dissection of the intestines on both ears, that is, on the intact and paralyzed vessels, was compared. In the other case, together with this comparative observation on the vascular lumen of both ears, the blood pressure in the art. carotis was measured.

Both series of experiments definitely proved that the constriction of vessels in the rabbit's ear under the dissection of the abdominal cavity is caused by a reflex transmission of the stimulation, since in the ear, on the side where the sympathicus was sectioned, no change whatever was observed in the lumen of the vessels, whereas in the ear vessel of the intact side, in all cases without exception, the dissection of the intestines led not only to the disappearance of the lumen, but also to the complete disappearance of the vessel branch. Measurement of the blood pressure revealed the phenomenon already observed by Ludwig and Cyon, namely, no decline whatever; on the contrary, increased blood pressure followed dissection of the peritoneum—a state which lasted from fifteen to sixty-six seconds after the abdominal cavity had been closed.

By way of illustration we give below a description of two typical cases taken from a series of experiments.

I. A curarized *rabbit*. The right art. carotis is connected with a mercurial manometer. The vessels of the left ear are under observation. (Chiefly it is the changes in the lumen of the medium branch of the artery that are taken into consideration.)

Time	The lumen of the vessel	Blood pressure
	The peritoneum is opened	
1 h 07 m.	Of average width	
1 h. 08 m.	Narrower	
1 h. 09 m.	Still narrower	
1 h 10 m. 1 h. 11 m.	Wider	
1 h 12 m.	Narrower	
1 h. 13 m 1 h. 14 m. 1 h. 15 m.	Still narrower	88
	The peritoneum is closed	
1 h. 15 m. 30s.	Considerably widened	106
1 h. 16 m. 30s.	Narrower	95
1 h. 17 m.		92
1 h 18 m. 1 h. 19 m. 1 h. 20 m.	Still narrower	90 87 85
	The peritoneum is opened **One intestinal loop is stretched**	
1 h. 20 m. 30s.	Fully disappeared	115
1 h 21 m.	Appeared again	89
1 h. 22 m. 1 h. 23 m.	Wider	86 Not measured
1 h. 24 m.	Narrower	85

Time	The lumen of the vessel	Blood pressure
	The peritoneum is re-opened	
1 h 24 m. 30s	Practically disappeared	102
	The peritoneum is closed	
1 h 25 m. 1 h 26 m	Wider	85 80
1 h. 27 m 1 h. 28 m	Narrower	77 76
	The peritoneum is opened	
1 h 28 m. 30s.	Disappeared	100
	The peritoneum is closed	
1 h. 29 m 30s. 1 h. 30 m.	Wider	87 74
	The peritoneum is opened	
1 h. 30 m. 30s.	Disappeared	95
	The peritoneum is closed	
1 h. 31 m. 30s	Wider	77
1 h. 34 m.	Narrower	Not measured
1 h. 36 m.	Wider	74
	The peritoneum is opened	
1 h. 36 m. 30s.	Disappeared	97
	The peritoneum is closed	
1 h 37 m.	Appeared again	Not measured
	Artificial respiration interrupted	
1 h. 37 m. 30s.	Considerably widened	Not measured
	The peritoneum is opened	
1 h. 38 m.	Disappeared	Not measured

A detailed analysis of the above figures would yield conclusions of no small importance. For example, one can hardly disregard the regular decline of the effect of stimulation of the intestines on the rise of the blood pressure, which represents, apparently, a phenomenon of fatigue. For the time being we shall abstain from such an analysis, especially since this case, as stated previously, must be regarded as only one of an extensive series of experiments.

In conclusion we should like to make one more casual observation.

When the abdominal cavity remained open for a longer time (one minute), or when opened more frequently for shorter periods, there was observed towards the end of the experiment, under interrupted respiration, a decline in the still considerable blood pressure (more than 60 mm. Hg), without any preliminary increase.

II. A curarized *rabbit*. The manometer is connected with the right art. carotis. The medium vessel of the left ear is under observation.

Time	The lumen of the vessel	Pressure in the art. carotis
4 h. 23 m	Dilated	77
4 h 24 m		77
4 h 25 m.		76
4 h. 26 m.		74
4 h 27 m		74
	The abdominal cavity is opened One intestinal loop is stretched	
4 h. 28 m.	Constricted, almost disappeared	95
	The peritoneum is closed	
4 h. 29 m.	The medium artery disappears	75
4 h. 30 m		74
4 h. 31 m.	Some branches of the vessel appear	70
4 h. 32 m		69
4 h. 33 m	The medium vessel appears	67
4 h 34 m	The vessels are filled to a still greater degree	64
4 h. 35 m.		Not measured
4 h 36 m.	Constriction	60
4 h. 37 m.	Dilated	73
4 h 38 m.	Continues to dilate	81
4 h. 39 m.	Considerably dilated	87
4 h. 40 m		90

Time	The lumen of the vessel	Pressure in the art carotis
	The peritoneum is opened	
4 h. 41 m	Insignificant constriction	97
	The peritoneum is closed	
4 h 42 m.	The lumen of the medium vessel is considerably constricted	88
4 h 43 m		83
4 h. 44 m		79
4 h 45 m		76
4 h 46 m		75
4 h. 47 m.		76
4 h 48 m		79
4 h 49 m		76
4 h. 50 m.		75
4 h. 51 m		75
4 h. 52 m		77

In similar cases stimulation of the ischiadici,[17] even under a current of considerable strength, either did not produce any effect, or resulted in a decline of blood pressure instead of the usual increase. The ear vessels, on the contrary, remained unchanged. We leave the interpretation of this phenomenon until a detailed account of our experiments is published.*

* The above-mentioned observation is one of a series of experiments conducted in our laboratory by Mr. Pavlov in the autumn of 1876. Publication of the results of these experiments has been delayed for the reason that a number of similar papers on the same subject were published before Mr. Pavlov had completed his experiments. They will be published in the near future. (An editorial note of the *Pfluger Archiv*.)

CONCERNING TROPHIC INNERVATION[18]

It is perfectly clear that the horizon of medical observation of life is immeasurably wider than the sphere of vital phenomena which the physiologists have before their eyes in their laboratories. Hence the permanent incongruity between that which medicine knows, sees and empirically applies, and that which physiology can reproduce and explain. This relates, incidentally, also to the shock and neurotrophic phenomena of the clinic. For the former the physiologists have no generally accepted explanation; as for the latter, until now they cannot be observed under conditions of precise experimentation.

In the laboratory, however, not experimentally, but also clinically, I gradually came to the conclusion of the clinicians that there are special trophic nerves. Having operated for years on the digestive canals of animals (various fistulae, artificial separation and connection of different parts of the canal, etc.), for the purpose of facilitating experimentation during weeks, months and even years, I often unexpectedly observed extraneous and striking symptoms in surviving animals. I have read a number of papers on these symptoms at gatherings of the Russian Medical Society in St. Petersburg. I have seen various trophic disturbances of the skin and of the mucous membrane of the oral cavity as well as tetany and paresis; on one occasion I observed a case of acute and typically progressive paralysis of the spinal cord which lasted from ten to twelve days, on another occasion I observed a case of disease of the cerebral hemispheres (in the form of strong infiltration) with complete distortion, of the animal's normal attitude towards the external world; and finally I have seen shock phenomena, now quickly resulting in death, now manifesting themselves in temporary syncope of the animal almost fully simulating death. And all the cases were of a nervous character, either steadily progressive, or the reverse.

These observations gradually strengthened my supposition that such phenomena could be interpreted as reflexes coming from the abnormally stimulated centripetal nerves of the alimentary canal to the special inhibitory trophic nerves of various tissues. It has been assumed that the intensity of the chemical processes taking place in each tissue are regulated by special centrifugal nerves and in accordance with the principle inherent in the entire organism, i.e., in two opposite directions. Certain nerves intensify these processes and thereby increase the vitality of the tissue, while others weaken them, and, when subjected to excessive stimulation, deprive the tissue of its ability to resist the diverse destructive influences always acting inside and outside the organism.

On the basis of this assumption the observed shock phenomena were interpreted as being an acute, rapidly developing effect of an extremely strong reflex stimulation of the trophic inhibitory nerves, while the chronic pathological changes taking place in the tissues were seen as another effect of the same reflex stimulation, but weaker and more protracted.

In 1920 O. S. Rosenthal and myself deliberately operated on animals in a somewhat different way. Straining the nerves by means of displacing and fixing different parts of the alimentary canal, however, without any previous derangement of its integrity, we again observed many of the early symptoms, such as trophic diseases of the skin and of the mucous membrane of the oral cavity, paresis, and a considerable lowering of body temperature.

In this way we obtained additional proof for our contention that the phenomena observed by us are not conditioned by direct disturbance of the digestive process, as was the case in earlier experiments, when the animal was deprived of a more or less considerable quantity of digestive juices.

But, unfortunately, the pathological phenomena even now remained impermanent and fluctuating, and for this reason we were unable to go ahead with a strict and thorough analysis of their nervous mechanism. But these latest experiments strengthened our supposition, and at present we are trying out other methods in the hope of imparting greater stability to the phenomena which are of interest to us, especially since a thorough consideration of the subject brings together very many facts, both from the field of physiology and medicine, which lend weight to our supposition.

It may be that the trophic nerves, which to us are still hypothetical, have already been discovered by physiologists, and in the chief organ of the animal at that. Forty years ago physiology established the existence, along with the earlier known pair of rhythmic cardiac nerves—the retarding and accelerating nerves—another pair of cardiac nerves which might be described as influencing—also in an antagonistic way—the vitality of the cardiac muscle, i.e., raising it and lowering it. One of these nerves intensifies the heart-beat, conditions a more rapidly proceeding systole, increases the excitability of the muscle, eliminates the dissociation of the heart's sections and, generally speaking, heart troubles of all kinds whenever they emerge under unfavourable conditions. The influence exerted on the heart by the other nerve is the very opposite. What then, are these nerves? Perhaps they are the vascular nerves of the coronary system? But there are weighty experimental facts to disprove this: the action of these nerves is manifested on an excised, bloodless heart. And so one has to admit that they are trophic nerves.

Here is another case from the field of physiology. Long ago the late Heidenhain established two kinds of nerves for the salivary glands: one stimulating secretory activity of the glands in general, and the other accumulating in secretion their special organic substances. The first of these he named the secretory, the other the trophic nerve—with the reservation that the latter adjective was used conditionally, not in the generally accepted sense. Heidenhain's experiments, which later on were disputed in certain respects by some physiologists, have been definitely confirmed by the recent experiments of Professor B. P. Babkin. But is Heidenhain correct in regarding the term "trophic" conditional in his particular case? Indeed, no matter how liquid the saliva may be, it always contains all its components under stimulation of the secretory fibres. Consequently, the action of the trophic fibres must, undoubtedly, be interpreted as intensification of the constant vital chemism of the saliva, but then this relates to the function of the trophic nerves in the ordinary sense of this word. Just as the salivary glands have but one nerve, stimulating their function and having no antagonist, the trophic nerve, too, is a single nerve and acts positively.

Now for the medical aspect. I shall not dwell on special cases—these are well known to physicians and they are usually regarded as manifestations of neurotrophic disorders. I shall deal with the aetiology and therapy of some pathological cases, the mechanisms of which have not yet been disclosed by modern physiology.

Why do abnormalities in the digestive canal, especially of children, lead to various skin diseases? And on the contrary, why do certain influences on the skin cause diseases of the internal organs—of the pleura, lungs, kidneys, etc.? In the laboratory I observed in our dogs many cases of osteomalacia which often assumed a general and very acute character. Observation and even experimentation led me to conclude that this is caused by the chronic application of damp cold to the skin, i.e., when subjected to cold the skin is continuously moistened.

Let us turn now to certain therapeutic methods. Why and how do compresses, mustard plasters, cupping glasses, etc., bring relief to the patient? Does physiology provide a satisfactory answer to this question? Obviously, there is a tremendous gap in modern physiology in this respect. But all the above-mentioned aetiological moments and therapeutic agents would become clear as to the mechanism of their action if we assumed the existence of an antagonistic pair of trophic nerves, now increasing the vitality of the tissue, now lowering it. They would then be cases of reflex stimulation of these nerves, at times causing illness due to a lowering of the tissue's vitality under strong, excessive stimulation of the retarding trophic nerves, and at others helping the tissue to overcome the morbific agents by increasing its vitality through stimulation of the positive trophic nerves.

Of course, this pair of nerves must constantly function also during normal working of the animal organism, but so far we, naturally, do not know when and how they are normally stimulated, the more so since we are not sure whether they exist or not. However, hypothetically we can visualize certain extreme cases of their physiological work under extraordinary conditions. Let us take for example the old and regular medical fact—a badly furred tongue due to indigestion. What does it mean and what mechanism is responsible for it? Indeed, we cannot always assume a continuous pathological process spreading from the stomach to the oral cavity. It may be assumed that the derangement of the stomach, and of the digestive canal in general, stimulates a reflex on the inhibitory trophic nerves of the mucous membrane of the mouth, and mostly of the tongue; this conditions a certain abnormal state leading to distortion and even loss of taste, since the receiving apparatus of the gustatory stimuli are located in the mucous membrane. But loss of taste causes abstention from food, and this gives the digestive canal a rest, which is a highly important therapeutic remedy against the pathological process. Thus, this would be a self-healing reflex on the part of the organism.

Let us take another instance. In cases of starvation the heart and brain, being the most important parts of the organism, preserve their normal weight longer than the other organs. It can be assumed that only in these organs is the normal energy of the vital chemical process maintained by corresponding reflexes on their positive trophic nerves, while in all other organs it is restricted and reduced, resulting in particularly rapid atrophy.

From a consistent point of view, the pair of trophic nerves must be the last, most direct distributor of the alimentary resources of the organism among its parts.

Thus, as we see it, each organ should be under ternary nervous control—the functional nerves initiating or inhibiting its functional activity (muscular contraction, glandular secretion, etc.); the vascular nerves regulating the bulk supply of chemical substances (as well as elimination of waste) by increasing or diminishing the supply of blood to the organ; and, finally, the trophic nerves which determine in the interests of the organism as a whole the exact quantity of material to be used ultimately by each organ. We have demonstrated this ternary control in the case of the heart.

Confining myself now to this insignificant factual report and continuing with the help of several colleagues laboratory investigation of our complex and difficult subject in different directions, I have taken the liberty of drawing your attention to this, mostly raw, working material of our laboratory research for a special reason. From the physiological aspect I wanted to spread among physicians the idea of trophic nerves, by introducing the concept of an antagonistic pair of these nerves and by stressing their probable universal and constant role in the organism. This, perhaps, will contribute to a more appropriate and, consequently, more fruitful analysis of the available clinical material.

III

WORKS ON DIGESTION

LECTURES ON THE WORK OF THE PRINCIPAL DIGESTIVE GLANDS

LECTURE ONE

GENERAL SURVEY OF THE SUBJECT. METHODS

Gentlemen,

The physiology of the digestive glands has engaged the attention of my laboratory, i.e., of myself and my co-workers, for many years, and we have obtained certain results which, it seems to me, are both of theoretical and practical importance. The secretory activity of the digestive canal, of its chief organs—the gastric glands and the pancreas—proved to be quite different from that usually described in text-books and, consequently, as pictured by the physician. We, therefore, considered it necessary to help in every way in establishing a revised and fuller teaching to replace the antiquated doctrines of the text-books. With this object I delivered a speech* at a meeting of the Society of Russian Physicians in St. Petersburg, dedicated to the memory of S. P. Botkin, outstanding Russian clinician. However, in the space of an hour I could only outline in general terms the results of years of work. It was impossible, in view of the shortness of time, to corroborate my words with docu-

* Proceedings of the Society of Russian Physicians in St. Petersburg, 1894-95. *(Note by I. P. Pavlov.)*

mentary references, to convince my hearers by facts, by actual experiments. The lectures which I now submit to your esteemed attention are designed to make good these deficiencies. The facts referred to in these lectures are taken from works which, for the most part, have already been published, but some unpublished facts obtained by our laboratory will also be adduced.

The digestive canal, in respect to its chief function in the organism, recalls a chemical factory where the raw material—food—undergoes a predominantly chemical treatment; this makes possible its absorption by the juices of the organism and its utilization by the organism for the maintenance of the vital process. This factory, then, consists of a series of departments in which the food, according to its properties, is more or less graded and then it is either retained for a time or immediately transmitted to the next department. The factory and each of its departments are supplied by special reagents produced, so to speak, in a primitive manner by the neighbouring small workshops situated in the walls of the factory itself, or by more distant and separate organs which may be compared with large chemical mills and which are connected with the factory by a system of tubes transmitting the reagents. These are the so-called glands with their ducts. Each factory delivers a special fluid, a particular reagent, possessing definite chemical properties; due to this, the reagent acts only on certain components of the food, usually a complex mixture of different substances. These properties of the reagents are chiefly determined by the presence of special substances in them, the so-called ferments. Definite reagents or digestive juices, as they are called, either act only on a single ingredient of the food, or on several, thus combining the inherent properties of many individual reagents, although each produces its own particular effect. But even a simple reagent, having only one ferment, represents a complex solution, since, in addition to the ferment, it may contain alkalies, acids, protein, etc.

All this has been studied by physiology through obtaining the above-mentioned reagents or pure ferments from the organism and investigating in test tubes their effects on the components of the food, as well as their interrelation. It is chiefly on this knowledge that the scientific theory of the processing of food in the organism, or as we say, of digestion, is based.

However, this theory of the digestive process, which is largely of a deductive character, obviously suffers from many serious defects. Without doubt there is still a considerable gap between the knowledge acquired, on the one hand, and the physiological reality, as well as the empirical rules of dietetics, on the other. Many problems still remain unsolved, or have not even been raised. Why are the reagents poured out on the raw material in one definite way and not in another? Why are the properties of separate reagents repeated and combined in other reagents? Are all the reagents always poured out into the digestive canal on any kind of food? Is each individual reagent subject to variation, and if so, when, how and why does it occur? Does the composition of all the reagents change simultaneously, or do individual reagents alter in different cases differently, depending on the kind of the raw material? What happens to the reagents when the activity of the entire factory increases or diminishes? Is there not something in the nature of a contest between definite components of the food, i.e., does it not happen that some of them require a special reagent which may interfere with the successful action of other reagents on the remaining components?, and so on, and so forth. No one, of course, can doubt that these questions are relevant to the case. The mechanism of the digestive process cannot be presented in the abstract manner typical of present-day physiology. The individual properties and the diversity of the reagents clearly indicate that the work of the digestive canal is highly complex, delicate and strictly adapted to the given digestive function. Upon reflection, we must admit a priori that for any food, i.e., for any combination of substances which are to be processed, there is a definite combination of reagents with their special properties. No wonder that dietetics is, if not in its general empirical principles, then in its explanations and particularities, one of the most intricate branches of therapy. The physiologist must have knowledge not only of the elements of digestion—of the effects of individual reagents; in order fully to master the subject he must also include in the sphere of his observation the entire actual process of digestion. This, of course, was realized by many investigators who attempted to accomplish it, and they would have succeeded had the knowledge been more easily attainable.

Full knowledge of the digestive process can be acquired in one of two ways—on the one hand, by investigating the state of elaboration of the raw material in each part of the digestive canal (the method of Brücke, Ludwig's[19] school, etc.) and on the other hand, by strictly ascertaining when and what quantity of the reagent is poured out into the digestive canal on each kind of food, as well as on the entire meal, and what its properties are (this way was taken by numerous researchers who investigated the secretory activity of the digestive glands).

Our investigations belong to the second category. The earlier investigations were hindered by the inadequate methods employed. It is often said, and not without reason, that science advances in leaps, depending on the development of experimental methods. With every advance in method, we rise, so to speak, a step higher, and a wider horizon with hitherto imperceptible objects unfolds before us. Our first aim, therefore, was to develop a method. We had to observe how the reagents were poured out on the food coming into the digestive factory. Ideal accomplishment of this task required the fulfilment of many and difficult conditions. It was necessary to have the reagents at hand *at any time*, otherwise important things might escape us; the reagents had to be obtained *in an absolutely pure* *condition*, otherwise we would not have been able to establish the variations taking place in their composition; we had to *ascertain their quantities* accurately, and, finally, it was necessary that *the digestive canal should function normally*, and that the animal *should be in good health.*

It is understandable that physiology approached the solution of this problem gradually, much effort having been spent in vain, and a number of attempts having been unsuccessful, although many outstanding scientists devoted attention to this problem.

We shall begin our consideration with the pancreas—a fairly simple matter. It might seem that here our task is quite easy. We need only find the duct through which the gland secretion is transmitted to the digestive canal, and then, by attaching a cannula to it, let the fluid flow to the outside, into a graduated vessel. This, actually, is not such a difficult matter, but, unfortunately, it does not solve the problem. Although the digestive process in the animal under experiment is in full swing, after this operation, in most cases, there is no flow of pancreatic juice at all, or if there is any its quantity is abnormally small. In this case observations on the process of secretion, as well as on alterations in the composition of the juice caused by different kinds of food, are out of the question. Further investigation showed that the pancreas is a very delicate organ, and as a result of the conditions inevitably accompanying the operation (narcotization, dissection of the abdominal cavity, etc.) its state of disturbance is such that in most cases no traces of normal activity remain. This method is known in science as the temporary pancreatic fistula. Its failure, naturally, resulted in attempts being made to find new methods.

A possible way out was to obtain the juice from the duct not during the operation period but after it, when the inhibitory influence of the operation had fully vanished. For this it was necessary to let the juice escape from the duct for a considerable length of time. It was believed that this for any combination of substances which are to be processed, there is a definite combination of reagents with their special properties. No wonder that dietetics is, if not in its general empirical principles, then in its explanations and particularities, one of the most intricate branches of therapy. The physiologist must have knowledge not only of the elements of digestion—of the effects of individual reagents, in order fully to master the subject he must also include in the sphere of his observation the entire actual process of digestion. This, of course, was realized by many investigators who attempted to accomplish it, and they would have succeeded had the knowledge been more easily attainable.

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A possible way out was to obtain the juice from the duct not during the operation period but after it, when the inhibitory influence of the operation had fully vanished. For this it was necessary to let the juice escape from the duct for a considerable length of time. It was believed that this could be done either by attaching a glass tube to the animal's duct and bringing it out to the exterior through the abdominal wall (Claude Bernard),[20] or by placing in the duct a T-shaped piece of twisted lead wire (Ludwig's school). These methods were called permanent pancreatic fistula. They proved effective, but only for a short time, usually for three to five days and in exceptional cases up to nine days. After this the glass tube usually fell out and the fistula closed up; the lead wire, too, failed to prevent this. And so these methods too had to be regarded as bearing a temporary character. But this was not their only defect. In two or three days when the inhibitory influence of the operation had passed away, there was manifested in many cases another abnormal state—a continuous excitation of the gland irrespective of the fact whether the dog was fed or not. This prompted the question, which of the two was better—the temporary or the permanent fistula? But it was obvious that both were defective. Whereas with a temporary fistula the normal conditions were almost invariably distorted due to the inhibitory influence of the operation, with the so-called permanent fistula there was often observed an inflammatory process in the pancreas which manifested itself a few days after the operation (especially in those performed in the old laboratories) and which also distorted the normal activity of the gland.

It only remained to find a means of access to the gland lumen which would keep the duct open for any length of time, until the above-mentioned unfavourable conditions had disappeared completely. Such a means was first suggested by me in 1879 and a year later, in 1880, by Heidenhain independently.[21]*

My method was this (I shall describe the method of my operation which differs slightly from that of Heidenhain): from the wall of the duodenum a diamond-shaped piece, containing the natural opening of the pancreatic duct, is

* Hermann's *Handbuch der Physiologie*, Bd. V.

cut out; the intestine, the lumen of which is not appreciably narrowed, is stitched up, and the separated piece of intestine is sewn (with the mucous membrane outwards) into the opening in the abdominal wall. The wounds heal quickly, and the entire operation requires no special skill; it does not last long (about half an hour) and is easily endured by the animal. After two weeks the animal is absolutely ready for observation. In the place of the healed-up abdominal wound there appears a roundish elevation of the mucous membrane, 7 to 10 mm. in diameter, with a cleft-like orifice which in the more successful cases is located exactly in the centre of the elevation. If the animal is now fastened in the stand, the juice can be collected either directly, as it drops from the mucous papilla, or if it flows along the abdominal wall, by properly fixing a funnel, with the wide end upward, to the abdomen. The two obstacles, which hindered the work of the investigators when the temporary and so-called permanent fistulae were employed, have been removed. The gland, undoubtedly, is now in a normal condition; however, the trials of the experimenter are by no means over.

In a short time the abdominal wall, owing to the action of the escaping juice, becomes greatly eroded and large areas of it even begin to bleed. This irritates the animal and interferes with the collection of pure juice by means of the funnel. What is to be done? Many things may help—frequent washing of the affected skin with water and application of emollient ointments; even better results can be obtained if the animal is kept fastened in the stand for a number of hours every day, with the funnel attached to its abdomen. But best of all is to let the animal, when free from experimental work, to lie on a bed of porous material, such as sawdust, sand, or old mortar. Many animals find the most suitable position in which to lie, namely, on the abdomen, so that the escaping juice is immediately absorbed by the porous material and the overflow of juice and skin abrasion is fully and readily avoided. It is worth mentioning that this method was adopted as a result of a hint given by one of the dogs subjected to the operation.

I shall take the liberty of telling you about this interesting case in detail. In one of the dogs operated according to our method the eroding action of the juice began to manifest itself ten to fifteen days after the operation. The dog was tied in the laboratory. One morning, much to our annoyance, a heap of plaster torn from the wall was found beside the animal which was generally known for its quiet behaviour. The dog was then chained in another part of the room. Next morning we observed the same thing—another part of the wall had been damaged. At the same time it was noticed that the dog's abdomen was dry and that the cutaneous irritation considerably diminished. Only then did we realize what had caused the dog's strange behaviour. When we prepared a bed of sand for the dog, the wall was no longer damaged and the flow of juice ceased to trouble the animal. We (Dr. Kuvshinsky and I) gratefully acknowledged that by its manifestation of common sense the dog had helped us as well as itself. It would be a pity if this fact were lost for the psychology of the animal world. And so another obstacle had been overcome, but the final goal had still to be reached.

Three or four weeks after the operation, the animals, which previously seemed in a normal state, suddenly became ill; they began to reject the food and showed signs of rapidly developing weakness, which in most cases was accompanied by convulsive symptoms and sometimes even by violent convulsions, followed, after two or three days, by death. Obviously, this was a peculiar form of disease. To think in terms of inanition was out of the question, since animals often die with their weight almost at the normal level; the supposition of some form of post-operative disease, such as chronic peritonitis, was also excluded, since neither the state of the animals before death nor the findings of the autopsy justified this. Finally, we had to give up the idea of the possibility of any self-intoxication caused by food insufficiently or incorrectly digested as a consequence of the digestive canal losing a considerable quantity of pancreatic juice—an idea suggested by Dr. Agrikoliansky* in his dissertation. In the first place, no symptoms of digestive disorder were observed in many animals before death—neither vomiting, nor diarrhoea, nor constipation. In the second place, our experiments, in which the pancreatic duct was specially ligatured and sectioned, had demonstrated the absolute harmlessness of this operation. There remained but one assumption, namely, that together with the escaping pancreatic juice the animal had lost something that was essential to the proper course of the vital processes. Proceeding from this idea we applied two means of protecting our animals against possible complications. Aware of the powerful influence exerted by different kinds of food on the composition and quantity of the secreted pancreatic juice, we (Dr. Vasiliev) excluded meat from the diet of the dogs, feeding them solely on bread and milk. On the other hand, taking into account that with the escaping pancreatic juice the organism loses a large quantity of alkali, we regularly added a certain quantity of sodium bicarbonate to the food (Dr. Yablonsky).

With the help of these two measures it is quite easy to obtain an animal provided with a permanent pancreatic fistula and at the same time fit for experimentation for a period of months and even years, without additional precautionary measures. Of course, the difficulties encountered in handling different animals greatly vary. As a rule one of every four or five dogs endures the operation without any special subsequent care. The way in which the sodium bicarbonate helps is not yet clear. It is possible that the sodium really compensates for the injurious deficiency of alkali in the blood; however, it is likewise pos-

* "The Influence of Strychnine Nitrate on the Secretion of Pancreatic Juice in the Dog," Dissertation, St. Petersburg, 1893.

sible that its action consists, as shown by Dr. Becker, in reducing the secretion of the juice. In the latter case the nature of the substance the loss of which proves so injurious to the organism, would remain obscure. Quite clearly this question is of great importance, since here we have a new, experimentally induced, pathological state of the organism. In our laboratory, investigation of this problem has been undertaken by Dr. Yablonsky.

The collection of the juice is performed by means of a glass, or, better still, of a metallic funnel, with its wide end upwards and pressed to the spot containing the opening of the pancreatic duct with the help of elastic bands or simply rubber tubes tied round the body. On the funnel there are hooks to which small graduated cylinders are attached; the animal is placed in the experimental stand. While these arrangements are very convenient for the observer, the animal is not at all comfortable, especially when the experiment lasts a long time; it becomes tired and restless. However, it gradually learns to sleep soundly even in these conditions, especially when its position in the stand is eased, for example, by supporting its head. In cases when dogs are first used for laboratory work it is better to collect the juice in a lying posture, placing a vessel under the opening of the duct and slightly pressing it to the body.

I have deliberately described the series of misfortunes experienced by us in connection with the formation of a permanent pancreatic fistula; I wanted to show how difficult it is to solve apparently easy problems when dealing with material such as ours.

There is no doubt that our solution of the problem is also far from being ideal. What is badly needed is a method that would allow the juice to flow outside during the experiment and into the intestine during the intervals. In addition to saving much juice for the organism, this method would be of particular importance because it would preclude the possibility of any considerable changes in the work of the digestive glands in general. There are certain grounds for assuming that the steady flow from the digestive canal of such important a reagent as the pancreative juice is compensated for, to a degree, on the one hand, by a heightened or otherwise changed activity of the remaining digestive glands, and, on the other hand, by the expedient depreciation of the juice which is uselessly and continuously poured out on the floor. But the significance of these somewhat far-fetched hypotheses must not be overrated. Later we shall see how clear, unquestionable and instructive are the results of the investigations carried out with the help of this method. The method recently published by the Italian scientist Fodera* approximates, in a way, to the perfect, irreproachable method. He succeeded in placing in the duct a T-shaped metallic cannula which, apparently, makes it possible to collect the juice on the outside, or to direct it to the intestine by closing the outer end of the cannula. This method, however, suffers from one essential defect: there is no guarantee that simultaneously with the flow of juice to the outside a certain quantity of it may not enter the intestine.

No less difficult and protracted was the evolution of methods for obtaining the gastric juice and for observing its secretion. Leaving aside the older and obviously inadequate methods, we shall dwell in detail on the formation of a gastric fistula, as the starting-point for the method employed at present. In 1842, our countryman, Professor Basov** and in 1843, the French physician Blondlot*** independently, suggested the idea of artificially reproducing in animals the condition observed by an American physician in one of his patients; the latter had a permanent unhealable opening in the abdominal wall leading to the stomach —it had been caused by a bullet wound.[22] Both Basov and

* *Moleschotts Untersuchung zur Naturlehre des Menschen und der Tiere*, Bd. XVI, 1896.

** *Bulletin de la Soc. des natur. de Moscou*, t. XVI.

*** *Traité analytique de la digestion*, 1843.

Blondlot, using dogs, made an opening through the abdominal wall into the stomach and fastened into it a metallic tube corked from the outside. The tube heals into the wound and can remain in this position for years without causing even the slightest harm to the animal.

This method raised great hopes at the time, since it provided easy and free access to the inside of the stomach at any moment. But as time went on these hopes gave way to an ever-increasing disappointment. For the purpose of investigating the properties of the ferment of the gastric juice almost all researchers had to use extracts prepared from the mucous membrane of the stomach, since only very little and highly impure juice could be obtained through the fistula. It was also very difficult to observe the course of gastric secretion during digestion and to obtain an idea of the properties of the gastric juice in different conditions, since the juice was mixed up with the mass of food. The result was that voices began to be raised saying that the gastric fistula had justified none of the hopes, that it was hardly of any use at all. However, this was an exaggeration due, apparently, to the disappointment at the slow progress in elaborating the theory of the secretory activity of the digestive canal, and of the gastric glands in particular. Indeed, many important observations had been made earlier with the help of the gastric fistula. Now it was only necessary to introduce a slight modification in it in order, with its help, to make possible the final solution of a number of fundamental problems.

In 1889, we (Mrs. Shumova-Simanovskaya and I) performed the oesophagotomy operation on a dog with an ordinary gastric fistula: we severed the oesophagus at the dog's neck and sutured both its ends separately to the edges of the skin wound. We accomplished thereby the complete anatomical separation of the mouth and stomach cavities. Animals subjected to this operation fully recover if well cared for, and live for many years in perfect health. In feeding, the food, naturally, is introduced direct into the stomach. The following interesting experiment can be performed with such animals. The dog is given meat, which, of course, falls out through the upper opening of the oesophagus. However, in the perfectly empty stomach, preliminarily washed out with water, there begins a profuse secretion of absolutely pure gastric juice, which continues all the time the animal is eating, and even for some time longer. Hundreds of cubic centimetres of gastric juice can be easily obtained in this way. I shall discuss in future lectures the causes responsible for the secretion of gastric juice under such conditions, as well as the significance of this phenomenon for the entire process of digestion. Now I shall merely remark that the problem of obtaining pure gastric juice has been definitely solved by means of this method; at present it is possible to collect from an animal thus operated upon a few hundred cubic centimetres of gastric juice every two days or even every day, without causing any apparent harm to its health, i.e., to obtain gastric juice from a dog almost as regularly as one obtains milk from a cow.

For our ferment experiments we no longer need to prepare an infusion of the mucous membrane; we now obtain from the living animal enormous quantities of the purest ferment with much greater ease and in less time. The animal subjected to the operation becomes an inexhaustible source of the most refined product. It seems to me that the pharmaceutist, too, should devote attention to this fact, since the physician has always regarded pepsin and hydrochloric acid as being beneficial and, in many cases, essential. Comparative experiments carried out in detail by Dr. Konovalov with solutions of commercial pepsin and natural gastric juice obtained from dogs as described above, showed that the former could by no means compete with the latter. The possible objection that the gastric juice is obtained from dogs can hardly be regarded as a serious obstacle to its widespread use as a pharmaceutical preparation. In the laboratory we tried it out on ourselves, and the tests revealed beneficial rather than injurious effects. The taste is by no means unpleasant and it contains nothing extra compared with a corresponding solution of hydrochloric acid. In view of the prejudice, it is quite possible to obtain gastric juice in a similar way from other animals whose flesh is consumed by man. I cannot but express regret that this method which, in any case, deserves a serious trial, is not promoted in Russia, although I have frequently called the attention of my medical colleagues to it. The desire to try my luck once more has made me dwell on this collateral subject when describing our methods. Since last year pure gastric juice, obtained by Dr. Fremont from the isolated stomach of the dog by the method of Thiry's well-known intestinal fistula, has been recommended abroad as a therapeutic remedy for various affections of the digestive canal. Perhaps this product, actually long known to us, would have more success in our country if it appeared under a foreign flag!

But to return to the subject of our methods. As already mentioned, the problem of obtaining pure gastric juice has been solved, but as yet no progress has been made in providing the means which would make it possible to observe the secretion of the juice and to study its properties during digestion.

Obviously this requires adherence to an absolutely exceptional condition—normal gastric digestion together with strict collection of perfectly pure juice. That which is quite simple in the case of the anatomical relations of the pancreas (where the cavity containing the food is fully separated from the cavity containing the juice), becomes a matter of the greatest difficulty in the case of the stomach, for its glands are microscopic and are situated in the walls of the cavity containing the food. A truly fortunate idea for overcoming these difficulties was suggested by Thiry. In order to procure pure intestinal juice, which is also produced by microscopic glands situated in the intestinal wall, and to be able to study the course of its secretion, Thiry cut out a cylindrical piece of intestine, shaped it into a cul-de-sac and sewed it into the opening of the abdominal wound. This idea was used by Klemensiewicz* in 1875 for obtaining pure juice from the pyloric end of the stomach, but his dog died three days after the operation. Heidenhain,** however, succeeded in nursing such a dog and keeping it alive. Shortly afterwards Heidenhain*** isolated a piece of the stomach fundus and gave it the shape of a cul-de-sac, which secreted its juice externally.

Thus the above-mentioned requirement was met. When, in the normal way food reached the large stomach, which remained in its usual position, the isolated pouch began to secrete perfectly pure juice, the quantity of which could be accurately measured at any interval of time. However, in order to arrive at well-founded conclusions concerning the normal work of the stomach during normal digestion, judging by the activity of the isolated pouch, it was necessary to ensure its absolute nervous inviolability. Evidently in Heidenhain's operation this was not the case, since in making the transverse incisions by which the piece of stomach was cut out, the branches of the vagus extending lengthwise along the wall of the stomach were severed. Consequently, before the method could be improved this defect had to be eliminated.

In order to do this, we (Dr. Khizhin and I) modified Heidenhain's operation in the following way. The first incision, which begins on the side of the fundus two centimetres from the pars pyloris, is carried in a longitudinal direction for 10 or 12 centimetres through the posterior and anterior walls. In this way a triangular flap is formed. A second incision is made precisely at the base of this flap, but only through the mucous membrane, the muscular and serous coats being left intact. The edges of the incised mucous membrane are separated for one to one and a half centi-

* *Sitzungsbericht der Wiener Akademie*, 1875.

** Pflüger's Archiv f. d. ges. Physiologie, Bd. XVIII. 1878.

*** *Ibid.*, Bd. XIX, 1879.

metres from the subjacent tissue on the side of the stomach, and on the side of the flap for two to two and a half centimetres. The edge belonging to the large stomach is folded and stitched together. The edge of the flap is shaped into a cupola. The stitching along the edges of the first incision both in the stomach and the flap forms a septum between their respective cavities consisting of two layers of mucous membrane; one of these layers is intact, the other being sutured along the middle. Only thanks to the above-mentioned cupola it is possible to obtain an experimental animal with a permanent fistula; if both layers of the mucous membrane were sewn along the middle, then after a shorter or longer period of time a communication would be formed between the stomach and the cul-de-sac, and this would make the animal unfit for our purpose. Better still would be to form cupolas out of the mucous membrane on both sides of the stomach. To make a long story short, we cut out an elongated piece from the stomach, shape it into a cylinder, suturing its free end into the opening of the abdominal wound and allowing the other end to remain connected with the other part of the stomach; the stomach becomes separated from the cul-de-sac by a septum of the mucous membrane. For the sake of illustration I give here schemes of the operation, taken from the work by Dr. Khizhin (Fig. 1).

Naturally our addition to Heidenhain's operation makes it much more complicated, but, as we shall see later from experiments, this difficulty is compensated for by the absolutely intact condition of the nervous relations of our artificial stomach; this is clear from the fact that the fibres of the n. vagi pass between the serous and muscular layers of the bridge into the isolated pouch. This operation does not cause any serious discomfort to the animal and does not endanger its life.

It would be appropriate now to answer the question whether the activity of our miniature stomach provides a true reproduction of the secretory work of the large stomach, since in the latter the food comes into contact with the walls during the normal process of digestion, while the former remains empty. However, I shall answer this question fully in a later lecture, when we have in our possession more facts for the solution of the problem. Now I shall merely state that, in addition to strict conclusions

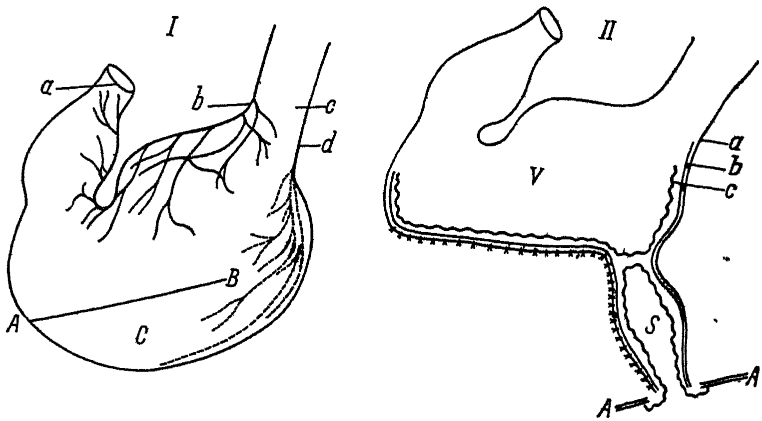

Fig 1 I· *a*—Pylorus; *b*—Plexus gastricus anterior vagi; *c*—Oesophagus; *d*—Plexus gastricus posterior vagi; *AB*—Line of incision; C—Flap for forming stomach pouch; II: *a*—Serosa; *b*—Muscularis; *c*—Mucosa; *A*—Anterior abdominal wall; *S*—Cavity of stomach pouch; *V*—Cavity of stomach.

drawn from a series of unquestionable facts, we carried out *numerous experiments in which the miniature and large stomachs were directly compared* as to the conditions of work and properties of secretions; as a result no room was left for doubt that the miniature stomach, *on which* we base our study of normal gastric activity, is fully valid for our investigations. In my next lecture the miniature stomach will appear as an instructive object worthy of close attention.

As mentioned previously, Dr. Fremont succeeded recently (after publication of our method) in isolating the whole stomach of a dog in accordance with Thiry's principle; he connected the lower end of the oesophagus with the duodenum, and fixed an ordinary fistular cannula in the stomach closed at both ends. This method, however, can only serve for certain special experiments on gastric secretion, as I shall show later on. As a general method it suffers from two essential defects. First, in ordinary digestion in such dogs it is impossible to reckon on absolutely normal conditions of gastric secretion, since the mucous membrane of the stomach is not in the slightest degree reflexly excited by contact with food; secondly, when food is introduced directly into the stomach it mixes with the gastric juice. As to obtaining juice for practical purposes from such a stomach, it seems to us that our method of combining an ordinary gastric fistula with oesophagotomy possesses greater advantages compared with Dr. Fremont's method. Our method is incomparably simpler from the surgical point of view, and, given proper conditions for the operation, does not result in useless sacrifice of animal; the animals subjected to the operation live for years, enjoying perfect health. Can this be said of Dr. Fremont's dogs?

The usual method of collecting juice from our miniature stomach is as follows: a glass, or better still, a rubber tube is introduced with its perforated end into the cul-de-sac. This tube either remains there of itself, or it is secured by means of an elastic band round the animal's body. The juice is collected either in the lying or standing posture.

It seems to me now that the method of forming an isolated miniature stomach must be regarded as the only possible one and fully correct in principle. There still remain some minor defects, such as the erosion of the edges of the wound and the loss of a certain quantity of gastric juice, but they can be easily eliminated or regarded as being of little importance; in time they may be altogether avoided.

In the interests of a better study of the entire secretory activity of the digestive canal simplification of the technical side of the described methods is to be desired; it is necessary to remove the minor defects so that it may be possible to make several fistulae on one and the same animal without causing any danger to its life or health.

It is clear from the foregoing general survey of the digestive process that the study of the concordant work of the separate glands is of great importance; but it can be carried out with absolute exactitude as regards time, intensity, etc., only when the activity of all or many glands is simultaneously observed on one and the same animal.

In concluding this description of methods I consider it essential to dwell for a moment on the importance of surgical technique in physiology. It seems to me that in modern physiology a firmer stand is to be taken by the surgical method (I counterpoise it to the purely vivisectional method), which implies performing (skilfully and creatively) more or less complex operations with the aim of either extirpating certain organs, or of ensuring access to physiological phenomena taking place in the depths of the body; of disrupting one or another connection linking the organs, or, on the contrary, establishing a new connection, and so on; it also implies ability subsequently to heal the animal and restore its state, in the measure that the nature of the operation allows, to normalcy.

I regard the promotion of such surgical technique to be a matter of the greatest importance, because the usual method of simply vivisecting the animal in an acute experiment is, as is now becoming clearer day by day, a major source of errors, since the act of crude violation of the organism is accompanied by a mass of inhibitory influences on the functions of the different organs. The organism as a whole, the realization of the most delicate and most expedient linking of an enormous number of separate parts, cannot, in the nature of things, remain passive to destructive agents; it must, in its own interests, strengthen one part and weaken another, i.e., temporarily leaving aside, so to speak, all other aims, and concentrating on saving whatever can be saved. While this circumstance has been and still is a big obstacle in the way of analytical physiology, it appears to be an insurmountable obstacle to the development of synthetic physiology where it is necessary to determine exactly the true course of one or another physiological phenomenon in an intact and normal organism. At the same time discovery in the sphere of performing operations, as a means of physiological research, has in no way disappeared; on the contrary, as life shows, it is just coming into its own. Recall, for example, the extirpation of the pancreas performed by Minkovsky;[23] the transference of the portal blood into the vena cava by Dr. Eck;[24] and, finally, the remarkable operations of Goltz in which he extirpated different parts of the central nervous system. Have not many physiological problems been solved in this way, and do they not give rise to numerous new problems? It may be argued that such operations have been performed already. Yes, but, in the first place, they are very rare and performed only by the few. If, for instance, the number of physical instruments devised annually and introduced for the investigation of physiological phenomena, as well as the number of physiologico-chemical methods and their variations, be compared with the number of new physiological operations after which the animal must survive, the meagreness of the latter stands out in marked contrast to the richness of the former. In the second place, it is noteworthy that many of these operations were performed first by surgeons and not by physiologists; the latter, so to speak, do not regard these problems as being essential for their work, or do not possess the means necessary for their solution. Finally, the fact that surgical methods have not yet taken their proper place in physiology is demonstrated in the most striking fashion by the absence in modern physiological laboratories of properly equipped surgical departments, whereas provision is made for chemical, physical, microscopic and vivisectional departments.

The ordinary laboratory rooms cannot be used for frequent and complicated operations ensuring the survival of the animals, without the sacrifice of much time and labour; such operations require all the methods and conditions provided by present-day surgery. There is no doubt that certain operations, even performed with the aid of antiseptic and aseptic precautions, would not be successful in an ordinary laboratory, since, when dealing with animals, it is almost impossible to maintain absolute cleanliness during and immediately after the operation in the absence of a large surgical department specially equipped for this purpose. I shall refer by way of example to the well-known history of Eck's fistula which connects the vena cava inferior and the portal vein. In the conditions that prevailed in the old laboratories the inventor of this operation, despite his energy and resourcefulness, could not keep the animals alive for any considerable period after the operation. Similar failure overtook Prof. Stolnikov, who repeated the operation with the assistance of Dr. Eck sparing neither dogs nor effort. It was only in the surgical department of the physiological laboratory of the Institute of Experimental Medicine, which had just been opened (1891), and consequently, in a building which, in the surgical sense, was perfectly clean, that the first major success was registered. However, this happy period of successful operations lasted for only one year. The physiological laboratory in the Institute was a small place at that time, and therefore, despite precautionary measures, it quickly became so impure that the Eck operation, though performed by the same, now even more skilful hands, proved fruitless and a waste of time. This situation lasted for about a year, notwithstanding all the efforts made by the experimenters, until a new physiological laboratory was built in the Institute where considerable space was allotted to the surgical department.

I take the liberty of calling your attention to this, because, as far as I know, it is the first instance of a special surgical department in a physiological laboratory. Perhaps this example will give my physiological colleagues some useful hints for designing new institutes. The surgical department occupies half the upper floor which comprises a quarter of the entire laboratory. It consists of a set of operating rooms located along one side; in the first room the animal is washed in a bath and dried on special stands, in the next (the preparation-room) the animal is narcotized, and the site of the operation shaved and cleansed with antiseptic solutions; the third room is used for sterilizing the instruments and cloths, for washing hands and donning overalls; the fourth is a well-lighted operating room. The narcotized and prepared animal is carried, without any table, into this room by those who take part in the operation. As a rule the attendants are not allowed to go beyond the second room of the operating section. This set of rooms is separated by a solid wall from a series of special cabins where the dogs are kept for the first ten days after the operation. Each of these cabins has a large window with a small hinged pane for ventilation; its floor space is about one square sazhen,* and it is more than five arshins** high. Each cabin is heated with hot air and provided with electric light. There is a passage running along the cabins, each being shut off from it by a massive, tightly-fitting door. The entire department has cement floors with gutters in each room. In the cabins a lead pipe with small apertures in it runs along the walls near the floor, and by means of this pipe the floors can be watered from the corridor at any time without entering. The whole department is painted a white oil colour. The long series of operating rooms is a reliable protection against penetration of dirt into the last and main operating room. Although

* An old Russian measure of about seven English feet.—*Tr.*
** An old Russian measure of about twelve English feet.—*Tr.*

physiology owes much to the intelligence of the dog in general, it would be in vain to rely on the assistance of this clever animal in carrying out certain surgical tasks. Only by arranging this long series of barriers against penetration of dirt, was it possible, in the ordinary and surgical sense of the word, to maintain the surgical department in the proper condition for a considerable length of time. Two years of work in this department have not made it impure, which is proved by our criterion for surgical cleanliness—the successful performance of the Eck operation. When I recall the results of operations carried out in the course of the last twenty years in different buildings, and always upon equally healthy material, with a frequent repetition of the same operation, I am amazed, perhaps even to a greater degree than the surgeon, at this triumph of cleanliness which saved the lives of numerous animals and spared both the time and labour of the experimenters.

I hope you will forgive me for this long digression on the significance of surgical methods in physiology. I am sure that only the development of inventiveness and skill in performing operations on the digestive canal will disclose the magnificence of the chemical activity of this organ, some features of which can already be traced with the help of modern methods. I would ask you to remember these words at the end of my lectures, and I am convinced you will admit their truth.

LECTURE EIGHT

PHYSIOLOGICAL FACTS, HUMAN INSTINCT AND MEDICAL EMPIRICISM

Gentlemen,

The object of our discourse today is to consider the previously communicated results of our laboratory research from the point of view of the regulations relating to the partaking of food and of the therapeutic measures prescribed by the physician in disorders of the digestive apparatus. In the latter case, in order to perfect our knowledge and to secure its most useful practical application, the pathology and therapy of the digestive canal should, of course, be subjected to experimental investigation by the same methods and from the same point of view. Such investigation would now present no great difficulty; thanks to the progress of bacteriology many pathological processes can easily be produced in the laboratory, especially since in this case we are dealing, as it were, with external diseases: the methods used nowadays give access to any part of the surface of the digestive canal. On such pathological animals it would be possible precisely and thoroughly to study the functional disturbances of our apparatus, i.e., the changes which take place in the secretory activity —in the properties of the fluids and the conditions under which they are secreted. Therapeutic methods, too, could be experimentally tested on such animals by observing the entire course of healing and its final effect, i.e., by investigating the conditions of secretion during all phases of the healing process. It can hardly be doubted that only the development of experimental therapy, together with experimental physiology and pathology, can ensure for scientific, i.e., ideal, medicine its rightful position. Incontestable proof of this is provided by bacteriology, which has recently come into being and developed.

I have already described pathological therapeutic experiments with dogs whose vagi nerves were severed at the neck. I recall some other cases of a similar nature. At times our dog with the two stomachs suffered from a slight and usually transient gastric catarrh. It was very interesting to observe that the pathological disturbance caused by us in the large stomach made itself felt in the small one; the latter showed an almost continuous slimy secretion of very low acidity, but of strong digestive power. At the beginning of the illness or before it manifested itself, the psychic stimulation was strikingly effective—it furnished juice in normal quantity, while the local stimuli were almost completely ineffective. In this case one can assume that the deeper layers of the mucous membrane with the gastric glands still remained healthy, being easily excited to activity from the centres, while the surface of the mucous membrane with the peripheral apparatus of the reflex nerves was already considerably injured. I mention these, one might say, impressions rather than precise facts, for the purpose of showing the fruitful field awaiting any investigator who undertakes to study, with the help of modern methods and practice, the pathological states of our digestive organs and their treatment. Such a study is all the more desirable since clinical investigation of this same subject, despite big efforts in recent years, meets, of course, with serious difficulties. It should be borne in mind that the stomach-probe, the chief clinical instrument, is less convenient than the gastric fistula practised on animals; and yet we know that the physiology of the stomach, even after years of application of the latter method, has not made any serious advance. This is understandable. We had before us a mixture of substances comprehension of which was difficult and at times even impossible.

And so a strictly scientific solution of therapeutic problems is still a matter for future research. But this in no way excludes the possibility of fruitful influence being exerted by the latest physiological achievements on the work of the physician. Physiology, of course, cannot lay claim to authoritative guidance in the field of medicine; because of the incompleteness of its knowledge it is always more restricted than clinical reality. But physiological knowledge often elucidates the mechanism responsible for one or other illness and the intrinsic significance of appropriate empirical methods of treatment. To apply a remedy without knowing how it will act is one thing and to know what you do is another, ensuring immeasurably greater advantages. In the latter case the influence on the affected organ will, of course, be more effective and more adapted to the given conditions. Besides, medicine, being constantly enriched with new physiological facts, will, sooner or later, become what in the ideal sense it should be, namely, the art of repairing the damaged mechanism of the human body on the basis of exact knowledge; in other words, it will become applied physiology.

Let us return now to our basic subject. While it is generally recognized that human instinct is the result of everyday experience, which has turned into an unconscious striving for the best possible conditions of existence, in the physiology of digestion especially the phrase has become current that physiology merely confirms the rules of instinct. It appears to us that the foregoing physiological facts also furnish numerous instances of the triumph of instinct before the tribunal of physiology. Particularly impressive are the reasons underlying the daily empirical demand that food be enjoyed and eaten with relish. Everywhere the act of eating is connected with certain customs designed, as it were, to distract from the routine of daily life: a special time of the day is chosen; a group of relatives, acquaintances, or companions assemble; certain preparations are made (change of garments, as, for example, in Britain, grace is said by the oldest member of the family, etc.). In well-to-do houses there are special rooms for meals; musicians and others are invited to entertain the diners—in short, everything is done to distract the company from the cares and worries of daily life and to concentrate on the food. From this point of view it is also obvious why serious conversation, as well as serious reading, are considered inappropriate at meals. This, perhaps, partly explains also the use of alcoholic beverages at meals, since alcohol already in the early phases of its action has a mild narcotic effect which contributes to distraction from the burden of everday cares. It goes without saying that this highly developed hygiene of eating is met with predominantly in the intelligent and well-to-do classes, first, because here mental activity is more strenuous and the varied questions of life are more disturbing; and secondly, because food is usually served here in quantities in excess of the requirements of the organism. In the lower classes, where mental activity is of a more elementary nature, highly strained muscular activity and chronic insufficiency of nourishment normally evoke a strong and lively desire for food, without special measures for stimulating it. These conditions explain why the choice of food is so dainty in the case of the upper classes and can be so simple and at the same time harmless in that of the lower classes. All the condiments and all the appetizers used before a substantial repast are obviously designed to provoke curiosity, interest and a greater desire for food. It is a well-known fact that a person who at first displays indifference to his customary meal, afterwards begins to eat with gusto if his taste has been stimulated by something piquant. Thus, it is only necessary to give an impulse to the taste organs, to set them into action, in order that their further activity can be maintained by less powerfull stimulants. Naturally, a person who is hungry does not need these extraordinary stimulating measures, since satisfying hunger is in itself a matter of pleasure. It is often said and not without reason that "hunger is the best sauce." However, here, too, it is a matter of degree, since every normal individual, even every animal, must feel a certain appetizing taste. For example, a dog that has gone without food for many hours eats not all the things that dogs usually eat, but chooses the food it likes best. Hence, the presence of certain flavouring substances in the food is a general requirement, although naturally individual tastes greatly differ. On the other hand, an extravagant indulgence of the appetite for food, like any other over-indulgence, is easily understood (for example, Petr Petrovich Petukh in Gogol's *Dead Souls*, and other gluttons).

This passing description of the attitude towards the act of eating testifies that people always take care to maintain attention to and interest in food, to ensure that meals are enjoyed; in other words, they take care of what is generally called appetite. Everybody knows that food eaten with appetite and pleasure is normal and useful food, food eaten to order, or for the sake of convenience, becomes to a greater or lesser degree, harmful, and the instinct of human health acts against it. Hence, one of the most frequent requests addressed to the physician is to restore the lost appetite. In compliance with this, medical men at all times and in all countries until recently considered it important, in addition to combating fundamental disease, to take special measures for restoring appetite. It can be assumed that in this they were guided not only by the desire to free their patients from an unpleasant symptom, but also by the conviction that restoration of appetite facilitates the re-establishment of normal digestion. One can say that in the same measure as the patient wanted his appetite back the physician did all in his power to satisfy him. Hence the abundance of so-called remedies for restoring appetite. Unfortunately, modern medical science has considerably deviated from this correct and practical approach to appetite. It is astonishing how little attention modern text-books on digestive disorders devote to appetite as a symptom, and to its special therapy; only in some of them is the significance of appetite as a factor of the digestive activity mentioned in passing—in one or two parenthetical phrases. At the same time one comes across books in which the physician is practically advised not to treat bad appetite on the alleged grounds that it is an unimportant subjective symptom. From what I have said and demonstrated in previous lectures this attitude of modern medicine towards appetite cannot but be regarded as a serious misconception, since it is precisely here that symptomatic treatment is to a considerable degree concurrent with fundamental treatment. When in most cases of digestive disorders the physician finds it useful to stimulate secretory activity in every possible way, this aim can be achieved in the surest and most complete way by restoring the appetite. We have seen already that no other stimulant of gastric secretion can, in the matter of quantity and quality, compare with the craving for food. To a degree we can understand—and this helps to elucidate the matter—why modern medical science is so indifferent to loss of appetite as an object of treatment. Nowadays, with the experimental method penetrating deeper and deeper into medical science, many factors of complicated pathological states and therapeutic agents are appraised, so to speak, according to the attestation of the laboratory, i.e., in so far as they can be verified in laboratory conditions. Of course, the highly progressive significance of this trend is beyond doubt; but here, as in any other human undertaking, error and exaggeration are inevitable. It should be borne in mind that if one or other phenomenon cannot be reproduced in laboratory conditions, this is no reason for discarding it as fantastic; we do not know as yet all the actual conditions for the development of certain phenomena, nor are we able to grasp the complex connection between separate vital functions. Seeking support in the laboratory, but unable to find there anything bearing on appetite, the clinic and the pathology of digestion, naturally, lost interest in this factor and disregarded it in medical practice. As already stated, until recently the psychic secretion of gastric juice was mentioned in physiology only in passing, and even then not by all authors, and rather as some kind of curiosity. On the other hand, great importance was attached to mechanical stimulation, the effect of which, now that our knowledge is more complete, has proved illusory. This error committed by physiology has been experimentally disclosed and explained; each of the contending agents has been assigned its proper place, and if clinical medicine follows its rightful desire to investigate its problems experimentally, it is obliged in practice to accord to appetite its right to consideration and treatment.

Despite the above-mentioned indifference displayed by physicians to appetite, so to speak, per se, many medical methods even now are, in essence, based on stimulation of appetite. Such is the truth of empiricism! When the patient is directed to eat sparingly and to avoid over-eating, when he is advised to abstain from eating pending the special permission of the physician, when he is removed from his usual surroundings (according to Mitchell's method) or sent to a watering place, where life is riveted on the observance of certain physiological functions, and especially eating—in all these cases the physician is actually endeavouring to stimulate the patient's appetite and use it for curative purposes. In the first case, when the patient is counselled to eat sparingly, besides preventing a weak stomach from being overloaded, there undoubtedly takes place a recurrent secretion of appetite juice which is particularly profuse and strong in digestive power. I ask you to recall the previously described experiment in which the food given to a dog in small portions led to the secretion of a much stronger juice than a large portion eaten at once. This was an exact experimental reproduction of the clinical treatment of a weak stomach. This kind of diet regulation is all the more expedient since, in most frequent disorders of the stomach, only the surface layer of its membrane is affected. Thus the sensory surface of the stomach receiving the effect of the chemical stimulant, may not be able, so to speak, to cope with its duty, and the period of chemical stimulation of the gastric juice, which, with an abundant intake of food lasts for a long time, is for the most part deranged or even completely absent. Meanwhile a strong psychic excitation, a keen feeling of appetite, may be freely transmitted from the central nervous system to the gastric glands located in the deeper, yet unaffected layers of the mucous membrane. An example of this, taken from our laboratory pathological material, was mentioned by me at the beginning of the lecture. It is obvious that in these cases the surest way is to promote digestion only by exciting a secretion of appetite juice, and not juice excited by chemical stimulants. From this point of view the importance of removing a patient, suffering from chronic weakness of the stomach, from his customary surroundings, becomes quite clear. Let us take, for example, a mentally overstrained person during office hours. How often does it happen that he is unable to divert his thoughts from his work for a single moment. He eats, as it were, without noticing it, without interrupting his work. This is quite common with people in cities where life is extremely strenuous. Naturally this systematic inattention to the act of eating leads, sooner or later, to digestive disorders, with all their consequences. There is no appetite juice, no igniting juice, or at least very little. The secretory activity develops very slowly. The food remains in the digestive canal for a much longer time than it is normally required; due to the insufficiency of digestive juices it is subject to fermentation and, in this state, greatly irritates the mucous membrane of the digestive canal. Thus the latter is brought naturally and gradually to a state of disorder. No prescriptions on the part of the physician can help the patient so long as he remains in his old surroundings, since the fundamental cause of his complaint has not been eliminated. There is only one solution—remove the patient from his everyday surroundings, free him from his usual work, interrupt the train of persistent thought and for a time concentrate his attention exclusively on the care of his health, on eating. This is done by sending the patient on a tour, to a watering place, etc. The duty of the physician is not simply regulating the behaviour of individual patients in this respect, but taking care that a proper attitude towards the process of eating be widely established. This is the duty especially of Russian physicians, because among the so-called intelligent classes in Russia with their highly confused conceptions of life, generally speaking, there is often an absolutely unphysiological, and sometimes even scornful indifference towards eating. More methodical nations, like the English, have made the act of eating something of a cult. If gluttony is looked upon as a manifestation of bestiality, a scornful indifference towards eating is, on the contrary, a manifestation of imprudence. As is always the case, the best course lies between the two extremes—one must not over-indulge in eating, but at the same time proper attention should be devoted to it. Render unto Caesar the things that are Caesar's, and unto God the things that are God's.

With the firmly established fact that mental influence is exerted on gastric secretion, the question of flavouring substances enters on a new phase. Now we know why the empirical conclusion was drawn that food must be tasty as well as nutritious. And therefore the physician, who prescribes diets for individuals, or even for groups of people, must constantly bear in mind the phenomenon of psychic secretion, i.e., he is obliged to inquire and know how the given food has been eaten—whether with or without relish. In reality, however, those responsible for diets often focus their attention exclusively on the nutritive value of the food or are guided solely by their own taste. It is impossible, in the interests of public health, not to call attention also to the feeding of children. If taste determines the individual's attitude towards food—and this evokes the initial activity of the digestive glands—then it would be irrational from the point of view of vitality to accustom children solely to delicate and uniform gustatory sensations; this would but reduce their further adaptability to the conditions of life.

The question of the therapeutic importance of bitters seems to me to be very closely connected with appetite. After enjoying a very long period of high repute these substances have been all but excluded from the list of pharmaceutical remedies. Laboratory tests showed that they were unable to live up to their old reputations; when introduced directly into the stomach or into the blood, many of them failed to produce the secretion of digestive juices; they thereby became greatly discredited in the eyes of clinicians, so much so that some of them were quite ready to abandon them altogether. Obviously, their fate was determined by the simple conclusion that a weakened digestion could be aided only by a remedy that would excite secretory activity under given conditions. It was, however, overlooked that the experimentally tested conditions could not cover all the possible conditions of the process under investigation. The whole question of the therapeutic importance of bitters acquires quite a different aspect when linked with another question, namely, what is the effect of bitters on the appetite? The unanimous verdict of both the earlier and later physicians is that bitters definitely stimulate appetite; and that says everything. It follows then that bitters really stimulate secretion, since appetite, as has been frequently pointed out in these lectures, is the strongest stimulus to the digestive glands. There is nothing surprising in the fact that this was not observed in previous laboratory experiments. Bitters were injected directly into the stomach, and even into the blood of absolutely normal dogs. But their action is mainly bound up with the influence they exert on the gustatory nerves; and it is not accidental that this wide variety of remedies, covering substances of most diverse chemical composition, is grouped together chiefly because of a common bitter taste. The taste of a person suffering from digestive disorders is a blunted taste and displays a certain gustatory indifference. Ordinary food, agreeable to other people, and to himself when in health, is now tasteless; it not only does not excite appetite, but, on the contrary, rather evokes a feeling of distaste. In such patients the gustatory sensations, as it were, completely vanish or become distorted. Consequently, a powerful impulse should be given to the gustatory apparatus in order to restore strong and normal sensations. Experience has shown that this can be most quickly achieved by the application of sharp, unpleasant stimulants, which, by contrast, awaken the idea of pleasant gustatory sensations. In any case the indifference disappears and this makes it possible to excite appetite for one or another kind of food. This phenomenon reproduces a general physiological fact: light appears brighter after darkness, sound louder after silence, the joy of health more intense after illness, etc. This explanation of the stimulating action of bitters on the appetite proceeding from the mouth cavity does not exclude similar action from the stomach cavity. As pointed out in the fifth lecture, there are grounds for assuming that certain stimuli coming from the stomach also excite appetite. It is possible that bitters, besides acting on the gustatory nerves in the cavity of the mouth, produce a peculiar effect on the mucous membrane of the stomach. This engenders certain sensations—separate elements of the craving for food. The fact that these special sensations arise in the stomach after the administration of bitters has been confirmed by some clinicians. Consequently, this must be a matter not merely of a simple physiological reflex, but of a certain psychic effect which causes the physiological secretory activity. The same, apparently, holds good for other substances, such as spices, vodka, etc. In any case, irrespective of whether this explanation conforms to reality or not, the question of the therapeutic importance of bitters, I repeat, has been decided positively, since their obvious effect on appetite is generally acknowledged. And so experimental investigation of bitters has the job of establishing their influence on appetite, which is a difficult matter not yet attempted in the laboratory.

It is not sufficient, therefore, to verify the clinical observations in the laboratory on animals; one must have, in addition, the assurance that this verification is correctly carried out, i.e., that the investigation concerns the particular point of the process under clinical consideration. It is interesting to observe that the connection between appetite and gastric secretion is pictured in exactly the reverse way by many physicians and in many medical text-books; thus it is assumed that a certain therapeutic agent causes the secretion of gastric juice and that the presence of the latter in the stomach evokes appetite. Here we have, apparently, a wrong interpretation of a true fact, since what is overlooked is that a psychic effect could also be a strong excitant of the secretory nerves.

After one or other hors d'oeuvre or some vodka (especially customary in Russia) designed to excite the appetite, the main meal in most cases begins with something hot, with meat broth (bouillon, different soups, etc.). This is followed by the really nutritious food—meat of different kinds served in different ways, or in the case of poorer people, porridges rich in starch and protein. This sequence of foods is quite natural from the point of view of the physiological facts mentioned in these lectures. As we have seen already, meat broth is an essential chemical stimulant of gastric secretion. Consequently, practical experience secures two ways of exciting a profuse flow of gastric juice on the fundamental food: first by stimulating the secretion of appetite juice with the help of the hors d'oeuvres, and secondly by promoting the gastric secretion with the help of meat broth. Human instinct has thus developed a preliminary procedure for the digestion of the main food. However, only well-to-do people can afford a good meat broth; poorer people use for the excitation of early gastric secretion cheaper and less effective chemical stimulants. Russians, for instance, use kvass;* in Germany, where meat is quite expensive, strictly speaking, a slightly flavoured and warmed up water is used (Mehlsuppe, Semmelsuppe, etc.). Probably not without significance is the fact that the quantity of digestive juice is, generally speaking, closely connected with the water content in the organism. If this sequence of food holds good for healthy people, then it is all the more obligatory in pathological cases. A person suffering from loss of appetite, or with a bad appetite, has no psychic secretion of gastric juice at all, or if he has, it

* A Russian beverage made of malt, water and different varieties of bread.—*Tr.*

is very feeble. Consequently, his meal must inevitably begin with a strong chemical stimulant, i.e., with a solution of stimulative meat extracts. Otherwise solid food, especially non-meat foods, would remain undigested for a long time. Hence, it is quite expedient to prescribe meat juice, strong bouillon or a solution of the Liebig extract for patients suffering from loss of appetite. The same applies to forcible feeding, for example, of mental patients. In the latter case, the very method of introducing the food ensures the supply of a chemical stimulant, since the food can be introduced only in liquid form; in any case the addition of the Liebig extract to liquid food substances would be very useful. According to the strength of the chemical excitation, the liquid substances may be arranged in the following order: first, the substances just mentioned (meat juice, etc.), secondly—milk, and thirdly, water.

The usual termination of a dinner can also be easily understood from the present physiological standpoint. A dinner usually ends with the sweet course, and everybody knows from experience that sweets give certain pleasure. The meaning of this is quite plain. A repast which begins with satisfaction evoked by the desire for food, must end with the same sensation, despite the fact that the hungry feeling has been satisfied, moreover, the object of this satisfaction is a substance that calls for practically no digestion but agreeably excites the gustatory organs, namely, sugar.

Having considered the general arrangement of eating from the point of view of physiological facts, we shall now turn to some special points.

First of all, I shall touch on the acid reaction of the food. It is obvious that of all tastes acid occupies a very special place. A number of acid substances are in use—one of the commonest being vinegar, which is used in the preparation of numerous sauces and dressings. Many wines are also acid in taste. In Russia, kvass, especially acid kvass, is widely consumed. Then, large quantities of acid fruits and vegetables are consumed, some of them acid in themselves and some being made acid in the course of preparation. Medicine, too, makes use of this instinct, and solutions of acids, mostly hydrochloric and phosphoric, are often prescribed in disorders of digestion. Finally, nature herself constantly takes care to produce in the stomach, during normal digestion, along with hydrochloric acid, also lactic acid, which is formed from ingested food and, consequently, is always present. These facts have become physiologically comprehensible, because we know that an acid reaction in the digestive canal is not only required for the effective action of the chief gastric ferment, but is also a very strong stimulant of the pancreatic gland. It can even be assumed that in certain cases the entire digestion depends solely on the acid reaction (as a digestive stimulant), since the pancreatic juice has a fermentive action on all the components of the food. Thus, the above-mentioned acids now assist digestion, now serve as a remedy, and substitute the gastric juice when it is fully absent or relatively insufficient. From this point of view it is not difficult to understand why a close combination of kvass and bread is widely used by Russian peasants: the enormous quantity of starch consumed by them in the form of bread or porridge necessitates strong excitation of the pancreatic gland, and this is opportunely effected by the acid. In isolated stomach complaints, accompanied by loss of appetite, both instinct and medicine have recourse to acids, since, as we now know, they excite intensified activity of the pancreatic gland and thereby supplement the insufficient work of the gastric glands. In my view this knowledge of the special relation of acids to the pancreatic gland may be of great use to practical medicine, and may place the pancreatic gland, this powerful and important organ of digestion hidden so deep in the organism, under the strict control of the physician. It is possible, for instance, to exclude the stomach deliberately from the digestive process and transfer digestion direct to the bowel by prescribing acids that do not stimulate the gastric glands. It is possible, likewise, to restrict the activity of the pancreatic gland by reducing the acidity of the gastric contents. This may be necessary in treating various digestive disturbances, as well as certain general complaints.

No less instructive is a comparison of our experiments on fats with the demands of instinct and the counsel of dietetics and therapy. It is generally recognized that fatty food is heavy, i.e., difficult to digest; in cases of weak stomachs it is, therefore, usually avoided. Now we are able to explain this physiologically. The fat, when present in large quantities in the chyme, retards, in its own interest, the secretion of gastric juice and thus impedes the digestion of protein substances. This explains why a combination of fat and protein foods is particularly heavy, and only strong stomachs and persons with keen appetites can cope with them. A combination of bread and butter proves less difficult of digestion as can be judged from its widespread use. Bread, as we have already seen, requires little gastric juice and little acid, especially when calculated per unit of time; but the fat which excites the pancreatic gland ensures a simultaneous production of ferment for itself and for the starch and protein. Fat alone is by no means a heavy food, as is proved by the fact that large quantities of Ukrainian bacon can be consumed with impunity. This is understandable, because in this case the inhibitory action of the fat on the secretion of gastric juice is harmless; it contributes merely to assimilation of the fat itself. There is no conflict between the food components and consequently no one of them suffers. Fully in accordance with practical experience, the physician completely excludes fatty foods from the diets of patients in cases of weakness of the stomach and recommends red meat only, for example, game. But in those pathological cases where there is excessive activity of the gastric glands, fatty food or fat in the form of an emulsion, is prescribed by the physician. In this case, obviously, medicine has empirically learned to make use of the inhibitory action of fat on the gastric secretion, so strikingly manifested in the foregoing experiments on dogs.

Milk has an exceptional place in human food, and this is recognized both in everyday experience and in medical practice. It has always been regarded as the lightest food and is given in cases of weak and diseased stomachs, as well as in numerous other severe illnesses, such as heart and kidney affections. The extreme importance of milk as a food prepared by nature herself has now been elucidated to a considerable degree. We can indicate three essential properties of milk which characterize it as an exceptional food. As we already know, in comparison with the nitrogenous equivalents of other foods, the weakest gastric juice and the smallest quantity of pancreatic juice are poured out on milk. Thus, the secretory activity required for the assimilation of milk is considerably weaker compared with any other food. At the same time milk has another important property. When introduced directly into the stomach without the animal noticing it, the milk always causes a certain degree of secretory activity of the stomach and the pancreas, i.e., it acts as an independent chemical stimulant of the digestive canal; and it is really a mysterious phenomenon that no essential difference is observed between the secretory activity caused in the digestive canal when the milk is introduced unnoticed into the stomach and that which arises when the milk is ingested by the animal. In the case of meat, as we already know, the mode of introduction into the stomach is of extreme importance, even though meat is a better chemical stimulant. Consequently, it must be assumed that milk itself causes not only an absolutely adequate, but also a highly economical secretion, and not even appetite can make this secretion more abundant, so to speak, more luxuriant. Unfortunately, the secret of this specific relation of milk to the secretory activity of the digestive canal cannot yet be analysed and explained. It may be supposed that on the one hand, a certain role is played here by the fat which inhibits the activity of the gastric glands, and, on the other hand, by the alkaline reaction of the milk which inhibits the activity of the pancreatic gland. Thus, both the gastric glands and the pancreas, despite the presence of stimulants in the milk, are maintained, at a certain, not too high, level of activity, and this in its turn appears expedient in view of the easy digestibility of all the components of milk. Finally, the third characteristic property observed in milk, and which in all probability is only another expression of the first, is seen in the following. If we feed the animal with equal quantities of nitrogen, in one case in the form of milk, in the other in the form of bread, and then observe the hourly excretion of nitrogen in the urine, we find that the increase during the first seven to ten hours after the administration of milk (compared with the rate of excretion beforehand) comprises only from 12 to 15 per cent of the nitrogen taken in with the milk, whereas in the case of bread it rises to 50 per cent. Taking into consideration the course and rate of assimilation of milk and bread, one must admit that the increase in urinary nitrogen, which takes place immediately after eating, expresses the functional intensity of the working metamorphosis of the alimentary canal required for digestion, and that in the case of bread this intensity is three or four times greater than in the case of milk (Prof. Ryazantsev's experiments). Hence, in the case of milk a considerably larger portion of nitrogen is, so to speak, placed at the disposal of the organism than in that of any other kind of food. In other words, the price paid by the organism for the nitrogen (in the form of the work of the digestive canal) is much lower than that for nitrogen in other food substances. How wonderfully does the food prepared by nature distinguish itself compared with the other foods! These facts, obviously, pose the question of a new approach towards the comparative nutritive value of the different foods. The old criteria must give way to new, or, to be more precise, admit the latter to their midst.

Experiments on the assimilation of foods, with the aim of ascertaining what remains undigested and what enters the organism's juices, in themselves cannot solve the question in a satisfactory way. Suppose that we set the alimentary canal a certain task connected with the digestion of a given food. If it is sound, this task will be accomplished in the best possible way, i.e., with complete extraction of all the nutriment. In this way we would learn how much nutritive material is contained in the given kind of food in general, but the question of the digestibility of the food would still be obscure. The experiment does not disclose the magnitude of the effort of the digestive canal in extracting all the nutritives from the given food. Nor can experiments on artificial digestion fully solve the question of digestibility, since experiments with food normally ingested are quite different from those in the test tube, where we deal only with one juice, in the absence of any interaction with other juices and food components. That an essential distinction really exists here is clearly proved by the investigations made in our laboratory by Dr. Walther. Fibrin, which is generally considered the most digestible protein, when compared with milk of the same nitrogenous equivalent, proved to be a much stronger stimulant of the pancreatic gland, while apart from nitrogenous substances milk contains a good deal of non-nitrogenous nutritive material. It is obvious, therefore, that the question of digestibility and nutritive value of foods must be solved mainly by means of estimating the real energy used in the process of their digestion, i.e., the quantity and quality of the juices poured out on the given amount of nutritive material. The energy of the glandular metamorphosis must be deducted from that of the entire intake of food, the remainder will indicate the extent to which the food is utilized by the organism, i.e., the amount available for use by all the organs, with the exception of the digestive apparatus. From this point of view those food substances, the bulk of which is used to compensate for the expenditure by the alimentary canal on their digestion, must be regarded as not very nutritious and as indigestible, in other words, as foods whose nutritive value covers only the cost of their own digestion. It is, therefore, of great practical importance that one and the same kind of food but differently served should be compared from this aspect, for example, boiled and roast meat, hard- and soft-boiled eggs, boiled and unboiled milk, etc.

It remains for me now to touch on some purely medical questions. The first concerns the therapeutic administration of neutral and alkaline salts of sodium. Clinical, pharmacological and physiological text-books have always advanced as a well-grounded doctrine the thesis that these salts evoke a secretion of juice. However, we would search in vain for any serious experimental backing for this doctrine. The experimental facts adduced cannot be considered satisfactory. The experiments carried out by Blondlot who sprinkled sodium bicarbonate on meat, as well as the experiments of Braun and Grützner who injected solutions of sodium chloride direct into the blood, either suffered from methodological defects or were far removed from normal relations. We can hazard the guess that in this case the experimental insufficiency was benevolently made good by the clinic, since the experiment seemed to confirm the clinical observations. There is no doubt, of course, that salts of sodium (the chloride and bicarbonate) are useful in digestive disorders. But how do they act? It appears to me that here, as in some other similar cases, medical thought has fallen into error, since the effect of the action is one thing, and its mechanism—altogether different. Although medicine is broad and comprehensive in its empiricism, it often manifests narrow reasoning when it comes to interpreting the facts; it often gives a simplified explanation of the highly complex mechanism of healing processes merely on the basis of modern physiological data. It seems to me that this is also true in the given case. The following reasoning is current in medicine: "alkalies act favourably in disturbances of the digestive canal; consequently they provoke a flow of digestive juices." Of course, upon recovery the stomach begins to secrete the normal, i.e., in some cases a larger, quantity of gastric juice. But this must be the result of recovery from a disordered state and not of the direct physiological effect of the alkalies. The latter, however, should be thoroughly, that is, specially proved. The help given to the organism by the alkalies might be explained in another way, altogether different from the ordinary. In this case I venture to express the idea of the therapeutic effect of sodium chloride and of alkaline sodium salts, which is the exact opposite of the generally accepted idea. Both on the stomach and the pancreas we failed to convince ourselves of any juice-exciting influence of these salts; on the contrary, in our hands they exerted an inhibitory influence on secretion. In addition to the previously described experiments concerning the action of alkalies on the stomach and pancreas, I should like to mention the following observation. A dog which had been subjected to complex operations—a gastric fistula, a pancreatic fistula and an oesophagotomy—was given daily, for a period of weeks, an addition of soda to its food. The animal had a perfect appetite and was in good health. When we performed the first experiment with sham feeding, we were struck by the relatively weak effect of this generally powerful juice-exciting procedure. At the same time we observed that the pieces of meat which fell out of the upper end of the oesophagus contrary to the usual rule, had hardly been touched by the saliva. Consequently, this dog exhibited reduced activity of many digestive glands simultaneously, namely, of the gastric, pancreatic and salivary glands. The work of the salivary glands, of course, deserves closer investigation. I believe that the experimentally proved inhibitory action of alkalies on the digestive glands gives grounds for advancing the following concept of the mechanism of their healing effect in certain digestive disorders. Catarrhal complaints of the stomach are characterized by a constant or greatly protracted secretion of slimy gastric juice of extremely low acidity. Moreover, in certain cases the affection begins with hypersecretion, with abnormal excitability of the secretory apparatus manifested in an excessive and causeless flow of gastric juice. The same thing can be assumed in the case of disorders affecting the pancreatic gland, judging by its state after operations performed on it for physiological purposes. It can be supposed that when for some reason or other the abovementioned affections arise, they afterwards, so to speak, maintain themselves independently, since continuous activity is obviously injurious to the glands. The nourishment and restoration of the glandular organs proceeds best during rest; such is the normal course—after a period of external work there comes a break, followed by a period of internal work. Consequently, the elimination of the pathological state and the return to normal can be attained by means of a remedy which forcibly interrupts the external work of the affected glandular organ. Such, in my opinion, is the healing importance of the alkalies. One might draw a certain parallel between the effect of the alkalies in a pathological state of the digestive canal and that of digitalis in compensatory disturbances of the heart. A heart so affected usually beats rapidly, thereby aggravating its condition, shortening the period of its rest, i.e., of its recovery. A circulus viciosus sets in; the weak work of the heart reduces the blood pressure; in view of the constant physiological connection this leads to a quickening of the heart-beat, which, in its turn, causes a further weakening of the heart. Undoubtedly the favourable action of digitalis begins to manifest itself in the fact that it breaks through this vicious circle, slows the pulse and in this way gives new strength to the heart. Our explanation of the action of the alkalies accords with the usual practice of prescribing a strict diet simultaneously with their use, which ensures a certain rest for the digestive glands. It is interesting to note that clinical investigations with the help of the stomach tube, after a period when the alkalies were regarded as having a juice-exciting effect, recently entered into a new phase and that more and more is heard of the inhibitory effect of the alkalies.

The second point that we should consider is the following. The main difficulty encountered by the physician in determining the diet of patients suffering from digestive disorders is that a very important role is played here by idiosyncrasy. In cases of one and the same illness different patients react to the same kinds of food in an absolutely different manner. That which is agreeable to one patient, and which is easily borne by him and eases his condition, is almost poison for another patient. In one of the clinical manuals it is stated that while some patients easily bear milk and will not have fatty goose flesh, others have a reverse reaction to the same food. Hence the first and foremost rule in dietetics is to give no instructions with regard to diet until the taste and habits of the patient have been ascertained. What does this signify? Until recently physiology had no experimental answer to this question. But our facts, it seems to me, to a certain degree clarify the matter. Each kind of food leads to certain digestive activity, and a continuous diet sets up definite and fixed types of glands which cannot be quickly and easily altered. This explains why digestive disorders often arise when there is a sudden change from one diet to another, especially from a frugal to a richer diet, as is the case, for example, after the long Russian fasts; these disorders are manifestations of the temporary inability of the glands to adapt themselves to the new digestive task.

Finally, it may be useful to mention the following. There are cases of very acute and, as it were, absolutely unjustified disturbances of the digestive canal. From the point of view of modern physiology these cases might be explained by intereference of the secreto-inhibitory nervous system arising from excessive and abnormal excitation due to one or another cause. In any case this system now represents a factor which must be duly considered by the physician.

At this point, gentlemen, I conclude my lectures. I hope that the physiological facts communicated here, may help the physician to understand certain things in his sphere of activity, and that they will contribute to the elaboration of more correct and effective methods of treatment. The physician will derive more benefit by bringing to the attention of the physiologist in what way, in his opinion, the explanations given here need correction, and also by pointing out those new aspects of the digestive process which have been disclosed by him in the broad world of clinical observation but which have not yet come within the field of vision of the physiologist. It is my profound belief that the aims of physiology as a branch of knowledge and of medicine as an applied science can be attained solely by means of active exchange of experience between physiologist and physician.

NOBEL SPEECH DELIVERED IN STOCKHOLM ON DECEMBER 12, 1904[25]

It is not accidental that all the phenomena of human life are dominated by the matter of daily bread—the oldest link connecting all living things, man included, with the surrounding nature. The food which finds its way into the organism where it undergoes certain changes—dissociates, enters into new combinations and again dissociates—embodies the vital process, in all its fulness, from such elementary physical properties of the organism, as the law of gravitation, inertia, etc., all the way to the highest manifestations of human nature. Precise knowledge of what happens to the food entering the organism must be the subject of ideal physiology, the physiology of the future. Present-day physiology can but engage in the continuous accumulation of material for the achievement of this remote aim.

The first stage through which the food substances introduced from without must pass, is the digestive canal; the first vital action on these substances, or to be more exact and objective, their first participation in life, in the vital process, is effected by what we know as digestion.

The digestive canal is a kind of tube passing through the entire organism and communicating with the external world, i.e., also on external surface of the body, but turned inwards and thus hidden in the organism.

The physiologist who succeeds in penetrating deeper and deeper into the digestive canal becomes convinced that it consists of a number of chemical laboratories equipped with various mechanical devices.

These mechanical devices are formed by the muscular tissue which is a constituent part of the wall of the digestive canal. They either facilitate the passage of the components of food from one laboratory to another, or detain them for a certain time in a given laboratory or, finally, expel them when they prove harmful to the organism; moreover, they participate in the mechanical processing of the food, accelerating the chemical action on it by compact mixing, etc.

A special so-called glandular tissue which is either also a constituent part of the wall of the digestive canal, or lies beyond it in the shape of separate masses and communicates with it by means of branch tubes, produces chemical reagents, the so-called digestive juices which stream into separate segments of the digestive tube. The reagents, on the one hand, are aqueous solutions of such well-known chemical substances as hydrochloric acid, soda, etc., and, on the other hand, substances which are found only in a living organism and which break up the main components of food (proteins, carbohydrates and fats) much more easily, i.e., more rapidly and at a much lower temperature and in smaller quantities than any other chemically well-studied substances. These substances which act in vitro[26] just as well as in the digestive canal, and which, therefore, are a natural object for chemical investigation, have so far been difficult to analyse. As is known, they are called ferments.

From this general description of the digestive process I shall turn to facts relating to this process established by me and by the laboratory of which I am in charge. In doing so I deem it my duty to recall with profound gratitude my numerous laboratory co-workers.

It is perfectly clear that successful study of the digestive process, as of any other function of the organism, depends to a considerable degree on whether we succeed in finding the nearest and most convenient starting-point in relation to the process under observation and on whether all collateral processes between the phenomena under observation and the observer are removed.

For the purpose of investigating the development of secretion in the big digestive glands, which communicate with the digestive canal only by means of branch tubes, we cut from the wall of the digestive canal small pieces, in the centre of which were the normal openings of the secretory ducts; we then stitched the opening in the wall of the canal, and the excised pieces with the openings of the secretory ducts were sutured to a corresponding place on the surface of the skin, from the outside. Thanks to this procedure the juice was diverted from the digestive canal and collected in special vessels. For the purpose of collecting the juice produced by the microscopic glands located directly in the wall of the digestive canal, already long ago large pieces were cut out from the wall of the digestive canal and artificial pouches with openings to the outside were made; the defect in the digestive canal, naturally, was closed by stitching. In the case of the stomach the preparation of the artificially isolated pouch was always connected with sectioning the nerves of the glandular cells, and this, naturally, deranged the normal work of the stomach.

Taking into account more delicate anatomical relations, we modified the operation in a way that left the normal nervous paths fully intact when making an isolated pouch from parts of the stomach wall.

Finally, since the digestive canal is a complex system, a number of separate chemical laboratories, I used to cut the communication between them in order to investigate the course of phenomena in each particular laboratory; thus I divided the digestive canal into several separate parts. This, of course, necessitated laying short and convenient passage-ways from the outside into each separate laboratory. For this purpose metal tubes have long been in use; they are inserted into the artificial openings, and during the intervals between the experiments they can be sealed.

In this way we often performed very thorough operations and sometimes even several operations on one and the same animal. It goes without saying that the desire to accomplish the task with more confidence, to avoid wasting time and labour, and to spare our experimental animals as much as possible, made us strictly observe all the precautions taken by surgeons in respect to their patients. Here, too, we had to apply proper anaesthesia, observe irreproachable cleanliness during the operation, provide clean rooms after the operation, and take thorough care of the wounds. But these measures did not suffice. After remaking the animal's organism in accordance with our design, which naturally caused more or less damage to the experimental animal, we had to find a modus vivendi that would ensure an absolutely normal and long life for it. Only by observing this condition would the results of our work be regarded as fully conclusive and as having elucidated the normal development of the phenomena. We succeeded thanks to our correct appraisal of the changes evoked in the organism, and thanks to the expedient measures taken by us; our healthy and happy animals did their laboratory work with real gusto; they always rushed from their cages to the laboratory and readily jumped on to the tables where our experiments and observations were conducted. Believe me I am not exaggerating one iota. Thanks to our surgical methods in physiology we can demonstrate at any time phenomena of digestion without the loss of even a single drop of blood, without a single scream from the animal undergoing the experiment. At the same time this is an extremely important practical application of the power of human knowledge, which may also be of immediate use to man, who, due to the implacable fortuities of life, is often mutilated in similar, though more diversified ways.

In our observations on dogs, we soon noticed the following fundamental fact: the kind of substances getting into the digestive canal from the external world, i.e., whether edible or inedible, dry or liquid, as well as the different food substances, determined the onset of the work of the digestive glands, the peculiarities of their functioning in each case, the amount of reagents produced by them, and their composition. This can be proved by a number of facts. Take, for instance, the formation of saliva by the mucous salivary glands. With each meal, when edible substances find their way into the oral cavity, thick and viscous saliva containing much mucus flows out of these glands. With the introduction into the animal's mouth of substances that it finds offensive, such as salt, acid, mustard, etc., the saliva may flow in the same quantity as in the first case, but its quality is quite different—it is fluid and watery. If the dog is given now meat, now ordinary bread, then, other conditions being equal, the secretion of saliva in the second case will be more abundant than in the first. Similarly, some of the substances which are rejected by the animal, for example, such irritants as acid, alkali and others, evoke a more profuse secretion of saliva than other, chemically indifferent substances, like bitters; consequently here, too, different activity of the salivary glands is observed. The gastric glands react in the same way; they secrete their juice now in larger, now in smaller quantities, now of a higher and now of a lower acidity; its content of pepsin—a ferment dissolving protein—is sometimes greater, sometimes smaller. Bread evokes the secretion of gastric juice with the highest ferment content, but with a very low acid content; milk evokes the minimum ferment content, while meat evokes the maximum acid content. Under the action of certain quantities of protein introduced in the form of bread, the glands produce from two to four times as much protein ferment as in the case of meat or milk.

However, the diversity of the work of the gastric glands is not confined to the above-mentioned phenomena; it is manifested also in peculiar fluctuations in the quantity and quality of the reagents during the period of the functioning of the glands after the introduction of one or another food substance.

But that will suffice. I should only abuse your attention by giving an exposition of all the facts collected by us in this field. I shall merely remark that similar correlations were observed by us in the activity of all the other glands of the digestive canal.

Now it may be asked: what does this changeability in the work of the glands signify? In reply we shall revert to the phenomenon of salivary secretion. Edible substances evoke the secretion of thicker and more concentrated saliva. Why? The answer, obviously, is that this enables the mass of food to pass smoothly through the tube leading from the mouth into the stomach. Under the action of certain substances disagreeable to the dog the same glands secrete fluid saliva. What purpose does the saliva serve in such cases? Obviously, either to dilute these substances and thereby weaken their chemically irritating action, or, as we know from our own experience, to cleanse the mouth from such substances. In this case water, not mucus, is required, and the water is actually secreted.

As we have seen, bread, and especially dry bread, evokes secretion of considerably larger quantities of saliva than meat. This, too, is perfectly understandable: the eating of dry bread requires saliva, firstly, to dissolve the components of the bread and so make it possible to taste it (since something utterly inedible may get into the mouth!), and secondly, to soften the hard and dry bread, otherwise it would go down with difficulty and could even cause injury to the walls of the oesophagus while moving from the mouth to the stomach.

The relations inside the stomach are exactly the same. The bread protein induces secretion of more protein ferment than the protein of milk or meat, and a corresponding phenomenon is observed in the test tube: the protein of meat and milk is broken up by the protein ferment more easily than the vegetable protein.

Here again I could cite numerous additional examples of such expedient links between the work of the digestive glands and the properties of the substances entering the digestive canal (but this I shall do later, if and when opportunity offers). There is nothing surprising in this phenomenon; and no other relations could be expected. It is clear to all that the animal organism is a highly complex system consisting of an almost infinite quantity of parts connected both with one another and, as a single complex, with the surrounding world, with which it is in a state of equilibrium. The equilibrium of this system, as of any other system, is an indispensable condition for its existence. And if in certain cases we are unable to disclose the expedient connections in this system, the reason is that we lack knowledge; it does not mean that these connections are absent in a system that has the quality of permanence.

Now we shall pass to another question which arises from what has been said above: how is this equilibrium effected? Why is it that the glands produce and secrete in the canal the reagents needed for the successful treatment of the respective object? Clearly, it should be admitted that in some way the definite properties of the object act on the gland, evoke in it a specific reaction and cause its specific activity. Analysis of this influence on the gland is an extremely intricate matter and one that requires much time. The main thing is to reveal in the object those properties which, in this particular case, act as *stimuli* on the glands in question. An investigation of this kind is not so easy as it looks at first sight. Here are some facts to prove this. By means of the previously mentioned metal tube, we introduce meat into the empty and inactive stomach of the dog, without the animal noticing it. In a few minutes the gastric reagent, a solution of the gastric protein ferment, begins to exude from the walls of the stomach. But which property of the mass of meat has acted as the stimulus on the gastric glands? The simplest way would be to assume that this action has been caused by its mechanical properties—pressure, or friction against the walls of the stomach. But such an assumption would be absolutely wrong. Mechanical influences are completely ineffective with regard to the gastric glands. We can mechanically influence the wall of the stomach in any way—strongly or feebly, continuously or with interruptions, on limited areas or in a diffused way—but without obtaining a single drop of gastric juice. Actually it is the components of meat dissolved in water that are the stimulating substances. However, as yet we lack sufficient knowledge of these substances since the extractive substances of meat form a vast group that still awaits investigation in full measure.

Here is one more example. A few minutes after the chyme finds its way into the nearest section of the digestive canal—into the duodenum—one of the glands of this section comes into action; this is the *pancreas*—a large organ located at the side of the digestive canal and connected with it by an excretory duct. But which of the properties of the chyme advancing in the bowels act as a stimulating agent on the gland? Contrary to our expectations, it turned out that this action was exerted not by the properties of the consumed food, but by the properties of the juice which joined it in the stomach, namely, by its acid content. If we pour into the stomach or directly into the intestine pure gastric juice, or simply the acid which it contains, and even some other acid, our gland will begin to function just as vigorously, or even more vigorously, than in the case of the normal chyme passing from the stomach into the bowels. The profound significance of this unexpected fact is quite clear.

The gastric laboratory uses its protein ferment under an acid reaction. Different intestinal ferments, and, among them, naturally, pancreatic ferments, cannot develop their activity in an acid medium. Hence, it is clear that the first task of the laboratory is to provide the neutral or alkaline reaction necessary for its fruitful activity. These relations are effected by the above-mentioned interconnections, since the acid content of the stomach, as already stated, induces secretion of alkaline pancreatic juice (and the higher the acid content, the greater the secretion). Thus, the pancreatic juice acts first of all as a solution of soda.

One more example. It has been known for a long time that the pancreatic juice contains all the three ferments which act on the major food substances—the protein ferment, which is different from the gastric, the starchy ferment and the fatty ferment. As proved by our experiments, the protein ferment in the pancreatic juice is, constantly or at times, wholly or partly (this is still a matter of argument), in an inert, latent form. This can be explained by the fact that an active protein ferment might endanger the other two pancreatic ferments and destroy them. Simultaneously we established that the walls of the upper section of the bowels send into its lumen a special fermentative substance the purpose of which is to transform the inert pancreatic protein ferment into an active one. The active ferment, upon coming into contact with the protein substances of the food in the bowels, loses its noxious action with regard to other ferments. *The above-mentioned special intestinal ferment is secreted by the wall of the intestine due solely to the stimulating action of the pancreatic protein ferment.*

Thus, the expedient connection of phenomena is based on the specific properties of the stimuli and on the similarly specific reactions corresponding to them. But this by no means exhausts the subject. Now the following question should be put: how does the given property of the object, the given stimulant, reach the glandular tissue itself, its cellular elements? The system of the organism, of its countless parts, is united into a single entity in two ways: by means of the specific tissue which exists solely for the purpose of maintaining mutual relations, that is, the nervous tissue, and by means of tissue fluids which wash all the tissue elements. It is these very intermediaries that transmit our stimuli to the glandular tissue. We have thoroughly investigated the first of these interrelations.

Long before us it was established that the work of the salivary glands is regulated by a complex nervous apparatus. The endings of the centripetal sensory nerves are irritated in the oral cavity by different stimuli; the irritation is transmitted via these nerves to the central nervous system and thence, with the help of special centrifugal, secretory nerve fibres directly connected with the glandular cells, it reaches the secretory elements and induces them to certain activity. As is known, this process, as a whole, is designated as a *reflex* or as a reflex stimulation.

We have asserted, and we have proved experimentally, that normally this reflex is always of a specific nature, that is, that the endings of the centripetal nerves receiving the stimulation are different, each sending out a reflex only when there are definite external stimuli. Accordingly, the stimulus reaching the glandular cell must also be of a specific, peculiar character. This is a very profound mechanism securing the expedient dependence of the work of the organs on the external influences, and the connection which is effected with the help of the nervous system.

As was to be expected, the discovery of the nervous apparatus of the salivary glands immediately impelled physiologists to seek a similar apparatus in other glands lying deeper in the digestive canal. And despite the big expenditure of effort, positive results in this respect baffled researchers for a long time. Obviously the new objects of investigation had important properties which prevented the researchers, using the old methods, from disclosing anything.

Having taken into account these specific relations, we were able, fortunately, to achieve what for a long time had been regarded as a pium desiderium.[27] Physiology has, at last, gained control over the nerves which stimulate the gastric glands and the pancreas. Our success was mainly due to the fact that we stimulated the nerves of animals that freely stood on their feet and were not subjected to morbid irritation either during stimulation of their nerves or immediately before it.

Our experiments proved the existence not only of a nervous apparatus in the above-mentioned glands, but also disclosed facts clearly showing the participation of these nerves in normal activity. Here is a striking example.

We performed two simple operations very easily endured by dogs, and after which, if taken good care of, they live for years absolutely healthy and normal. The operations were as follows: 1) The oesophagus was severed at the neck and both ends separately sutured to the skin of the neck in a way that prevented food passing from the mouth into the stomach of the animal—it fell through the upper opening of the digestive canal; 2) a metal tube was introduced into the stomach through the abdominal wall—an operation mentioned earlier and already practised long ago. It will be understood that the animals were fed in a way that allowed the food to enter direct into the stomach through the metal tube. When, after a fast of several hours and after the empty stomach of the dog had been thoroughly washed, the animal was fed in the normal way (the food, as already mentioned, falling out of the oesophagus without reaching the stomach), in a few minutes the empty stomach began to secrete pure gastric juice. The secretion lasted as long as the animal was given food, sometimes even persisting long after the discontinuance of the so-called sham feeding. In these conditions the secretion of juice is very abundant, and it is possible to obtain in this way hundreds of cubic centimetres of gastric juice. In our laboratory we perform this operation on many dogs and the gastric juice thus obtained not only serves the purposes of research, but is also a good remedy for patients suffering from insufficient activity of the gastric glands. Thus a part of the vital supplies of our animals, which live for years (more than seven or eight years) without revealing even the slightest deviation from normal health, proves beneficial to man.

From the above-mentioned experiment it is clear that the mere process of eating, even when the food does not reach the stomach, stimulates the gastric glands. If we sever at the neck of this dog the so-called vagus nerves, the sham feeding will not cause any secretion of gastric juice, no matter how long the dog lives and how well it feels. Thus, the stimulation produced by the process of eating reaches the gastric glands via the nervous fibres contained in the vagus nerves.

Now I shall take the liberty of deviating briefly from the main topic of my lecture. The severing of nn. vagorum is an operation that has been performed on animals for a long time and has always proved fatal. In the course of the 19th century physiologists studied the numerous influences exerted by the vagus nerves on the different organs, and their respective investigations revealed at least four disturbances which take place in the organism after the sectioning of these nerves, each of which is by itself of a lethal character. Appropriate measures were taken by us to prevent these disturbances in our dogs; one of these measures related to the digestive system; thanks to this the animals whose vagus nerves were severed enjoyed a healthy and happy life. Thus, four simultaneously acting lethal factors were deliberately eliminated. Here we have striking proof of the power of science, which regards the organism as a machine!

Some ten years ago the great man to whom science owes its annual gatherings in Stockholm honoured me and my late friend, Prof. Nentsky,[28] with a letter enclosing a considerable gratuity for the best laboratory in our charge; in that letter Alfred Nobel displayed his keen interest in physiological experiments and suggested some of his own highly edifying schemes for experiments touching on the supreme tasks of physiology, the problems of the ageing and dying away of organisms. Indeed, physiology can justly anticipate big victories in this field; the power of physiology is by no means confined to what has already been achieved. This may be accomplished in the future only if our knowledge of the organism, which is an extremely complex mechanism, is deepened and extended. An example in support of this has been just cited by me.

I shall now revert to the subject of my lecture. Among the stimuli of the digestive glands there is one category—it has not yet been mentioned—which, quite unexpectedly, came right into the foreground during our investigations. True, it has long been known that the sight of tasty food makes the mouth of a hungry man water; absence of appetite, too, has always been regarded as undesirable, from which it can be deduced that appetite is closely linked with the process of digestion. In physiology mention was made also of the psychical stimulation of both the salivary and gastric glands. It should be pointed out, however, that psychical stimulation of the gastric glands has not been universally recognized, and generally speaking, the outstanding role of psychical stimulation in the processing of food in the digestive canal has not met with proper acknowledgement. Our investigations forced us to bring these influences to the fore. Appetite, the craving for food, is a constant and powerful stimulus to the gastric glands. There is not a dog in which skilful teasing with food does not evoke a more or less considerable secretion of juice in the empty and hitherto inactive stomach. At the mere sight of food nervous and excitable animals secrete several hundred cubic centimetres of gastric juice, while the sedate and quiet animal secretes only a few cubic centimetres. By changing the experiment in a definite way, an extremely profuse secretion of juice is observed in all animals without exception; I have in mind the previously mentioned experiment with sham feeding, when the food cannot get from the mouth into the stomach. A very thorough and frequently repeated analysis of this experiment convinced us that in this case the secretion of juice cannot be regarded as being the result of a simple, reflex stimulation of the mouth and throat by the ingested food. Any chemical irritant can be introduced into the mouth of a dog operated upon in this way, and still the stimulation will not induce the secretion of even a single drop of gastric juice. From this one might conclude that the oral cavity is stimulated not by every chemical substance but only by specific substances contained in the ingested food. However, continued observations did not confirm this supposition. The action of one and the same food, as a gland stimulus, differs, depending on whether the food was eaten by the animal with avidity or unwillingly, in response to command. Generally, the following invariable phenomenon is observed: each kind of food ingested by the dog during the experiment acts as a strong stimulus only when it suits the dog's taste. We must assume that in the act of eating the craving for food, that is, appetite—and therefore a psychical phenomenon—serves as a powerful and constant stimulus. The physiological significance of this juice, which we termed *appetite* juice, proved exceptionally great. If we introduce bread into the dog's stomach via a metal tube so as to prevent the dog from noticing it, i.e., without stimulating its appetite, the bread may remain in the stomach unchanged for a whole hour, without evoking even the slightest secretion of juice, since it lacks the substances that would stimulate the gastric glands. But when the same bread is swallowed by the animal, the gastric juice secreted in this case, that is, the appetite juice, exerts a chemical influence on the protein substances of the bread, or, in everyday terminology, digests it. Some of the substances obtained from protein subjected to this change act in turn on the gastric glands as independent stimuli; they thereby carry on the work begun by the first stimulus, the appetite, which is now, in the normal course of things, receding.

In the course of our study of the gastric glands we became convinced that appetite acts not only as a general stimulus to the glands, but that it also stimulates them in *varying degree*, depending on the object on which it is directed. For the salivary glands the rule obtains that all the variations of their activity observed in physiological experiments are exactly duplicated in the experiments with psychical stimulation, i.e., in those experiments in which the given object is not brought into direct contact with the mucous membrane of the mouth, but attracts the animal's attention from a distance. For example, the sight of dry bread evokes a stronger secretion of saliva than the sight of meat, although the meat, judging by the animal's movements, may excite a much livelier interest. On teasing the dog with meat or any other edible substance a highly concentrated saliva flows from the submaxillary glands; on the contrary, the sight of disagreeable substances produces the secretion of a very fluid saliva from the same glands. In a word, the experiments with psychical stimulation prove to be exact, but miniature, models of the experiments with physiological stimulations by the same substances. Thus, with regard to the work of the salivary glands, psychology occupies a place close to that of physiology. More than that! At first sight the psychical aspect of this activity of the salivary glands appears even more incontrovertible than the physiological. When any object that attracts the attention of the dog from a distance produces salivary secretion, one has all the grounds for assuming that this is a psychical and not a physiological phenomenon. When, however, the dog has eaten something or substances have been forcibly introduced into its mouth, saliva begins to flow, it is still necessary to prove the presence in this phenomenon of a certain physiological cause, to demonstrate that it is not of a purely psychical character, but is reinforced because of the special conditions accompanying it. These concepts correspond all the more to reality, since, after the severance of all the sensory nerves of the tongue, most substances entering the mouth in the process of eating or forceful feeding, evoke, strange as it may seem, the identical pre-operative action of the salivary glands. It is necessary to go further and resort to more radical measures such as poisoning the animal or destroying the higher parts of the central nervous system, in order to become convinced that between substances stimulating the oral cavity and the salivary glands there is not only a psychical but also a physiological connection. Thus we have two series of obviously different phenomena. But how is the physiologist to regard the psychical phenomena? It is impossible to disregard them because they are closely bound up with the purely physiological phenomena in the work of the digestive glands with which we are preoccupied. And if the physiologist intends to pursue his study of them he finds himself faced with the question: How?

Since we based ourselves on the experience acquired by us in the lowest organized representatives of the animal kingdom, and, naturally, desired to remain physiologists instead of becoming psychologists, we preferred to maintain a purely objective attitude also in regard to the psychical phenomena in our experiments with animals. Above all, we tried to discipline our thought and our speech in order completely to ignore the mental state of the animal; we limited our work to thorough observation and exact description of the influence exerted by distant objects on the secretion of the salivary glands. The results corresponded to our expectations—the relations between the external phenomena and the variations in the work of the glands could now be systematized; they proved to be of a regular character since they could be reproduced at will. To our great joy, we saw for ourselves that we had taken the right path in our observations, leading us to success. I shall cite some examples illustrating the results achieved by us with the help of these new methods.

If the dog is repeatedly teased with the sight of objects inducing a salivary secretion from a distance, the reaction of the salivary glands becomes weaker and weaker and finally drops to zero. The shorter the intervals between separate stimulations, the quicker the reaction reaches zero, and vice versa. These rules are fully manifested only when the conditions of the experiments remain unchanged. Identity of the conditions, however, may be only of a relative character; it may be confined only to those phenomena of the external world that were previously associated with the act of eating or with the forceful introduction of corresponding substances into the animal's mouth; the change of other phenomena is of no significance. This identity is easily attained by the experimenter so that an experiment in which a stimulus repeatedly applied from a distance gradually loses its effect, can be readily demonstrated even in the course of one lecture. If in a repeated stimulation from a distance a certain substance becomes ineffective, this does not mean that the influence of other substances is thereby eliminated. For example, when milk ceases to stimulate the salivary glands, the action of bread remains strongly effective, and when the bread loses its effect owing to repetition of the experimental stimulation, acid or other substances still produce their full action on the glands. These relations also explain the real meaning of the above-mentioned identity of experimental conditions; every detail of the surrounding objects appears as a new stimulus. If a certain stimulus has lost its influence, it can be restored only after a rest of several hours duration. However, the lost action can be restored without fail at any time by special means.

If bread repeatedly shown to the dog no longer stimulates its salivary glands, it is only necessary to let the animal eat it and the effect of the bread placed at a distance is fully restored. The same result is obtained when the dog is given some other food. More than that. If a substance producing a salivary secretion, for instance, acid, is introduced into the dog's mouth, even then the original distant effect of bread is restored. Generally speaking, everything that stimulates the salivary glands restores the lost reaction; the greater their activity, the more fully it is restored.

However, the reaction can be inhibited with the same regularity by certain artificial means, if, for example, some extraordinary stimuli act on the eye or ear of the dog, evoking in the latter a strong motor reaction, say, a tremor of the whole body.

Since time is short I shall limit myself to what I have said and pass to a theoretical consideration of these experiments. Our facts fit in readily with physiological thought. The stimuli which act from a distance may be rightly termed and regarded as reflexes. Careful observation shows that the activity of the salivary glands is always excited by certain external phenomena, that like the usual physiological salivary reflex, it is caused by external stimuli. But while the latter emanates from the oral cavity, the former comes from the eye, nose, etc. The difference between the two reflexes is that our old physiological reflex is constant and unconditioned, whereas the new reflex is permanently subject to fluctuation, and is, therefore, *conditioned.* Examining the phenomena more closely we can see the following essential distinction between the two reflexes: in the unconditioned reflex the properties of the substance act as a stimulus with which the saliva has to deal physiologically, for example, the hardness, dryness, definite chemical properties, etc.; in the conditioned reflex, on the contrary, the properties of the substance which bear no direct relation to the physiological role of the saliva act as stimuli, for example, colour, etc. These last properties appear here as *signals* for the first ones. We cannot but notice in their stimulating action a wider and more delicate adaptation of the salivary glands to the phenomena of the external world. Here is an example. We are getting ready to introduce acid into the dog's mouth; in the interest of the integrity of the buccal mucous membrane it is obviously very desirable that before the acid enters the mouth, there should be more saliva; on the one hand the saliva hinders direct contact of the acid with the mucous membrane and, on the other hand, it immediately dilutes the acid, thus weakening its injurious chemical effect. However, in essence the signals have only a conditional significance: on the one hand, they are readily subject to change, and on the other, the signalizing object cannot come into contact with the mucous membrane of the mouth. Consequently, the finer adaptation must consist in the fact that the properties of the signalling objects now stimulate the salivary glands, and at other times do not. And that is what really happens. Any phenomenon of the external world can be made a temporary signal of the object which stimulates the salivary glands, provided the stimulation of the mucous membrane of the mouth by the object has been associated once or more times with the action of the given external phenomenon on other receptor areas of the surface of the body. In our laboratory we are trying out many such highly paradoxical combinations; and the experiment is proving successful. On the other hand, rapidly acting signals can lose their stimulating effect if repeated over a long period without bringing the corresponding object into contact with the mucous membrane of the mouth. If ordinary food is shown to a dog for days and weeks, without giving it to him to eat, then the sight of the food will, finally, cease to produce a salivary secretion. The mechanism of stimulation of the salivary glands through the signalling properties of the objects, i.e., the mechanism of "conditioned stimulation," can be easily conceived from the physiological point of view as a function of the nervous system. As we have just seen, at the basis of each conditioned reflex, i.e., of stimulation through the signalling properties of an object, there is an unconditioned reflex, that is, a stimulation through the essential attributes of the object. Thus, it must be assumed that the point of the central nervous system which is strongly stimulated during the unconditioned reflex, attracts to itself weaker stimuli proceeding from the external world to other points of the central nervous system, i.e., thanks to the unconditioned reflex there is opened for all other external stimuli a temporary, casual path leading to the central point of this reflex. The conditions influencing the opening and closing of the path, its practicability and desolation, constitute the internal mechanism of the effectiveness or ineffectiveness of the signalling properties of the external objects; they are the physiological basis of the most delicate reactivity of the living substance, of the most delicate adaptation of the animal organism.

It is my firm conviction that physiological research will be successfully and greatly advanced along the lines which I have sketched here.

In point of fact only one thing in life is of actual interest for us—our psychical experience. But its mechanism has been and still remains wrapped in mystery. All human resources—art, religion, literature, philosophy and historical science—have combined to throw light on this darkness. Man has at his disposal yet another powerful resource—natural science with its strictly objective methods. This science, as we all know, is making big headway every day. The facts and considerations which I have placed before you are one of the numerous attempts to employ—in studying the mechanism of the highest vital manifestations in the dog, the representative of the animal kingdom which is man's best friend—a *consistent*, purely scientific method of thinking.

IV

PROBLEM OF THE STUDY OF HIGHER NERVOUS ACTIVITY AND THE WAYS OF ITS EXPERIMENTAL SOLUTION

EXPERIMENTAL PSYCHOLOGY AND PSYCHOPATHOLOGY IN ANIMALS[29]

Regarding the language of facts as most eloquent, I shall take the liberty of proceeding directly to the experimental material, which gives me the right to speak on the subject of my present communication.

To begin with, this is the history of the transition of the physiologist from research into purely physiological problems to the sphere of phenomena usually called psychical. Although this transition took place suddenly, it occurred in a perfectly natural way, and what seems to me most important in this respect, without changing the, so to speak, methodological front.

In studying over a period of years the normal working of the digestive glands, and analysing the constant conditions of this work, I came upon conditions of a psychical character, which, incidentally, had been observed by others before me. There were no grounds for neglecting these conditions, since they participated constantly and prominently in the normal physiological process. I was obliged to investigate them if I wanted to make a really thorough study of my subject. But how? All that follows in my exposition supplies the answer to this question.

From all our material I shall select only the experiments with the salivary glands—organs which apparently play a very insignificant physiological role; however, I am convinced that they will become classical objects for the new type of research about which I shall have the honour of telling you today; part of this research has already been carried out and part is in the planning stage.

In observing the normal working of the salivary glands one cannot but be amazed by the high degree of their adaptability.

Give the animal dry, hard food substances and there will be an abundant salivary secretion—give it liquid food and the secretion will be much smaller.

It is obvious that for the chemical testing of the food, for mixing it and converting it into a lump to be swallowed, water is required—and the salivary glands supply it. From the mucous salivary glands there flows for every kind of food, saliva rich in mucin—a lubricating saliva, which facilitates the smooth passage of the food into the stomach. All highly irritant substances, such as acids, salts, etc., also produce a salivary secretion which varies in accordance with the strength of their stimulating action, clearly, as we know from everyday experience, the purpose of this secretion is to neutralize or dilute the substances and to cleanse the mouth. In this case the mucous glands secrete fluid saliva containing little mucin. For what would be the purpose of the mucin here? If pure insoluble quartz pebbles are placed in the mouth of a dog it will move them around, try to chew them, and finally, it will drop them. There is either no secretion of saliva at all, or at most two or three drops flow out. Again, what purpose would the saliva serve here? The pebbles are easily ejected by the animal and nothing remains in the mouth. But if sand is placed in the dog's mouth, i.e., the same pebbles but in pulverized form, there will be an abundant flow of saliva. It is clear that without saliva, without fluid in the oral cavity, the sand could neither be ejected, nor forwarded to the stomach.

Here we have exact and constant facts—facts which seem to imply intelligence. But the entire mechanism of this intelligence is absolutely plain. On the one hand, physiology has long known about the centrifugal nerves of the salivary glands, which now chiefly cause water to enter into the saliva, and now accumulate in the saliva special organic substances. On the other hand, the internal lining of the oral cavity consists of separate areas which act as receptors of different special stimuli—mechanical, chemical, thermal. Moreover, these stimuli may be further subdivided, the chemical, for example, into salts, acids, etc. There are grounds for assuming that the same thing is true of the mechanical stimuli. It is in the areas acting as receptors of special stimuli that the specific centripetal nerves have their origin.

Thus, the reactions of adaptation are based on a simple reflex originated by definite external conditions acting only on certain kinds of centripetal nerve endings; from here the excitation passes along a definite nervous path to the centre, and thence, also along a definite path, to the salivary gland, evoking its specific function.

In other words, this is a specific external agent evoking a specific reaction in living matter. At the same time we have here a typical example of what we call adaptation or fitness. Let us dwell for a moment on these facts and terms, since they play, obviously, an important role in modern physiological thought. What, exactly, is the fact of adaptation? It is, as we have just seen, simply the exact co-ordination of the elements making up a complex system and of the entire complex with the surrounding world.

But the same thing can be observed in any inanimate object. Take, for example, a complex chemical object. This object exists thanks to equilibration between its separate atoms and groups, between the object as a whole and the surroundings.

In exactly the same way the immense complexity of the higher and lower organisms exists as a whole so long as all its constituents are delicately and strictly co-ordinated and equilibrated both with one another and with the external conditions.

The analysis of the equilibration of this system is the prime task and aim of physiological investigation as purely objective investigation. There can hardly be two opinions on this point. Unfortunately, so far we have no purely scientific term to denote this fundamental property of the organism, its external and internal equilibrium. Many people hold that the terms now in use—fitness and adaptation (despite their natural-scientific, Darwinist analysis)—bear the stamp of subjectivism, which leads to misunderstanding in two opposite directions. The rigid adherents of the physico-mechanical theory of life see in these words an anti-scientific tendency—a retreat from pure objectivism to speculation and teleology.[30] On the other hand, philosophically inclined biologists see in every fact relating to adaptation and fitness proof of the existence of a special vital force, or, as it is now more and more often called, spiritual force (vitalism, apparently, gives way to animism[31]), which defines its own goal, chooses its means, adapts itself, etc.

And so, in the afore-mentioned physiological experiments with the salivary glands we, in our investigation, remain strictly within the bounds of natural science. We shall now pass to another sphere of phenomena which, it would seem, belong to quite a different category.

All the foregoing objects, which, after being placed in the mouth, influenced the salivary glands in different and at the same time definite ways, exert on these glands exactly the same action, at least qualitatively, when placed at a certain distance from the dog. Dry food produces much saliva—moist food only a little. A thick, lubricating saliva flows from the mucous glands to the food substances. Various inedible irritants also produce secretion from all the glands, including the mucous glands. But it is fluid and contains but a small amount of mucin. Pebbles, when shown to the animal, have no effect on the glands, while sand evokes profuse salivation. These facts were partly obtained and partly systematized in my laboratory by Dr. S. G. Wolfson. The dog sees, hears, and smells all the substances, pays attention to them, rushes to them if edible or agreeable, but turns away from them and resists their introduction into the mouth when disagreeable. Everybody would say that this is a psychical reaction, psychical stimulation of the animal's salivary glands.

How should the physiologist regard these facts? How can he establish them? How to analyse them? What are they compared with physiological facts? What are their common features and in what way are they distinguished from one another?

Must we, for the purpose of getting to know the new phenomena, penetrate into the inner state of the animal, visualize its feelings and desires in our own way?

It seems to me that for the naturalist there is only one answer to the last question—an emphatic "No." Where is there even the slightest indisputable criterion that our conjectures are correct, that we can, for the sake of a better understanding of the matter, compare the inner state of even such a highly developed animal as the dog with our own? Further: is not the eternal sorrow of life the fact that in most cases human beings do not understand each other and cannot enter into the inner state of the other? And then, where is the knowledge, where is the power of knowledge that might enable us correctly to comprehend the state of another human being? At first, in our psychical experiments with the salivary glands (for the time being we shall use the term "psychical"), we conscientiously endeavoured to explain our results by imagining the subjective state of the animal. But nothing came of this except sterile controversy and individual views that could not be reconciled. And so we could do nothing but conduct the research on a purely objective basis; our first and especially important task was completely to abandon the very natural tendency to transfer our own subjective state to the mechanism of the reaction of the animal undergoing the experiment and to concentrate instead on studying the correlation between the external phenomena and the reaction of the organism, i.e., the activity of the salivary glands. Reality had to decide whether elaboration of the new phenomena was possible in that direction. I make bold to say that the following account will convince you, as I am convinced, that a boundless field of fruitful research opens before us in the given case; it is another and immense part of the physiology of the nervous system, a system which mainly establishes the correlation not between the separate parts of the organism, our main subject so far, but between the organism and the surroundings. Unfortunately, to date the influence of the surrounding world on the nervous system has been studied mainly in relation to subjective reactions—the content of the modern physiology of the sense organs.

In our psychical experiments we have before us definite external objects, exciting the animal and evoking in it a definite reaction, in the given case—secretion of the salivary glands. As has been said, the effect of these objects is substantially the same as in the physiological experiments, when they come into contact with the oral cavity. Consequently, we have before us simply further adaptation—the object acts on the salivary glands the moment it is being brought close to the mouth.

What are the specific features of these new phenomena compared with the physiological ones? Above all, the difference seems to be that in the physiological form of the experiment the substance comes into direct contact with the organism, while in the psychical form it acts from a distance. But this circumstance in itself, if we reflect on it, does not, obviously, signify any essential difference between these, in a way specific, experiments, and the purely physiological ones. The point is that in these cases the substances act on other special receiving surfaces of the body—nose, eye, ear—through the medium in which both the organism and the stimulating substances exist (air, ether). How many simple physiological reflexes are transmitted by the nose, eye and ear, that is, originate at a distance! Hence, the essential difference between the new phenomena and the purely physiological does not lie here.

It lies much deeper, and should be sought, in my view, in a comparison of the following facts. In the physiological case the activity of the salivary glands is connected with the properties of the substance on which the effect of the saliva is directed. The saliva moistens dry substances and any ingested material; it neutralizes the chemical effect of the substances. These properties constitute the special stimuli of the specific mouth surface. Consequently, in the physiological experiments the animal is stimulated by the essential, unconditioned properties of the object in relation to the physiological role of the saliva.

In the psychical experiments the animal is excited by the properties of the external object, which are unessential for the activity of the salivary glands, or even entirely accidental. The visual, acoustic and even purely olfactory properties of our objects, when they are present in other objects, do not of themselves exert any influence on the salivary glands which, in their turn, so to speak, have no business relations with these properties. In the psychical experiments the salivary glands are stimulated not only by the properties of the objects unessential for the work of the glands, but absolutely by all the conditions surrounding these objects, or with which they are connected one way or another—for example, the dish in which they are contained, the article on which they are placed, the room, the people who usually bring the objects, even the noises produced by these people, though the latter may not be seen at the given moment—their voices, even the sound of their steps. Thus, in psychical experiments, the connection of the objects acting as stimuli on the salivary glands becomes more and more distant and delicate. Here, undoubtedly, we have a phenomenon of further adaptation. We can admit in this case that such a distant and delicate connection as that between the step of the person who usually feeds the animal and the working of the salivary glands has no specific physiological significance other than its delicacy. But we need only recall those animals whose saliva contains protective poison, to appreciate the great vital significance of this timely provision of a protective means against an approaching enemy. The significance of the distant signs of objects producing a motor reaction in the organism, is, of course, easily recognized. By means of distant and even accidental characteristics of objects the animal seeks its food, evades enemies, etc.

If that is so, then the following questions are of decisive significance for our subject: can this seemingly chaos of relations be included in a definite scheme? Is it possible to make the phenomena constant, to disclose the laws governing their development and their mechanism? It seems to me that the examples which I shall now present entitle me to give an emphatically positive answer to these questions, to find at the basis of all psychical experiments the one and same special reflex as the chief and most general mechanism. True, in its physiological form, our experiment, excluding, of course, all extraordinary conditions, always yields one and the same result; it is the unconditioned reflex. But the main feature of the psychical experiment is its impermanence, its obvious capriciousness. However, the results of a psychical experiment undoubtedly recur too, otherwise we would not speak of them at all. Consequently, the point is in the greater number of factors which influence the results of a psychical experiment compared with a physiological one. This, then, is a conditioned reflex. Here are facts which show that our psychical material may also be included in a definite scheme and that it is subject to certain laws. These facts were obtained in my laboratory by Dr. I. F. Tolochinov.

It is not difficult to recognize during the first psychical experiments the chief conditions guaranteeing their success, i.e., their constancy. If an animal is stimulated (i.e., its salivary glands) by food placed at a distance, the result of the experiment depends solely on whether the animal has been prepared for it by a certain period of fasting. An animal experiencing keen hunger yields positive results; on the contrary, the most voracious and least fastidious animal, if it has just had a good meal, fails to respond to food placed at a distance. Thinking in terms of physiology we can say that we have here a different degree of excitability of the salivary centre—greatly increased in the first case, and greatly decreased in the second. We may rightly assume that just as the carbonic acid contained in the blood determines the energy of the respiratory centre, so the different composition of the blood in a hungry animal and in one that is sated determines the above-mentioned fluctuations in the excitability and reactivity of the salivary centres. From the subjective point of view this could be designated as attention. When the stomach is empty, the sight of food easily causes the mouth to water; in sated animals the same reaction is either very weak or entirely lacking.

Let us proceed. If the animal is shown food or certain disagreeable substances, and if this is repeated several times, then with each repetition the experiment will produce a weaker result, and in the end there will be no reaction whatever. There is, however, a sure method of restoring the reaction; it can be achieved by giving the dog food or by introducing into its mouth substances which ceased to act as stimuli. This, of course, produces the usual strong reflex, and the object begins to act from a distance again. For the subsequent result it is immaterial whether food is placed in the mouth or any disagreeable substance. For example, if meat powder no longer stimulates the animal from a distance, its effect can be restored either by letting it eat the powder or by introducing into the mouth an undesired substance, e.g., acid. We can say that thanks to the direct reflex the excitability of the salivary centre has been heightened, and the weak stimulus—the object at a distance—has become sufficiently strong. Do we not experience the same thing ourselves when appetite comes with eating, or when, after unpleasant, powerful excitation, we begin to have the appetite that we previously lacked?

Here is a number of other facts of a constant character. The object placed at a distance stimulates the salivary glands not only by the entire complex of its properties, but also by its individual properties. If a hand smelling of meat or meat powder, is brought into proximity with the dog, it often proves sufficient to induce a salivary reaction. Similarly the sight of food placed at a distance, and consequently the mere optical effect of the object, may also stimulate the activity of the salivary glands. But the combined, simultaneous action of all these properties of the object always produces a better and greater effect, i.e., the action of the sum of the stimuli is more powerful than each individual stimulus.

The object acts on the salivary glands from a distance not only by means of its inherent properties but also by means of incidental qualities deliberately imparted to it. If we colour the acid black, then even water to which the same colour is added will influence the salivary glands from a distance. However, all incidental qualities deliberately imparted to the distant object begin to act as stimuli of the salivary glands only when the object with its newly acquired properties is brought into contact with the oral cavity at least once. Black-coloured water began to stimulate the salivary glands from a distance only after preliminary introduction of black-coloured acid into the dog's mouth. The stimuli of the olfactory nerves belong to the same group of conditioned properties. The experiments carried out in our laboratory by Dr. A. T. Snarsky showed that simple physiological reflexes from the nasal cavity acting on the salivary glands are conducted only through the sensory nerves lying along the trigeminal nerve. Ammonia, mustard oil, etc., always produce an invariable effect even in a curarized animal. However, if the trigeminal nerves are severed, this action fails. Odours lacking a local stimulating effect have no influence on the salivary glands.

If, for example, oil of anise is placed for the first time before a normal dog with constant salivary fistulae there will be no secretion of saliva. But if simultaneously with the odour the oil of anise (which produces a strong local irritation) is brought into contact with the dog's oral cavity, saliva secretion will be induced afterwards by the odour alone.

If food is combined with a disagreeable substance or with a certain property of the disagreeable substance, for example, if you show the dog meat moistened with acid, then, despite the fact that the dog reaches for the meat, a saliva secretion comes from the parotid gland (for meat alone there is no secretion from this gland), i.e., a reaction to the disagreeable substance. Moreover, if owing to repetition the action of the disagreeable substance placed at a distance becomes insignificant, then upon combining it with food which attracts the animal, the reaction always becomes intensified.

As mentioned above, dry food causes abundant saliva secretion, while moist food, on the contrary, produces either a weak flow of saliva or none at all. If one acts on a dog from a distance by showing it two extremes, for instance, dry bread and moist meat, the result will depend on the object which stimulates the dog more strongly, and this can be judged by its motor reaction. If, as usually happens, the dog is stimulated more strongly by the meat, then the only reaction will be the one peculiar to meat, i.e., there will be no saliva secretion. Thus, the bread, although it is before the dog's eyes, remains ineffective. It is possible to impart the smell of sausage or meat to dry bread so that the bread alone acts on the dog's eye, with the sausage or meat only leaving a smell, and yet the only reaction will be that induced by the sausage or meat.

The action of objects from a distance can be inhibited in other ways. If in the presence of a greedy, excitable dog we feed another dog, for example with dry bread, then the salivary glands, which previously evinced a most vivid reaction to the sight of bread, become inactive.

When the dog is placed on the stand for the first time, the sight of dry bread, which produced a very strong action on the salivary glands when the dog was on the floor, now has not even the slightest influence.

I have placed before you a number of easily and exactly recurring facts. It will be obvious that many striking instances of animal training belong to the same category as some of our facts. It follows, therefore, that they have long since testified to the strictly law-governed nature of certain psychical manifestations in animals. It is to be regretted that they have been left so long without science giving them the attention they merit.

So far in my exposition I have not mentioned any phenomenon corresponding to what in the subjective world we call desires. Actually we have not encountered such phenomena. On the contrary, the following fundamental fact constantly recurred before our eyes: the sight of dry bread, to which the dog hardly turned its head, produced an abundant secretion of saliva, whereas meat, to which the dog rushed with avidity, breaking from the stand and gnashing its teeth, failed to exert any influence on the salivary glands when placed at a distance. Thus, what in the subjective world we designate a desire, was expressed in our experiments only by the animal's motor reaction, but did not manifest any positive action on the salivary glands. Hence, the phrase that ardent desire stimulates the salivary or gastric glands in no way corresponds to reality. This sin of confusing what are obviously different things can be imputed also to me in my earlier articles. In our experiments we must, therefore, clearly distinguish between the secretory and the motor reactions of the organism; and in respect to the glands, if we compare our results with the phenomena of the subjective world, we must regard not the desire of the dog, but its attention, as the chief condition for the success of the experiments. The salivary reaction of the animal might be regarded in the subjective world as a substratum of elementary, pure notion, thought.

The above-mentioned facts, on the one hand, provide certain, and in my view, important conclusions about the processes taking place in the central nervous system; on the other hand, they make possible further successful analysis. Let us consider from the standpoint of physiology some of our facts, and first of all our fundamental fact. When a given object—a certain food or chemical irritant—is brought into contact with the special surface of the oral cavity and stimulates it by means of those of its properties on which the activity of the salivary glands is specially directed, then the other properties of the object that have nothing to do with the working of the salivary glands or even with the entire environment of the object, but simultaneously stimulating other sensory surfaces of the body, become connected, apparently, with the same nervous centre of the salivary glands to which the stimulation emanating from the essential properties of the object is conducted through a fixed centripetal path. It can be assumed in this case that the salivary centre acts in the central nervous system as a point of attraction for stimuli coming from other sensory surfaces. Thus, a certain path is opened from the other excited areas of the body to the salivary centre. But this connection of the centre with accidental points is very fragile and tends to disappear of itself. Constant repetition of simultaneous stimulation by means of the essential and unessential properties of the object is required to make this connection increasingly durable. In this way a temporary relation is established between the activity of a certain organ and the external objects. The temporary relation and its law—to become stronger as a result of repetition and to disappear when not repeated—play a big role in the well-being and integrity of the organism; by means of it the adaptability of the organism and the conformity of its activity to the surroundings become more perfect and delicate. The two parts of this law are equally important: if the temporary relation to the object is of great significance for the organism, then the rupture of this relation is essential when it is no longer justified by reality. Otherwise the relations of the animal, instead of being delicate, would assume a chaotic character.

Let us turn to another point. From the standpoint of physiology how do we regard the fact that the sight of meat destroys in the parotid gland the reaction to the sight of bread, i.e., that the saliva earlier secreted at the sight of bread ceases to flow when there is a simultaneous meat stimulation? One could assume that strong excitation in a definite motor centre corresponds to the strong motor reaction provided by the meat, as a consequence of which, according to the above-mentioned law, the stimulation is diverted from other parts of the central nervous system and in particular from the salivary centres, i.e., their excitability is diminished. This interpretation is supported by another experiment in which the secretion of saliva at the sight of bread is inhibited by the sight of another dog. Here the motor reaction to bread is really greatly intensified. Even more convincing would be an experiment in which the dog would prefer dry food to moist and display a stronger motor reaction to it. We should be quite right in our interpretation of this experiment if in the dog in question the sight of dry food did not evoke secretion of saliva, or if the secretion should be much less than in usual dogs. It is a well-known fact that a very strong desire often inhibits certain special reflexes.

But among the above-mentioned facts there are some which, from the physiological point of view, can be explained only with great difficulty; for example, why does a conditioned reflex, when repeated, invariably become ineffective? The natural explanation of fatigue is hardly acceptable, since in this case we are dealing with a weak stimulus. Actually the repetition of a strong stimulus of an unconditioned reflex does not bring on early fatigue.

Probably we have here altogether peculiar conditions for the excitation which is conducted along accidental centripetal paths.

From the above it is obvious that our new subject can be investigated quite objectively and that, in essence, it is a purely physiological subject. One can hardly doubt that analysis of this group of stimuli, coming into the nervous system from the external world will reveal to us laws of nervous activity and disclose its mechanism from aspects which so far have not been even touched upon by investigation of nervous phenomena in the organism, or have been touched upon only in rough outline.

Despite the complexity of the new phenomena, this investigation entails considerable advantages. In the present study of the mechanism of the nervous system, first, the experiments are conducted on animals that have just been injured by operations, and, secondly, and this is the chief thing, the nerve trunks of the animals are subjected to stimulation, i.e., the excitation extends simultaneously and in a uniform manner over a mass of highly diverse nervous fibres; such combinations, however, never occur in reality. Naturally, we experience great difficulty in discovering the laws of the normal activity of the nervous system, since we bring it to a state of chaos by our artificial stimulation. But in normal conditions, such as we maintained in our latest experiments, the stimulation is effected in an isolated manner, the correlations of the intensity being regulated.

Generally speaking this applies to all psychical experiments, but in the case of our psychical phenomena, observed in the activity of the salivary glands, there is another special advantage. For successful investigation of a subject, complex by its very nature, it is important to simplify it in some way or other. In the given case we have this simplification. The role of the salivary glands is so clear that their relation to the external environment of the organism must be equally clear and accessible to investigation and interpretation. However, it must not be imagined that the physiological role of the salivary glands is confined to the above-mentioned functions. By no means. For example, saliva is used by the animals for licking and healing wounds, a thing that we constantly see. This is probably the reason why we can obtain saliva by stimulating various sensory nerves. And yet the complexity of the physiological relations of the salivary glands is much less than that of the skeletal muscles through which the organism is connected with the external world in an endless number of ways. At the same time a simultaneous comparison of the secretory, especially salivary, reaction with the motor reaction enables us, on the one hand, to distinguish between the particular and the general, and on the other hand, to get rid of our stock of routine anthropomorphic concepts and interpretations relating to the motor reaction of the animals.

Having established the possibility of analysis and systematization of our phenomena we come to the next stage of our work—systematic division and derangement of the central nervous system in order to see how the previously established relations change. Thus, there will be an anatomical analysis of the mechanism of these relations. This will be the future and, I feel sure, the already approaching experimental psychopathology.

Here, too, the salivary glands as objects of investigation are of great value. The nervous system, which has a bearing on movement, is so highly intricate and predominates to such an extent in the brain that even the slightest damage to it often causes undesirable and very complicated results. The nervous system of the salivary glands, because of their inconsiderable physiological significance, comprises, it may be assumed, only a negligible portion of the brain substance, and is, consequently, so thinly distributed in the brain that its partial, isolated destruction does not bring about, even remotely, the difficulties which in this respect exist in the innervation motor apparatus. Of course, psychopathological experiments had their beginning at a time when the physiologists first removed these or other parts of the central nervous system and investigated the animals that survived these operations. In this respect the past twenty or thirty years have supplied us with a number of fundamental facts. We already know the drastic decline that takes place in the adaptive capacity of animals as a result of complete or partial extirpation of their cerebral hemispheres. But the investigation of this subject has not yet developed into a special branch, which could be studied without interruption and according to a definite plan. The reason for this, as I see it, is that the investigators still lack the more or less considerable and detailed knowledge of the animal's normal relations with the surrounding world that would enable them to make an objective and exact comparison of the state of the animal before and after the operation.

Objective investigation alone will gradually bring us to the complete analysis of that infinite adaptability in all its manifestations which constitutes life on earth. Are not the movements of plants towards light and the seeking of truth through mathematical analysis essentially phenomena of one and the same order? Are they not the last links of an almost endless chain of adaptation taking place throughout the living world?

We can analyse adaptation in its most elementary forms on the basis of objective facts. Is there any reason for changing this method in the study of adaptability in the higher orders?

Work in this direction has been started at different levels of life and has advanced without encountering obstacles. The objective study of living matter, which begins with the theory of tropisms of elementary living things, can and must remain objective also when it reaches the highest manifestations of the animal organism, the so-called psychical phenomena in the higher animals.

Guided by the similarity or identity of external manifestations, science, sooner or later, will apply the objective facts also to our subjective world and thereby shed a bright light on our mysterious nature, elucidate the mechanism and the vital significance of that which occupies the human mind most—his consciousness and its torments. This explains why in my exposition I have some words which sounded as if they were contradictory. In the title of my paper and throughout my exposition I have used the term "psychical," at the same time bringing forward only objective investigation and leaving aside everything subjective. The vital phenomena that are termed psychical, despite the fact that they are objectively observed in animals, are only distinguished from purely physiological phenomena by degree of complexity. It makes no difference whether they are termed psychical or complex-nervous as distinct from the simple physiological, once it is realized and recognized that the naturalist should approach them only objectively, leaving aside the question of the essence of these phenomena.

Is it not clear that contemporary vitalism, that is, animism, confuses the different points of view of the naturalist and of the philosopher. The former always bases his grandiose success on the study of objective facts and their comparisons, disregarding on principle the question of the essence and final causes; the latter, personifying the highest aspiration of man for synthesis—although up to now it has been of a fantastic nature—and seeking to provide the answer to everything relating to the human being, must right now create an entity from the objective and the subjective. For the naturalist everything lies in the method, in the chance of obtaining an unshakeable, lasting truth; and solely from this point of view, which for him is obligatory, the soul, as a naturalistic principle, is not only unnecessary but even harmful to his work, in vain limiting his courage and the depth of his analysis.

V

METHODS OF INVESTIGATION AND FUNDAMENTAL LAWS OF DEVELOPMENT

LECTURES ON THE WORK OF THE CEREBRAL HEMISPHERES[32]

LECTURE ONE

The substantiation and the history of the fundamental methods employed in the investigation of the activity of the cerebral hemispheres. The concept of the reflex. The variety of reflexes. Signalling activity as the most general physiological characteristic of the cerebral hemispheres.

Gentlemen,

One cannot but be struck by a comparison of the following facts. First, the cerebral hemispheres, the higher part of the central nervous system, is a rather impressive organ. In structure it is exceedingly complex, comprising millions and millions (in man—even billions) of cells, i.e., centres or foci of nervous activity. These cells vary in size, shape and arrangement and are connected with each other by countless branches. Such structural complexity naturally suggests a very high degree of functional complexity. Consequently, it would seem that a boundless field of investigation is offered here for the physiologist. Secondly, take the dog, man's companion and friend since prehistoric times, in its various roles as hunter, sentinel, etc. We know that this complex behaviour of the dog, its higher nervous activity (since no one will dispute that this is higher nervous activity), is chiefly associated with the cerebral hemispheres. If we remove the cerebral hemispheres in the dog (Goltz and others), it becomes incapable of performing not only the roles mentioned above, but even of looking after itself. It becomes profoundly disabled and will die unless well cared for This implies that both in respect of structure and function, the cerebral hemispheres perform considerable physiological work.

Let us turn now to man. His entire higher nervous activity is also dependent on the normal structure and functioning of the cerebral hemispheres. The moment the complex structure of his hemispheres is damaged or disturbed in one way or another, he also becomes an invalid, he can no longer freely associate with his fellows as an equal and must be isolated.

In amazing contrast to this boundless activity of the cerebral hemispheres is the scant content of the present-day physiology of these hemispheres. Up to 1870 there was no physiology of the cerebral hemispheres at all, they seemed inaccessible to the physiologist. It was in that year that Fritsch and Hitzig first successfully applied the ordinary physiological methods of stimulation and destruction to their study. Stimulation of certain parts of the cerebral cortex regularly evoked contractions in definite groups of the skeletal muscles (the cortical motor region). Extirpation of these parts led to certain disturbances in the normal activity of the corresponding groups of muscles.

Shortly afterwards H. Munk, Ferrier and others demonstrated that other regions of the cortex, seemingly not susceptible to artificial stimulation, are also functionally differentiated. Removal of these parts leads to defects in the activity of certain receptor organs—the eye, the ear and the skin.[33]

Many researchers have been thoroughly investigating these phenomena. More precision and more details have been obtained, especially as regards the motor region, and this knowledge has even found practical application in medicine; however, investigation as yet has not gone far beyond the initial point. The essential fact is that the entire higher and complex behaviour of the animal, which is dependent on the cerebral hemispheres, as shown by the previously mentioned experiment by Goltz with the extirpation of the hemispheres in a dog, has hardly been touched upon in these investigations and is not included even in the programme of current physiological research. What do the factors relating to the cerebral hemispheres, which are now at the disposal of the physiologist, explain with regard to the behaviour of the higher animals? Is there a general scheme of the higher nervous activity? What kind of general rules govern this activity? The contemporary physiologist finds himself truly empty-handed when he has to answer these lawful questions. While the object of investigation is highly complex in relation to structure, and extremely rich in function, research in this sphere remains, as it were, in a blind alley, unable to open up before the physiologist the boundless vistas which might have been expected.

Why is this so? The reason is clear: the work of the cerebral hemispheres has never been regarded from the same point of view as that of other organs of the body, or even other parts of the central nervous system. It has been described as special *psychical* activity which we feel and apprehend in ourselves and which we suppose exists in animals by analogy with human beings. Hence the highly peculiar and difficult position of the physiologist. On the one hand, the study of the cerebral hemispheres, as of all other parts of the organism, seems to come within the scope of physiology, but on the other hand, it is an object of study by a special branch of science—psychology. What, then, should be the attitude of the physiologist? Should he first acquire psychological methods and knowledge and only then begin to study the activity of the cerebral hemispheres? But there is a real complication here. It is quite natural that physiology, in analysing living matter, should always base itself on the more exact and advanced sciences—mechanics, physics and chemistry. But here we are dealing with an altogether different matter, since in this particular case we should have to rely on a science which has no claim to exactness as compared with physiology. Until recently discussion revolved even around the question whether psychology should be considered a natural science or a science at all. Without going deeply into this question, I should like to cite some facts which, although crude and superficial, seem to me very convincing. Even the psychologists themselves do not regard their science as being exact. Not so long ago James, an outstanding American psychologist,[34] called psychology not a science, but a "hope for science." Another striking illustration has been provided by Wundt,[35] formerly a physiologist, who became a celebrated psychologist and philosopher and even the founder of the so-called experimental psychology. Prior to the war, in 1913, a discussion took place in Germany as to the advisability of separating the psychological branch of science from the philosophical in the universities, i.e., of having two separate chairs instead of one. Wundt opposed separation, one of his arguments being the impossibility of establishing a common and obligatory examination programme in psychology, since each professor had his own ideas of the essence of psychology. Is it not clear, then, that psychology has not yet reached the stage of an exact science?

This being the case, there is no need for the physiologist to have recourse to psychology. In view of the steadily developing natural science it would be more logical to expect that not psychology should render assistance to the physiology of the cerebral hemispheres, but, on the contrary, physiological investigation of the activity of this organ in animals should lay the foundation for the exact scientific analysis of the human subjective world. Consequently, physiology must follow its own path—the path blazed for it long ago. Taking as his starting-point the assumption that the functioning of the animal's organism, unlike that of the human being, is similar to the work of a machine, Descartes[36] three hundred years ago evolved the idea of the reflex as the basic activity of the nervous system. Descartes regarded every activity of the organism as a natural response to certain external agents and believed that the connection between the active organ and the given agent, that is, between cause and effect, is achieved through a definite nervous path. In this way the study of the activity of the animal nervous system was placed on the firm basis of natural science. In the eighteenth, nineteenth and twentieth centuries the idea of the reflex had been extensively used by physiologists, but only in their work on the lower parts of the central nervous system; gradually, however, they began to study its higher parts, until finally, after Sherrington's[37] classical works on spinal reflexes, Magnus,[38] his successor, established the reflex nature of all the basic locomotor activities of the organism. And so experiment fully justified the idea of the reflex which, thereafter, was used in the study of the central nervous system almost up to the cerebral hemispheres. It is to be hoped that the more complex activities of the organism, including the basic locomotor reflexes—states so far referred to in psychology as anger, fear, playfulness, etc.—will soon be related to the simple reflex activity of the subcortical parts of the brain.

A bold attempt to apply the idea of the reflex to the cerebral hemispheres not only of animals but also of man, was made by I. M. Sechenov, the Russian physiologist, on the basis of the contemporary physiology of the nervous system. In a paper published in Russian in 1863 and entitled *Reflexes of the Brain* Sechenov characterized the activity of the cerebral hemispheres as reflex, i.e., determined activity. He regarded thoughts as reflexes in which the effector end is inhibited, and affects as exaggerated reflexes with a wide irradiation of excitation. A like attempt has been made in our time by Ch. Richet who introduced the concept of the psychical reflex in which the reaction to a given stimulus is determined by its union with the traces left in the cerebral hemispheres by previous stimuli.

Generally, the recent physiology of the higher nervous activity related to the cerebral hemispheres tends to associate acting stimulations with traces left by previous ones (associative memory—according to J. Loeb; training, education by experience—according to other physiologists). But this was mere theorizing. The time had come for a transition to the experimental analysis of the subject, and from the objective external aspect, as is the case with any other branch of natural science. This transition was determined by comparative physiology[39] which had just made its appearance as a result of the influence of the theory of evolution. Now that it had turned its attention to the entire animal kingdom, physiology, in dealing with its lower representatives, was forced, of necessity, to abandon the anthropomorphic concept and concentrate on the scientific elucidation of the relations between the external agents influencing the animal and the responsive external activity, the locomotor reaction of the latter. This gave birth to J. Loeb's doctrine of animal tropisms;[40] to the suggestion by Beer, Bethe and Uexküll of an objective terminology for designating the animal reactions; and finally, to the investigation by zoologists of the behaviour of the lower representatives of the animal world, by means of purely objective methods, by comparing the effect of external influences on the animal with its responsive external activity—as for example in the classical work of Jennings,[41] etc.

Influenced by this new tendency in biology and having a practical cast of mind, American psychologists who also became interested in comparative psychology displayed a tendency to subject the external activity of animals to experimental analysis under deliberately induced conditions. Thorndike's[42] *Animal Intelligence* (1898) must be regarded as the starting-point for investigations of this kind. In these investigations the animal was kept in a box and food placed outside, within sight. The animal, naturally, tried to reach the food, but to do so it had to open the door which in the different experiments was fastened in a different way. Tables and charts registered the speed and the manner in which the animal solved this problem. The entire process was interpreted as the formation of an association, connection between the visual and the tactile stimulation and the locomotor activity. Afterwards by means of this method, and by modifications of it, researchers studied numerous questions relating to the associative ability of various animals. Almost simultaneously with the above-mentioned work by Thorndike, of which I was not then aware, I too had arrived at the idea of the need for a similar attitude to the subject. The following episode, which occurred in my laboratory, gave birth to the idea.

While making a detailed investigation of the digestive glands I had to busy myself also with the so-called psychical stimulation of the glands. When, together with one of my collaborators, I attempted a deeper analysis of this fact, at first in the generally accepted way, i.e., psychologically, visualizing the probable thoughts and feelings of the animal, I stumbled on a fact unusual in laboratory practice. I found myself unable to agree with my colleague; each of us stuck to his point of view, and we were unable to convince each other by certain experiments.[43] This made me definitely reject any further psychological discussion of the subject, and I decided to investigate it in a purely objective way, externally, i.e., strictly recording all stimuli reaching the animal at the given moment and observing its corresponding responses either in the form of movements or in the form of salivation (as occurred in this particular case).

This was the beginning of the investigations that I have carried on now for the past twenty-five years with the participation of numerous colleagues who joined hand and brain with me in this work and to whom I am deeply grateful. We have, of course, passed through different stages, and the subject has been advanced only gradually. At first we had but a few separate facts at our disposal, but today so much material has been accumulated by us that we can make an attempt to present it in a more or less systematized form. I am now in a position to place before you a physiological theory of the activity of the cerebral hemispheres which at any rate conforms much more to the structural and functional complexity of this organ than the theory which until now has been based on a few fragmentary, though very important, facts of modern physiology.

Thus, research along these new lines of strictly objective investigation of the higher nervous activity has been carried out mainly in my laboratories (with the participation of a hundred colleagues); work along the same lines has been carried out also by American psychologists. As for other physiological laboratories, so far only a few have begun, starting somewhat later, to investigate this subject, but in most cases their work is still in the initial stage. So far there has been one essential point of difference in the research of the Americans and in ours. Since in the case of the Americans the objective investigation is being conducted by psychologists, this means that, although psychologists study the facts from the purely external aspect, nevertheless, in posing the problems, in analysing and formulating the results, they tend to think more in terms of psychology. The result is that with the exception of the group of "behaviourists"[44] their work does not bear a purely physiological character. Whereas, we, having started from physiology, invariably and strictly adhere to the physiological point of view, and we are investigating and systematizing the whole subject solely in a physiological way.

I shall now pass to an exposition of our material, but before doing so I should like to touch on the concept of the reflex in general, on reflexes in physiology and the so-called instincts.

In the main we base ourselves on Descartes' concept of the reflex. Of course, this is a genuinely scientific concept, since the phenomenon implied by it can be strictly determined. It means that a certain agent of the external world, or of the organism's internal medium produces a certain effect in one or other nervous receptor, which is transformed into a nervous process, into nervous excitation. The excitation is transmitted along certain nerve fibres, as if along an electric cable, to the central nervous system; thence, thanks to the established nervous connections, it passes along other nerve fibres to the working organ, where it in its turn is transformed into a special activity of the cells of this organ. Thus, the stimulating agent proves to be indispensably connected with the definite activity of the organism, as cause and effect.

It is quite obvious that the entire activity of the organism is governed by definite laws. If the animal were not (in the biological sense) strictly adapted to the surrounding world, it would, sooner or later, cease to exist. If instead of being attracted by food, the animal turned away from it, or instead of avoiding fire threw itself into it, and so on, it would perish. The animal *must* so react to the environment that all its responsive activity ensures its existence. The same is true if we think of life in terms of mechanics, physics and chemistry. Every material system can exist as an entity only so long as its internal forces of attraction, cohesion, etc., are equilibrated with the external forces influencing it. This applies in equal measure to such a simple object as a stone and to the most complex chemical substance, and it also holds good for the organism. As a definite material system complete in itself, the organism can exist only so long as it is in equilibrium with the environment; the moment this equilibrium is seriously disturbed, the organism ceases to exist as a particular system. Reflexes are the elements of this constant adaptation or equilibration. Physiologists have studied and are studying numerous reflexes, these indispensable, machine-like reactions of the organism, which at the same time are inborn, i.e., determined by the peculiar organization of the given nervous system. Reflexes, like the belts of machines made by human hands, are of two kinds: the positive and the negative inhibitory, in other words, those which excite certain activities and those which inhibit them. Although investigation of these reflexes by physiologists has been under way for a long time, it is, of course, a long way from being finished. More and more new reflexes are being discovered; the properties of the receptor organs, in which the external and especially the internal stimuli produce certain impulses, still remain in many cases unexplored. The paths along which nervous excitation is conducted within the central nervous system are often little known or not known at all. The central mechanism of inhibitory reflexes, excluding those which manifest themselves along the inhibitory efferent nerves, is quite obscure; the combination and interaction of the various reflexes have not yet been sufficiently elucidated. Nevertheless, physiologists are penetrating deeper and deeper into the mechanism of this machine-like functioning of the organism, and have every reason for believing that sooner or later they will elucidate it in full measure and exercise complete control over it.

Akin to the usual reflexes that have long been the object of physiological investigation in the laboratory and which concern mainly the functions of separate organs, are other inborn reactions; these reactions also take place in the nervous system, and are governed by definite laws, i.e., they are strictly determined by definite conditions. They are the reactions of different animals in relation to the functioning of the organism as a whole, manifested in the general behaviour of the animals and designated by the special term "instincts." Since full agreement has not yet been attained with regard to the essential similarity of these reactions to reflexes, I shall dwell on this question somewhat longer.

Physiology owes to Herbert Spenser, the English philosopher, the first suggestion that instinctive reactions are reflexes too. Afterwards zoologists, physiologists and comparative psychologists produced numerous facts in support of this suggestion. I shall try to systematize the various arguments to the effect that there is not a single essential feature distinguishing reflexes from instincts. First of all there are numerous, imperceptible stages of transition from the usual reflexes to instincts. Take, for example, a newly hatched chick; it reacts by pecking movements to any stimulus in the field of its vision, be it a tiny object or a stain on the surface on which it is walking. In what way does it differ, say, from inclining the head and closing the lids when something flashes near the eye? We should call the latter a defensive reflex, and the first an alimentary instinct, although in the case of the pecking, if it is caused by the sight of a stain, nothing but inclining the head and a movement of the beak occurs.

Further, it has been noted that instincts are more complex than reflexes. But there are exceedingly complex reflexes which no one designates as instincts. Take, for example, vomiting. This is a highly complex action and one that involves extraordinary co-ordination of a large number of muscles, both striated and smooth, usually employed in other functions of the organism and spread over a large area. It also involves the secretion of various glands which normally participate in quite different activities of the organism.

The fact that instincts involve a long chain of successive actions, while reflexes are, so to speak, one-storeyed, has also been regarded as a point of distinction between them. By way of example let us take the building of a nest, or of animal dwellings in general. Here, of course, we have a long chain of actions: the animal must search for the material, bring it to the site and put it together and secure it. If we regard this as a reflex, we must assume that the ending of one reflex excites a new one, or, in other words, that these are chain-reflexes. But such chain activities are by no means peculiar to instincts alone. We are familiar with many reflexes which are also interlocked. Here is an instance. When we stimulate an afferent nerve, for example, the n. ischiadicus, there takes place a reflex rise of blood pressure. This is the first reflex. The high pressure in the left ventricle of the heart and in the first part of the aorta acts as a stimulus to another reflex: it stimulates the endings of the n. depressoris cordis[45] which evokes a depressor reflex moderating the effect of the first reflex. Let us take the chain-reflex recently established by Magnus. A cat, even deprived of the cerebral hemispheres will in most cases fall on its feet when thrown from a height. How does this occur? The change in the spatial position of the otolithic organ of the ear causes a certain reflex contraction of the muscles in the neck, which restores the animal's head to a normal position in relation to the horizon. This is the first reflex. The end of this reflex—the contraction of the muscles in the neck and the righting of the head in general—stimulates a fresh reflex on certain muscles of the trunk and limbs which come into action and, in the end, restore the animal's proper standing posture.

Yet another difference between reflexes and instincts has been assumed, namely, that instincts often depend on the internal state or condition of the organism. For instance, a bird builds its nest only in the mating season. Or, to take a simpler example, when the animal is sated, it is no longer attracted by food and stops eating. The same applies to the sexual instinct, which is connected with the age of the organism, as well as with the state of the reproductive glands. In general the hormones, products of the glands of internal secretion, are of considerable importance in this respect. But this, too, is not a peculiar property of the instincts alone. The intensity of any reflex, as well as its presence or absence, directly depends on the state of excitability of the reflex centres which in turn always depends on the chemical and physical properties of the blood (automatic stimulation of the centres) and on the interaction of different reflexes.

Finally, importance is sometimes attached to the fact that reflexes are related to the activity of separate organs, whereas instincts involve the activity of the organism as a whole, i.e., actually the whole skeleto-muscular system. However, we know from the works of Magnus and de Kleyn that standing, walking, and bodily balance in general, are reflexes.

Thus, reflexes and instincts alike are natural reactions of the organism to certain stimulating agents, and consequently there is no need to designate them by different terms. The term "reflex" is preferable, since a strictly scientific sense has been imparted to it from the very outset.

The aggregate of these reflexes constitutes the foundation of the nervous activity both in men and animals. Consequently, thorough study of all these fundamental nervous reactions of the organism is, of course, a matter of great importance. Unfortunately, as already mentioned, this is a long way from having been accomplished, especially in the case of those reflexes which are called instincts. Our knowledge of these instincts is very limited and fragmentary. We have but a rough classification of them—alimentary, self-defensive, sexual, parental and social. But almost each of these groups often includes numerous separate reflexes, some of which have not been even identified by us, while some are confused with others or, at least, they are not fully appreciated by us as to their vital importance. To what extent this subject remains unelucidated and how full it is still of gaps can be demonstrated by this example from my own experience.

Once, in the course of our experimental work which I shall describe presently, we were puzzled by the peculiar behaviour of our animal. This was a tractable dog with which we were on very friendly terms. The dog was given a rather easy assignment. It was placed in the stand and had its movements restricted only by soft loops fastened round its legs (to which at first it did not react at all). Nothing else was done except to feed it repeatedly at intervals of several minutes. At first the dog was quiet and ate willingly, but as time went on it became more and more excited: it began to struggle against the surrounding objects, tried to break loose, pawing at the floor, gnawing the supports of the stand, etc. This ceaseless muscular exertion brought on dyspnoea and a continuous secretion of saliva; this persisted for weeks, becoming worse and worse, with the result that the dog was no longer fit for our experimental work. This phenomenon puzzled us for a long time. We advanced many hypotheses as to the possible reason for this unusual behaviour, and although we had by then acquired sufficient knowledge of the behaviour of dogs, our efforts were in vain until it occurred to us that it might be interpreted quite simply—as the manifestation of a freedom reflex, and that the dog would not remain quiet so long as its movements were constrained. We overcame this reflex by means of another—a food reflex. We began to feed the dog only in the stand. At first it ate sparingly and steadily lost weight, but gradually it began to eat more—until it consumed the whole of its daily ration. At the same time it became quiet during the experiments; the freedom reflex was thus inhibited. It is obvious that the freedom reflex is one of the most important reflexes, or, to use a more general term, reactions of any living being. But this reflex is seldom referred to, as if it were not finally recognized. James does not enumerate it even among the special human reflexes (instincts). Without a reflex protest against restriction of an animal's movements any insignificant obstacle in its way would interfere with the performance of certain of its important functions. As we know, in some animals the freedom reflex is so strong that when placed in captivity they reject food, pine away and die.

Let us turn to another example. There is a reflex which is still insufficiently appreciated and which can be termed the investigatory reflex. I sometimes call it the "What-is-it?" reflex. It also belongs to the fundamental reflexes and is responsible for the fact that given the slightest change in the surrounding world both man and animals immediately orientate their respective receptor organs towards the agent evoking the change. The biological significance of this reflex is enormous. If the animal were not provided with this reaction, its life, one may say, would always hang by a thread. In man this reflex is highly developed, manifesting itself in the form of an inquisitiveness which gives birth to scientific thought, ensuring for us a most reliable and unrestricted orientation in the surrounding world. Still less elucidated and differentiated is the category of negative, inhibitory reflexes (instincts) induced by any strong stimuli, or even by weak but unusual stimuli. So-called animal hypnotism belongs, of course, to this category.

Thus, the fundamental nervous reactions both of man and animals are inborn in the form of reflexes. And I repeat once more that it is highly important to have a complete list of these reflexes and properly to classify them, since, as we shall see later, all the remaining nervous activity of the organism is based on these reflexes.

However, although the reflexes just described constitute the fundamental condition for the safety of the organism in the surrounding nature, they in themselves are not sufficient to ensure a lasting, stable and normal existence for the organism. This is proved by the following experiment, carried out on a dog in which the cerebral hemispheres have been extirpated. Besides the internal reflexes, such a dog retains the fundamental external reflexes. It is attracted by food; it keeps away from destructive stimuli; it displays the investigatory reflex pricking up its ears and lifting its head to sound. It possesses the freedom reflex as well, and strongly resists any attempt at capture. Nevertheless, it is an invalid and would not survive without care. Evidently something vital is missing in its nervous activity. But what? It is impossible not to see that the number of stimulating agents evoking reflex reactions in this dog has decreased considerably, that the stimuli act at a very short distance and are of a very elementary and very general character, being undifferentiated. Hence, the equilibrium of this higher organism with the environment in a wide sphere of its life has also become very elementary, limited and obviously inadequate.

Let us now revert to the simple example with which we began our investigations. When food or some unpalatable substance gets into the mouth of the animal, it evokes a secretion of saliva which moistens, dissolves and chemically alters the food, or in the case of disagreeable substances removes them and cleanses the mouth. This reflex is caused by the physical and chemical properties of the above-mentioned substances when they come in contact with the mucous membrane of the oral cavity. However, a similar secretory reaction is produced by the same substances when placed at a distance from the dog and act on it only by appearance and smell. Moreover, even the sight of the vessel from which the dog is fed suffices to evoke salivation, and what is more, this reaction can be produced by the sight of the person who usually brings the food, even by the sound of his footsteps in the next room. All these numerous, distant, complex and delicately differentiated stimuli lose their effect irretrievably when the dog is deprived of the cerebral hemispheres; only the physical and chemical properties of substances, when they come in contact with the mucous membrane of the mouth, retain their effect. Meanwhile, the processing significance of the lost stimuli is, in normal conditions, very great. Dry food immediately encounters plenty of the required liquid; unpalatable substances, which often destroy the mucous membrane of the mouth, are removed from it by a layer of saliva rapidly diluted and so on. But their significance is still greater when they bring into action the motor component of the alimentary reflex, i.e., when the seeking of food is effected.

Here is another important example of the defensive reflex. The strong animals prey on those smaller and weaker, and the latter must inevitably perish if they begin to defend themselves only when the fangs and claws of the enemy are already in their flesh. But the situation is quite different when the defensive reaction arises at the sight and sound of the approaching foe. The weak animal has a chance of escaping by seeking cover or in flight.

What, then, would be our general summing up of this difference in attitude of the normal and of the decorticated animal to the external world? What is the general mechanism of this distinction and what is its basic principle?

It is not difficult to see that in normal conditions the reactions of the organism are evoked not only by those agents of the external world that are essential for the organism, i.e., the agents that bring direct benefit or harm to the organism, but by other countless agents which are merely signals of the first agents, as demonstrated above. It is not the sight and sound of the strong animal which destroy the smaller and weaker animal, but its fangs and its claws. However, the signalling, or to use Sherrington's term, the distant stimuli, although comparatively limited in number, play a part in the afore-mentioned reflexes. The essential feature of the higher nervous activity, with which we shall be concerned and which in the higher animal is probably inherent in the cerebral hemispheres alone, is not only the action of countless signalling stimuli, rather it is the important fact that in certain conditions their physiological action changes.

In the above-mentioned salivary reaction now one particular vessel acted as a signal, now another, now one man, now another—strictly depending on the vessel that contained the food or the unpalatable substances before they were introduced in the dog's mouth, and which person brought and gave them to the dog. This, clearly, makes the machine-like activity of the organism still more precise and perfect. The environment of the animal is so infinitely complex and is so continuously in a state of flux, that the intricate and complete system of the organism has the chance of becoming equilibrated with the environment only if it is also in a corresponding state of constant flux.

Hence, the fundamental and most general activity of the cerebral hemispheres is signalling, the number of signals being infinite and the signalization variable.

LECTURE TWO

Technical methods used in objective study of the work of the cerebral hemispheres. Signalling as a reflex action. Unconditioned and conditioned reflexes. Conditions for the development of conditioned reflexes.

Gentlemen,

In the previous lecture I touched on the reasons that impelled us to adopt a strictly objective method of investigating the entire nervous activity in higher animals, i.e., of studying it from the purely external factual aspect; this is in keeping with the investigations in other branches of natural science, and rules out fantastic speculation as to the probable subjective state of the animals by analogy with ourselves. At the same time I stated that from this point of view the entire nervous activity of the animal appeared to us first of all as inborn reflexes, i.e., regular connections between certain external agents acting on the organism and its definite responsive functions. It has been established that these agents are comparatively few in number; they prove to be akin to each other, being of a general nature. Of course, this, to a degree, ensures the existence of the organism, but it is far from being sufficient (especially in the more highly developed animals); therefore, if we deprive an animal of a certain part of its nervous activity, it will be fully disabled and, if left to itself, although retaining its inborn reflexes, doomed to death. Everyday life demands more detailed and specialized correlations between the animal and the surrounding world. And this further correlation is established only with the help of the higher part of the central nervous system—the cerebral hemispheres; to be more precise, a large number of natural stimuli act as temporary and alternate signals for the relatively small number of fundamental agents that determine the inborn reflexes. Only in this way is a precise and delicate equilibration of the organism with the environment attained. I have designated this function of the cerebral hemispheres signalling activity.

Now I should like to touch on the technical side of the methods used by us in our investigation. How shall we study the signalling activity of the hemispheres—which organ shall we select and what methods shall we use? It is obvious that any reflex can be chosen for investigation since signalling stimuli are connected with all the reflexes. But, as already mentioned, the particular conditions of our work made us concentrate on the study of two reflexes—the alimentary reflex and the usual defensive reflex which manifested itself when an unpalatable substance was introduced into the mouth of the dog used in our experiment. This was a fortunate choice in many respects. Whereas a strong defensive reflex, evoked, for example, by the application of an electric current to the skin, greatly excites the animal and makes it restless, and while the sexual reflex requires special conditions (to say nothing of its protracted periodic character and dependence on age), the alimentary reflex and the mild defensive reflex to unpalatable substances introduced into the mouth are normal and ordinary phenomena.

Here is another essential feature of our method of investigation. The alimentary reflex, and the reaction to unpalatable substances when they find their way into the animal's mouth, each consist of two components. On the one hand, the animal takes the food, masticates it and swallows it, or, in the case of unpalatable substance, ejects it from the mouth. On the other hand, this muscular activity is joined by a secretory one. Both the food and the unpalatable substances evoke an immediate secretion of saliva, needed in the first case for the physical and chemical processes of digestion, and in the second case for cleansing the mouth. In our experiments we used only the secretory component of the reflexes, the motor reactions being taken into account only in special circumstances. The secretory reflex proved most suitable for our experiments, since it is possible to take accurate measurements of the intensity of salivation, either by counting the number of drops or by means of a special graduated tube. It would be much more difficult to obtain accurate measurements for the motor component of the reflexes, which in this case is of a very complex and diversified character. The most delicate instruments would be required for this purpose, and even then they would not give the precision in measuring the motor reaction that is achieved in the case of the secretory component. Of certain importance in the early phase of our work was the fact that during observations on the secretion of saliva there was a lesser tendency towards anthropomorphic interpretations than was the case during observations of the motor reactions.

All the dogs used in our experiments are preliminarily subjected to a minor operation which consists in transplanting the opening of the salivary duct to the external surface of the skin. For this purpose we cut out a small piece of the mucous membrane surrounding the natural opening of the salivary duct in the mouth, then we separate the duct for a certain depth, bring out its end to the external surface of the skin through a special incision in the cheek and suture it to the edges of the incision. As a result of this operation the saliva flows not into the mouth, but outside, on to the cheek or under the chin. This greatly facilitates observation of the work of the salivary glands. It is only necessary to fix a small glass funnel with the help of cement (we utilize Mendeleyev's cement for the purpose), and the work of the glands can be observed in different ways and with remarkable exactness. Sometimes a hemispherical bulb is hermetically adjusted by us over the fistula; the bulb is provided with two projecting tubes, one pointing up and the other down. The lower tube is used for drawing off the saliva which accumulates after each stimulation, while the upper tube is connected by air transmission with a horizontal glass tube filled with coloured fluid. When the saliva flows into the hemispherical bulb it displaces the coloured fluid which begins to move along the graduated tube, and thus the amount of secretion is accurately recorded. It is also easy to fix up an automatic electric device accurately recording the number of drops of exactly equal volume.

Now I shall turn to the general conditions of our experiments. Since our research deals with the activity of the cerebral hemispheres, a highly complex signalling apparatus of the finest sensitiveness, it is obvious that numerous and diverse stimuli constantly act on the animal through it. Each of these stimuli has a certain effect on the animal and in the aggregate they collide and interact. Consequently, if we do not take precautions against these influences, often of a chaotic character, we should not be able properly to understand the phenomena under investigation, everything being confused and entangled. It is, therefore, important to simplify the conditions of the experiment. First of all the animal is usually placed in a stand. At first the experimenter alone was allowed to remain with the dog in the research chamber. But this precaution proved insufficient, since the experimenter himself is a source of numerous stimuli. His slightest movement, respiration, eye movements, etc., all act on the animal undergoing the experiment and interfere with the phenomena under investigation. Therefore, we were compelled to station the experimenter beyond the research chamber so as to exclude as much as possible his influence on the animal. But even this precaution proved inadequate in the conditions of an ordinary laboratory. Actually, the environment of the dog in an ordinary laboratory is constantly changing: sounds penetrate from the outside, footsteps, the noise of street traffic, a chance conversation, vibration of the walls caused by a passing van, shadows cast through the windows, and so on—any of these extraneous casual stimuli falling on the cerebral hemispheres must be reckoned with. For this reason a special laboratory was built at the Institute of Experimental Medicine, the necessary funds being provided by an enlightened Moscow businessman. The primary task was to prevent as much as possible the access of extraneous stimuli. For this purpose the laboratory was surrounded with a deep trench, and other structural devices were used. Inside, the rooms (four on each floor) were isolated by a cross-shaped corridor; the top and ground floors, housing the working rooms, were separated by an intermediate floor. Finally, each research chamber was thoroughly partitioned by means of certain sound-proof materials into two compartments—one for the animal and the other for the experimenter. Pneumatic or electric transmission was used for the purpose of stimulating the animal and recording its reactions. Thus, the maximum simplification and stability of the experimental conditions were ensured.

Lastly, one other point should be mentioned, which to a considerable degree still remains a pium desiderium. Since the entire complex of external influences on the animal is subjected to investigation, it is understandable that this complex must be fully under the control of the experimenter. He must have at his disposal a large number of instruments of various kinds in order to act on the animal by different kinds of stimuli and to combine certain stimuli so as to reproduce actual natural conditions. But we often experienced and still experience a shortage not only of specially perfected instruments but of modern instruments used in research. The functioning of the cerebral hemispheres each time proves too delicate to be fully investigated with the instruments at our disposal.

It may be that someone will say that the experimental conditions just described by me are artificial. Our reply to such an objection would be this. Firstly, in view of the infinite variety of living relations it is hardly possible to use something really unusual and absolutely new. Secondly, in investigating phenomena of a chaotic and complex nature, we must inevitably break them up and divide them into groups. Has not the physiology of animals constantly employed and is it not employing now the methods of vivisection and even the method of isolated organs and tissues? We subject our animal to a restricted number of definite conditions, and thus make it possible to study their influences independently of one another. You will see later how the conditions of our experimentation and the variations in the state of the animal furnished us with facts of vital importance.

Such are our general principles and the technical side of our methods.

Let us pass now to the subject of the signalling activity of the cerebral hemispheres itself. Here are a few demonstrations:

Demonstration. The animal used in this experiment has been operated upon as previously described. As you see, so long as no special stimulating agent acts on the animal, its salivary glands remain inactive and there is no secretion of saliva. Now we begin to act upon the dog's ear by beating a metronome. Salivary secretion begins in nine seconds, and in the course of forty-five seconds eleven drops have been secreted. Thus, before your eyes a stimulus utterly alien to food (the metronome) has evoked the activity of the salivary gland, and this activity must be regarded as a component of the alimentary reflex. You have also seen the motor component of this reflex: the dog turned in the direction from which the food is usually brought and began to lick its lips.

It is this central phenomenon, originating in the cerebral hemispheres, that will be the object of our further attention. A decorticated dog would never have reacted by a secretion of saliva to a stimulus of this kind. At the same time it is quite obvious that this is a signalling activity:

the beats of the metronome are signals for food, since the animal reacts to them in the same way as if it were food. A similar effect is produced by the sight of real food.

Demonstration. Food is shown to the animal. As you see, the secretion of saliva begins after five seconds, and in fifteen seconds six drops of saliva have been collected. Here, then, we have the same effect as observed under the action of the metronome.

This is also a case of signalling due to the activity of the cerebral hemispheres; it has been acquired in the course of the animal's individual existence and is by no means an inborn reaction. This was revealed by the experiments conducted by I. S. Tsitovich in the laboratory of the late Prof. V. I. Vartanov.[46] Tsitovich took a number of pups from their mother and for quite a while fed them exclusively on milk. When they were a few months old, he performed fistula operations on their salivary ducts and in this way he was able to record the secretion of saliva. When the pups were shown other food, namely, meat and bread, no salivary secretion was observed. Consequently, the sight of food does not, in itself, evoke a salivary reaction, and does not represent an inborn agent of this reaction. Only after the pups had had several meals of meat and bread did the sight of these items produce a salivary secretion.

The following experiment will demonstrate a phenomenon generally known as a reflex.

Demonstration. We suddenly introduce food into the dog's mouth and the secretion of saliva begins after a second or two. This is due to the action of the mechanical and chemical properties of the food on the mucous membrane of the mouth; it is a reflex. This experiment explains why a decorticated dog may die of starvation in the presence of food; it will begin to eat only when the food comes into contact with its mouth.

This experiment brings out the insufficiency of the inborn reflexes, their imperfection and their limited character; at the same time it brings out clearly the great importance of signals.

Now comes the fundamental question: what is the nature of signalization and how should it be considered from the purely physiological point of view?

We know that a reflex is an indispensable, natural reaction of the organism to an external agent effected by a definite part of the nervous system. It is quite obvious that in signalization there are present all the components of the nervous activity which is called a reflex. An external stimulus is required for the development of a reflex; in our first experiment this stimulus was provided by the beats of a metronome. They set in motion the auditory receptor of the dog, and the stimulation was further transmitted along the auditory nerve to the central nervous system; here it was transferred to the nerves of the salivary glands which excited a secretion of saliva. It is true that in the experiment with the metronome we observed an interval of nine seconds between the beginning of the action of the metronome and the beginning of the salivary secretion, whereas for the reflex this interval was only one to two seconds. But the longer latent period was due to special conditions deliberately created by us in the course of the experiment. Generally, the effect produced by signalization far from being belated, is evoked as quickly as that induced by ordinary reflexes; this question, however, will be discussed in another lecture. A reflex is a reaction strictly determined by definite conditions. The same holds true for signalization, the only difference being that in the latter case the effect depends on the greater number of conditions. But this, of course, does not make signalization differ fundamentally from reflexes, since in strictly definite conditions reflexes likewise often vanish, are inhibited. A thorough study of the subject shows that there is nothing accidental in the signalling activity of the hemispheres; here, too, the experiments are carried out strictly in accordance with our designs. In the special laboratory I have described, it often happens that the animal is under observation for one or two hours without secreting a single drop of saliva not caused by the stimuli applied; in the ordinary laboratories, of course, the experiments are often distorted by extraneous stimuli.

All these facts leave no grounds for regarding the phenomena, which up to now I have designated "signalization," as being other than reflexes. But there is another aspect which, at first sight, would seem to indicate an essential difference between the old reflex and this new phenomenon, which only a moment ago I also termed a "reflex." Food, through its mechanical and chemical properties, evokes the salivary reflex in any animal right from birth. But this new type of reflex, which you have seen illustrated, is developed gradually in the course of the animal's individual existence. Can this be regarded as an essential difference? Is it not an argument against terming this new phenomenon a reflex? Undoubtedly, it is a sufficient argument for distinguishing this type of reaction from the other, but by no means does it annul our scientific right to term it a reflex. Here it is a question not of the mechanism itself, but of the mode of formation of the reflex mechanism. Let us, by way of example, take the telephone system. Communication can be effected in two ways. My apartment can be connected directly with the laboratory by a special line which enables me to put a call through whenever I like, or, as is actually the case, a connection with the laboratory may be established through the central telephone exchange. But the result is the same, the only difference being that in the first case there is a readily available conducting line, while in the second a preliminary connection is required; in one case the mechanism effecting the communication is ready-made, in the other—it must be supplemented every time to make it complete. The same holds true for the reflex action: in the one case it is complete, in the other—a certain preliminary preparation is required.

Thus, we have to consider the question of the mode of formation of the new reflex mechanism. Since the new reflex develops easily and unfailingly in definite physiological conditions—a fact which will be illustrated later—there are no grounds for worrying about the subjective state of the dog. With complete knowledge of the matter, this phenomenon is fully under our control; it is strictly law-governed and there is no reason to regard it as being other than physiological activity, similar to all other activities with which physiology is concerned.

We have termed the new reflexes *conditioned* in contrast to the *unconditioned* inborn reflexes. The term "conditioned" is, more and more, coming into general use. From the point of view of research, it is fully justified, since in comparison with the inborn, these reflexes are conditioned in a special way: in the first place their formation requires definite conditions, and, in the second place, their action also depends on numerous conditions. Consequently, when investigating them, the researcher must take very many factors into account. Of course, our terms could, with justification, be replaced by others. Thus, for example, the old reflexes might be called "inborn" and the new ones—"acquired"; we could also term the former "species reflexes" since they are typical of the species as a whole, and the latter "individual reflexes," since they vary in different animals, and even in one and the same animal at different times and in different conditions. The terms "conductor reflexes" and "connection reflexes" would, likewise, be fully justified.

As for the assumption of the formation of new nervous connections within the cerebral hemispheres, there should be no objection to it from the theoretical point of view. The principle of connection is so often applied in modern technique, as well as in our everyday experience, that it would seem strange if it were regarded as an unexpected one in the mechanism of the central nervous system, the function of which is to establish highly complex and delicate relations. It is perfectly natural that along with the conductor mechanism there should also be a connector mechanism. The physiologist of all people should have no objection to this concept, especially since decades ago there was in general use the German concept "Bahnung"[47] which means laying down new paths, establishing new connections. The conditioned reflex is a common and widespread phenomenon. It is, evidently, what we recognize in ourselves and in animals under such names as training, discipline, education, habits; these are nothing but connections established in the course of individual existence, connections between definite external stimuli and corresponding reactions. Thus, the conditioned reflex opens to the physiologist the door to investigation of a considerable part, and possibly, even of the entire higher nervous activity.

I shall pass now to the question of the circumstances in which conditioned reflexes, or connections of new nervous paths are established. The fundamental requisite is that the external stimulus must coincide in time with the action of the unconditioned stimulus. In our experiment food acted as the unconditioned stimulus of the alimentary reaction. If the intake of food by the animal coincides in time with the action of a stimulus which previously had no relation to food, this stimulus begins to produce the same reaction as the food. Precisely this occurred in the case which passed before our eyes. We repeatedly stimulated the dog undergoing the experiment by the sound of the metronome and then fed the animal immediately, i.e., evoked the inborn alimentary reflex. After several repetitions the very sounds of the metronome began to produce a secretion of saliva and a corresponding motor reaction. The same occurs in the case of a defensive reflex to unpalatable substances introduced into the dog's mouth. If we introduce a weak acid solution we get an unconditioned acid reflex: the animal begins to make various movements, shaking its head violently, opening its mouth, trying to eject the acid with the help of the tongue, and so on; at the same time it manifests a profuse secretion of saliva. Exactly the same reaction is caused by any external stimulus repeatedly coinciding in time with the introduction of acid into the dog's mouth. *Thus, the first and foremost requisite for the formation of a conditioned reflex lies in the coincidence in time of the action of a previously indifferent agent with the action of an unconditioned agent which evokes a definite unconditioned reflex.*

The second important requisite is that the *conditioned reflex can be formed only if the indifferent agent somewhat precedes the action of the unconditioned stimulus.* If the order is reversed, i.e., if we apply the unconditioned stimulus first, and the indifferent agent afterwards, there will be no conditioned reflex.

A. N. Krestovnikov carried out a variety of experiments of this kind in our laboratory, and the effect was invariably the same. Here are some of his results. In the case of one dog 427 combinations of the odour of vanilin with the introduction of acid into the mouth were applied, the acid always preceding the odour of vanilin by five to ten seconds. Vanilin did not become a conditioned stimulus to an acid reaction. However, in subsequent experiments the odour of amyl acetate, which *preceded* the introduction of acid into the dog's mouth, became an effective conditioned stimulus after only twenty combinations. With another dog the sound of a loud electric bell, set buzzing five to ten seconds after it began to take food, did not produce a conditioned alimentary reaction after 374 combinations; but the rotation of an object in front of the dog prior to the administration of food, acquired the properties of a conditioned stimulus after only five combinations. Later, when the electric bell was rung *prior* to the administration of food, it also became a conditioned stimulus after a single combination. These experiments were tried on five dogs, and the result was always the same, no matter whether the new stimulating agent was applied ten seconds, five seconds or only two and even one second after the onset of the unconditioned stimulus. During the elaboration of conditioned reflexes, for the sake of greater certitude, we carefully observed not only the secretory but also the motor reactions of the animals. Thus, the first set of conditions includes the time relation between the unconditioned stimulus and the agent which becomes the conditioned stimulus.

As for the cerebral hemispheres themselves, only their active state makes possible the formation of conditioned reflexes. If the animal undergoing the experiment is in a more or less drowsy state, the formation of the conditioned reflex either acquires a protracted character, being considerably impeded, or becomes completely impossible. Consequently, the establishment of new connections, the process of coupling new nervous paths is a function which can be performed only when the animal is in an alert state. At the same time during the formation of a new conditioned reflex the cerebral hemispheres must be free from all other activity.

When elaborating a new conditioned reflex it is important to prevent extraneous stimuli from affecting the animal, since they are liable to give rise to altogether different reactions of the organism. If corresponding precautions are not taken, the formation of a conditioned reflex becomes exceedingly difficult and in many cases utterly impossible. For example, if during the elaboration of a conditioned reflex the dog is strongly irritated by a certain part of the stand in which it is fastened (causing pressure, strangulation, etc.), then no matter how many times we repeat the combination of our stimulus with the unconditioned stimulus, or at any rate with some of them, we shall not get a conditioned reflex. Another example is provided by the dog already mentioned which would not keep quiet when constrained in the stand. Hence the rule, almost without exception: in a new experimental animal, i.e., one which has not yet been subjected to the experiments in question, the establishment of the first conditioned reflex is difficult and often takes much time. This is obvious, since the experimental conditions themselves may provoke in different animals numerous special reactions, i.e., cause one or other extraneous activity of the cerebral hemispheres. It should be added that in cases when we are not in a position to disclose the nature of the extraneous reflexes that interfere with the formation of our conditioned reflex and when we are unable to get rid of them, the inherent properties of the nervous activity come to our aid. For if the environment of the animal during the experiment does not contain any particularly destructive elements, then almost all extraneous and interfering reflexes will gradually vanish of themselves.

Of course, this set of conditions also includes the state of health of the animal; sound health ensures the normal functioning of the cerebral hemispheres and precludes any influence of internal pathological stimuli coming into the cerebral hemispheres.

Finally, the last set of conditions relates to the properties of the agent which is to become a conditioned stimulus, as well as to the properties of the given unconditioned stimulus.

Conditioned reflexes are easily elaborated from more or less indifferent agents. Strictly speaking, there is no such thing as an absolutely indifferent agent. In a normal animal the slightest change in the environment—even the faintest sound, odour, or change in the lighting of a room—immediately evokes the above-mentioned investigatory, "What-is-it?" reflex in the shape of a corresponding motor reaction. But if this relatively indifferent agent recurs, then it rapidly loses its effect on the cerebral hemispheres, and the obstacle to the formation of a conditioned reflex is thereby removed. But if the agent belongs to the group of strong general stimuli, or, moreover, of special stimuli, the formation of our conditioned reflex will be greatly impeded and in extreme cases even impossible. It should also be borne in mind that in most cases the previous history of the dog was not known to us, we knew little of its life, the conditioned connections established in it, etc. On the other hand, we used as an agent even a strong unconditioned stimulus and were successful in transforming it into a conditioned stimulus. Take, for example, such a destructive stimulus as a strong electric current applied to the skin and causing injury and cauterization. This, obviously, is an unconditioned stimulus to the defensive reflex: the organism responds by a violent motor reaction directed either towards removal of the stimulus itself or to moving away from it. Nevertheless, even by means of such stimuli it is possible to elaborate other kinds of conditioned reflexes.

In one experiment this destructive stimulus was converted into an alimentary conditioned stimulus. When an extra strong electric current was applied to the skin of the dog, the latter did not display even the slightest defensive reaction; actually there was in evidence an alimentary reaction: the animal turned in the direction whence it usually received its food, licking its lips and exhibiting an abundant secretion of saliva.

Here is the original record of an experiment carried out by M. N. Yerofeeva.

Time	Electric current (distance between coils in cm)	Place of skin stimulated	Secretion of saliva in drops during 30 seconds	Motor reaction
4 23 p m.	4	Usual place	6	Alimentary
4.45 "	4	" "	5	No trace of
5.07 "	2	New place	7	defensive
5.17 "	0	" "	9	reaction
5.45 "	0	" "	6	

After each electric stimulation the dog was allowed to eat food for a few seconds.

A similar effect was obtained in a dog whose skin was repeatedly subjected to cauterization or to pricking deep enough to draw blood. When sensitive people expressed indignation at these experiments we were in a position to show that they were mistaken. Of course here, too, we had no intention of penetrating into the subjective world of the dog and of ascertaining its feelings. But we had absolutely reliable proof that even the most delicate objective phenomena usually manifested in the animals, when the latter are subjected to the action of strong and destructive stimuli, were not observed in this particular case. In our dogs, in which the reflexes had been transformed as described above, no appreciable change in the pulse or in the respiration was evoked by the stimulation, whereas such changes inevitably occur and assume a pronounced character when the destructive stimulus is not preliminarily associated with an alimentary reaction. Such is the remarkable result of diverting the nervous excitation from one path to another. But this transformation of reflexes depends on a definite condition—namely, a certain correlation between the two unconditioned reflexes. The conversion of the unconditioned stimulus for one reflex into the conditioned stimulus for another is possible only when the first reflex is physiologically weaker and biologically of less importance than the second. This conclusion, I believe, can be drawn from the further results obtained by Yerofeeva. A destructive stimulus applied to the dog's skin was transformed into a conditioned alimentary stimulus. But this, we think, was due to the fact that in the case of the damage to the skin, the alimentary reflex proved stronger than the defensive reflex. We know that dogs, when fighting for food, often sustain skin wounds, which means that the alimentary reflex predominates over the defensive reflex. But to this, too, there is a limit. There is a reflex that is stronger than the alimentary reflex—the life and death reflex, to be or not to be. This explains the following phenomenon observed in the course of our experiments: a strong electric current applied to skin overlying bone, without any intervening thick muscular layer, could not be converted into a conditioned stimulus for an alimentary reaction instead of a defensive reaction. This signifies that the afferent nerves, stimulated by the damage to the bone and signalizing a grave danger to the organism, establish with great difficulty, or fail to do so at all, a temporary connection with the part of the brain from which the alimentary reaction is controlled. It should be said in passing that the foregoing facts clearly show the advantage of employing the unconditioned alimentary reflex for our experiments, since it occupies a very high place in the hierarchy of reflexes.

On the one hand, as we have just seen, strong and even specialized agents become, in certain conditions, conditioned stimuli; on the other hand, there is, of course, a minimum strength below which the agent cannot function as a conditioned stimulus. Thus, for example, a thermal agent below 38°-39° C. applied to the skin cannot be made into a conditioned thermal stimulus (experiments of O. S. Solomonov).

Similarly, if by using such a very strong unconditioned stimulus as food—as was the case in our experiment—it is possible to transform a most unfavourable agent, already part of another reflex, even an unconditioned one, into a conditioned stimulus, the use of a weak unconditioned stimulus makes it extremely difficult or even impossible to transform even a favourable, i.e , almost indifferent agent, into a conditioned stimulus; even when such a conditioned stimulus is formed, it is inconsiderable. These are either constantly weak or temporarily weak unconditioned stimuli which, given other states of the organism, could be, on the contrary, very strong. Food can be taken as an example: in a hungry animal food naturally evokes a strong unconditioned alimentary reflex, and in this case the conditioned reflex develops rapidly and is also of considerable strength. In a permanently satisfied animal the unconditioned reflex is less powerful, and the conditioned reflex either is not formed at all or is established very slowly.

By complying with the conditions enumerated above—which is not a difficult task—we obtain a conditioned reflex *without fail*. Why, then, should we not regard the formation of a conditioned reflex as a purely physiological phenomenon? We act on the dog's nervous system by means of a number of definite external stimuli, and they, *necessarily*, result in the establishment of a new nervous connection; a certain nervous coupling takes place and, as shown above, a typical reflex reaction follows. Where, then, is there any place for any kind of non-physiological relations? Why, then, are the conditioned reflex and the laws governing its formation not regarded as physiology, but as something else? I see no reason for thinking about these phenomena in any other way, and it is my belief that human prejudice usually plays a harmful role in these questions by its reluctance to admit that the higher nervous activity is strictly determined; this is because of the extraordinary complexity of our subjective experiences, of our actions which in most cases at present cannot be traced to their ultimate definite stimuli.

NATURAL SCIENCE AND THE BRAIN[48]

One can truthfully say that for the first time since the days of Galileo the irresistible march of natural science has been held up quite perceptibly before the study of the higher parts of the brain, the organ of the highly complex relationship between the animal and the external world. And it would seem that this is not fortuitous, that this is indeed a critical moment in natural science, since the brain, which in its higher form—the human brain—created and is continuing to create natural science, itself becomes the object of this science.

But let us approach the matter more closely. For long the physiologist has persistently and systematically, in keeping with the strict rules of natural science, studied the animal organism. He has observed the vital phenomena unfolding before him in time and space; he endeavours with the help of experimentation to define the constant and elementary conditions of their existence, their coming and going. His foresight and his control over vital phenomena are increasing all the time, in the same way as natural science rises in all its grandeur over inanimate nature before our very eyes. When the physiologist deals with the basic functions of the nervous system—with the processes of nervous excitation and conduction—even though the nature of these phenomena is still obscure, he remains a naturalist, investigating one by one the varied external influences on these general nervous processes. Moreover, when the physiologist studies the lower part of the central nervous system, with the spinal cord, and finds out how the organism by means of this part responds to these or to other external influences, i.e., when he studies the law-governed changes taking place in the living substance under the action of one or another external agent, he remains exactly the same naturalist. This natural reaction of the animal organism to the external world, effected through the lower part of the central nervous system, is termed by the physiologist a reflex. The reflex, as one would expect, is strictly specific from the point of view of natural science; a certain external phenomenon causes strictly definite changes in the organism.

But when the physiologist turns to the higher levels of the central nervous system, a sudden and abrupt change takes place in his research. He no longer concentrates on the connection between the external phenomena and the animal's reactions to them; instead of dealing with these actual relations he begins to make suppositions about the internal states of the animals modelled on his own subjective state. So far he has based himself on the general concepts of natural science. But he now resorts to concepts that are utterly alien to him and in no way related to his earlier, psychological concepts; in short, he makes the leap from the measurable world to the immeasurable. This, obviously, is a step of extraordinary importance. But what caused it? What profound reasons impelled our physiologist to do this? What conflict of opinions preceded it? A totally unexpected answer must be given to these questions: in the world of science absolutely nothing preceded this extraordinary step. The natural scientist, in the person of the physiologist, investigating the higher parts of the central nervous system, has, so to speak, unconsciously and imperceptibly for himself, yielded to the common habit of regarding the animal's activity as analogous to his own and of explaining it by the same intrinsic causes which he feels and recognizes in himself.

This, then, is the point at which the physiologist departed from the firm position of natural science. And what has he acquired instead? He has borrowed concepts from that branch of human intellectual interest which, as those who work in this field readily admit, is not yet entitled to call itself science, despite its long existence. Psychology, as the knowledge of the human inner world, is still seeking its own true methods. And the physiologist has taken upon himself the ungratifying task of guessing the inner world of the animal.

After this one can easily understand why the study of the most complex nervous activity of the higher animals is hardly making any progress, although research has been carried on for about a hundred years. In the early seventies of the last century work on the higher part of the brain received what seemed to be a powerful impetus towards further development, but even this failed to bring research on to the highroad of science. A few basic facts were discovered in the first few years and then progress came to a standstill again. The subject, clearly, covers a vast field, and yet one and the same themes have been worked and reworked for the past thirty years and more, and hardly any new ideas have appeared. The impartial present-day physiologist is forced to admit that the physiology of the brain is now in a blind alley. Thus, psychology, as an ally, has not justified itself in the eyes of physiology.

In view of this state of affairs common sense demands that here, too, physiology should return to the path of natural science. But what must it do then? In investigating the activity of the higher parts of the central nervous system it must remain faithful to the methods that it uses in studying the lower parts, i.e., it must strictly compare the changes in the external world with the corresponding changes in the animal organism and disclose the laws governing these relations. But these relations are, apparently, intricate in the extreme. Is it possible to begin to record them objectively? To this really fundamental question there is but one serious answer: persevering and incessant effort is needed in this direction. An exclusively objective comparison of the external world and of the animal organism is now being attempted by a number of investigators on a great variety of species of animals.

I have the honour to submit for your esteemed attention an attempt to investigate the most complex activity of one of the higher animals, namely, the dog. Later on in my exposition I shall base myself on the results of ten years' research in my laboratories where I have been joined by a number of young scientists who are trying their luck in this new field of investigation. This decade of research, at first overshadowed by painful doubts, and then with growing frequency encouraged by the firm feeling that our efforts were not in vain, offers, as I am now convinced, an indisputable and positive answer to the above question.

All the activity of the higher parts of the nervous system, which was revealed before our eyes, appeared to us in the form of two main nervous mechanisms: first, the mechanism of a temporary connection, as it were, a temporary coupling of the conductor paths between the phenomena of the external world and the responsive reactions of the animal organism; secondly, the mechanism of analysers.

Let us consider these mechanisms separately.

I have already mentioned that long ago physiology established in the lower part of the central nervous system the mechanism of the so-called reflex, i.e., of a constant connection effected by the nervous system between certain phenomena of the external world and the corresponding definite reactions of the organism. Since this connection is simple and of a constant nature, it was natural to term it an unconditioned reflex. On the basis of our facts we came to the conclusion that temporary connection is effected in the higher part of the nervous system. By means of this part of the nervous system the phenomena of the external world are now reflected in the activity of the organism, i.e., excite the organism to activity, and now indifferent to the organism and inconvertible, just as if they did not exist at all. This temporary connection, these new reflexes were, naturally, termed conditioned reflexes. In what way does the organism benefit by the mechanism of temporary connection? When does the temporary connection, the conditioned reflex, appear? Let us take an actual example. The most essential connection between the animal organism and the surrounding world is that brought about by certain chemical substances which constantly enter into the composition of the given organism, i.e., the food connection. In the lower forms of the animal world it is the direct contact between food and the animal organism or vice versa, which chiefly leads to alimentary metabolism. In the higher forms these relations become more numerous and remote. Now odours, sounds and pictures attract the animals to food substances already in wide regions of the surrounding world. And in the highest formation the sound of speech, as well as written and printed characters, send human beings all over the world in search of daily bread. Thus, numberless, diverse and distant external agents act, as it were, as food signals, directing the higher animals to acquire it and making them establish food connection with the external world. Along with this variety and remoteness, there takes place a substitution of the temporary for the constant connection between the external agents and the organism; first, because, essentially, the remote connections are of a temporary and changeable nature, and, secondly, because, due to their variety and number, they cannot be covered as constant connections, even by the most capacious apparatus. The given food object may be now in one place, now in another; it may, consequently, be accompanied at one time by certain phenomena, at another time by quite different ones; it may be part of one or another system of the external world, and therefore now these now other natural phenomena must temporarily serve as stimulating agents producing in the organism a positive motor (in the broad sense of this word) reaction to this object. In order to make the second proposition more comprehensible—that distant connections cannot be of a constant nature—I shall make a comparison. Suppose that instead of the present system of telephonic communication effected through the central telephone exchange, that is, temporary communication, all the subscribers were permanently connected with one another. How expensive, inconvenient and indeed impracticable it would be! All that is lost in this case by the conditional nature of the connection (one cannot get connected every moment with every subscriber) is largely compensated by the wide range of possible connections.

How is the temporary connection, the conditioned reflex formed? For this purpose it is necessary that the new indifferent external agent should coincide in time once, or more than once, with the action of the agent already connected with the organism, i.e., which calls forth this or that activity of the organism. Given this coincidence, the new agent enters into the same connection and manifests itself in the same activity as the old one. Thus, a new conditioned reflex is formed with the help of the old one. In the higher nervous system, where the process of formation of conditioned reflexes occurs, the following procedure takes place: if a new, previously indifferent stimulus, upon entering the cerebral hemispheres, meets in the nervous system at that moment a focus of strong excitation, it begins to concentrate, as if working its way to this focus, and thence to the corresponding organ; thus it becomes a stimulus of that organ. On the contrary, when there is no such focus, it disperses in the mass of cerebral hemispheres without producing any pronounced effect. Such, then, is the formulation of the fundamental law of the higher part of the nervous system.

Allow me now, very briefly, to illustrate *with facts* what I have just said about the mechanism of forming conditioned reflexes.

So far all our research has been done exclusively on the small, physiologically insignificant organ—on the salivary gland. This choice, although at first accidental, proved most successful and even fortunate. In the first place, it corresponded to the fundamental requirement of scientific thought, namely, in the field of complex phenomena to begin with the simplest possible case; in the second place, this organ made it possible clearly to distinguish between simple and complex forms of nervous activity, so that they could be easily contrasted. It was this that led to comprehension of the matter. Physiology has known for years that the salivary glands begin to function, i.e., to secrete saliva in the mouth, when food or other stimulating substances are introduced into the oral cavity, and that this correlation is established by means of definite nerves. These nerves receive the stimulation produced by the mechanical and chemical properties of the substances introduced into the mouth, conduct them first to the central nervous system and thence to the salivary gland, causing there the formation of saliva. This is the old reflex, or, in our terminology, the unconditioned reflex, a constant nervous connection, a simple nervous activity which takes place in exactly the same way as in animals having no higher parts of the brain. At the same time everyone, not only physiologists, knows that the relation of the salivary gland to the external world is highly complex; for example, the sight of food or even the thought of it causes secretion of saliva in a hungry man or animal. According to the old terminology, this signified that secretion of saliva is excited also psychically. The higher parts of the brain are necessary for such complex nervous activity.

The analysis of this particular point revealed that at the basis of this complex nervous activity of the salivary gland, of its complicated relation to the external world, lies the mechanism of the temporary connection—the conditioned reflex, which I described in general terms earlier. Our experiments clarified the matter and brought out indisputable facts. Everything in the external world—every sound, picture, and odour—could be brought into temporary connection with the salivary gland and become an agent stimulating the secretion of saliva—the only condition being that it coincided in time with the unconditioned reflex, with the flow of saliva caused by the substances introduced into the mouth. In short, we were able to produce as many and as varied conditioned reflexes on the salivary gland as we wished.

At present the theory of conditioned reflexes, based on the work of our laboratories alone, constitutes an extensive chapter with a mass of facts and a number of strict rules connecting them. Here is a very general sketch, or, to be more exact, only the headlines of this chapter. First of all there are numerous details relating to the speed of formation of the conditioned reflexes. Then come various kinds of conditioned reflexes and their general properties. Further, since the centre of the conditioned reflexes is located in the higher part of the nervous system, where collision of numberless influences from the external world is always taking place, it is understandable that a never-ending struggle takes place between the various conditioned reflexes, or a selection of them at any given moment. Hence—constant cases of inhibition of these reflexes. Three kinds of inhibition have now been established—simple, extinguishing and conditioned. Taken together they form the group of external inhibition, since they are based on the addition of a collateral external agent to the conditioned stimulus. On the other hand, an already formed conditioned reflex, because of its internal relations alone, is subject to constant fluctuations, even to complete disappearance for brief periods, i.e., is inhibited internally. For example, if even a very old conditioned reflex is repeated several times without being accompanied by the unconditioned reflex, with whose help it was formed, it begins at once gradually but steadily to lose strength and, more or less quickly, is reduced to zero, i.e., if the conditioned reflex, as a signal of the unconditioned, begins to signalize incorrectly, it gradually loses its stimulating effect. This loss of effect occurs not by the destruction of the conditioned reflex, but solely because of its temporary inhibition, since the conditioned reflex thus extinguished is restored of itself after some time. There are still other cases of internal inhibition. Further experimentation revealed a new important side of the problem. It proved that, in addition to excitation and inhibition of excitation, inhibition of the inhibition is just as frequent, i.e., disinhibition. It is impossible to say which of these three acts is the most important. It should be simply stated that all higher nervous activity, as manifested in the conditioned reflexes, consists of a constant interchange, or to be more precise, equilibration of these three basic processes—excitation, inhibition and disinhibition.

I shall pass now to the second of the above-mentioned basic mechanisms—the mechanism of the analysers.

As stated above, the temporary connection is a necessity when the relation of the animal to the external world becomes complex. But this complexity of relations presupposes ability on the part of the animal organism to decompose the external world into separates. And it is actually the case that every higher animal possesses diverse and most delicate analysers. These are what until now have been known as the sense organs. The physiological teaching of these organs, as implied by their name, consists in large measure of subjective material, i.e., of observation and experimentation with the sensations and ideas of human beings, and is thus deprived of all the extraordinary means and advantages afforded by the objective study and the practically boundless field of experimentation on animals. It is true that this branch of physiology, thanks to the interest and participation of a number of brilliant investigators, is in some respects the most elaborated branch of physiology and contains much data of great scientific significance. But this elaborate research concerns mainly the physical side of the phenomena in the sense organs, for example, the conditions for the formation of clear pictures on the retina of the eye. But in the purely physiological part, i.e., in the study of the conditions and kinds of excitability of the nerve endings in the given sense organ, there is a multitude of unsolved problems. In the psychological part, i.e., in the teaching on sensations and ideas resulting from the stimulation of these organs, only elementary facts have been established, despite the skill and keenness displayed by investigators in this field. That which the great Helmholtz implied by the term "unconscious conclusion" evidently corresponds to the mechanism of the conditioned reflex.[49] When, for example, the physiologist becomes convinced that, for the purpose of getting an idea of the actual dimensions of an object, a certain dimension of its image on the retina is required, as well as a certain action of the external and internal muscles of the eye, he is thereby establishing the mechanism of the conditioned reflex. A definite combination of stimuli coming from the retina and ocular muscles, repeatedly coinciding with the tactile stimulus arising from an object of certain size, acts as a signal and becomes a conditioned stimulus produced by the real size of the object. From this point of view, which will hardly be disputed, the principal facts of the psychological part of physiological optics are, physiologically, simply a series of conditioned reflexes, i.e., of elementary facts relating to the complex activity of the eye analyser. Here, in the final analysis, as in all branches of physiology, more, immeasurably more, remains unknown than is known.

An analyser is a complex nervous mechanism which begins with an external receiving apparatus and ends in the brain, either in its lower, or in its higher part; in the latter case it is much more complex. The basic fact of the physiology of the analysers is that each peripheral apparatus is a special transformer of the given external energy into a nervous process. Then there are numerous problems that are far from having been solved or remain wholly unsolved: how is this transformation effected in its last stage? What underlies the analysis? Which part of the activity of the analyser is to be attributed to the construction and process in the peripheral apparatus, and which to the construction and process in the cerebral ending of the analyser? What are the consecutive stages of this analysis from their simplest to the highest forms? And finally, what are the general laws governing this analysis? At present these are questions for purely objective investigation on animals, by the method of conditioned reflexes.

By establishing a temporary connection between the organism and a certain natural phenomenon it is easy to determine the extent to which the given analyser can decompose the external world. For example, it can be revealed without any difficulty and at the same time with great precision that the ear analyser of the dog differentiates the finest timbres, separate small parts of tones, that it not only differentiates, but firmly retains this defferentiation (which in man is called "absolute pitch") and is much more susceptible to high-pitch stimulation than man; it reacts to oscillations of 80 to 90 thousand per second, whereas the limit of the human ear is but from 40 to 50 thousand oscillations per second.

In addition, objective investigation reveals the general rules according to which the analysis is effected. The most important of these is the gradualness of the analysis. The given analyser takes part in the conditioned reflex, in the temporary connection, at first, by its more general and gross activity and only afterwards, being gradually differentiated by the conditioned stimulus, does the activity become highly delicate and refined. For example, if a bright figure appears before the animal, the strong illumination acts first as a stimulus and only afterwards is a special stimulus elaborated from the figure itself, etc.

Further, these experiments on animals with conditioned reflexes clearly revealed that differentiation develops as a result of an inhibitory process, as if through a suppression of all other parts of the analyser except the given one. And it is this gradual development of this process that underlies the gradual analysis. That has been proved by many experiments. I shall refer to one convincing example. If the equilibrium between the excitatory and inhibitory processes is broken down in favour of the former by the administration of stimulants such as caffeine, then the well-elaborated differentiation is immediately and sharply deranged, and in many cases disappears altogether, although temporarily.

Objective study of the analysers also yielded favourable results in experiments with artificially damaged cerebral hemispheres. These experiments disclosed an important and exact fact: the more the cerebral end of the given analyser is damaged, the less delicate is its work; it continues to enter into the conditioned connection as previously, but only through its more general activity. For instance, when the cerebral end of the eye analyser is considerably damaged, one or another intensity of light easily becomes a conditioned stimulus, but separate objects, definite combinations of light and shadow irretrievably lose their specific stimulating effect.

Concluding this exposition of facts relating to the new field of research, I cannot refrain from a brief reference to the peculiarities of this work. The investigator always has the feeling that he is on sure and extremely fertile ground. He is besieged on all sides by questions, and his task is to establish their most expedient and natural order. Notwithstanding the speed of the research it invariably bears a practical character. One who has not tested the facts for himself can scarcely credit how often these, apparently highly complex relations, which, from the psychological point of view, seem truly enigmatic, are subject to clear and successful objective physiological analysis easily verified at all stages by corresponding experiments. Those working in this field are often struck by the incredible power of objective investigation in this new field of highly complex phenomena. I am convinced that extraordinary enthusiasm and a real passion for investigation will grip all who take to this new domain of research.

Thus, in a purely objective way, on the basis of natural science, the laws of complex nervous activity are being elaborated, and the secrets of its mechanisms gradually disclosed. It would be an unjustified claim to assert that the entire higher nervous activity of the higher animals is confined wholly and solely to the two general mechanisms described above. But this, too, is unimportant. The future of research is always obscure and fraught with surprises. In this case the essential point is that a vast and boundless domain for investigation has now been opened up, based on natural science and guided by fundamental, purely scientific concepts.

These basic concepts of the highly complex activity of the animal organism fully harmonize with the most general picture of it from the standpoint of natural science. As part of nature, each animal organism is a complex and integral system, the internal forces of which, so long as it exists, are equilibrated at every moment with the external forces of the surrounding medium. The more complex the organism, the more delicate, manifold and diverse are the elements of its equilibration. There are analysers and mechanisms both of constant and temporary connections which serve this purpose; they establish the most precise relations between the most minute elements of the external world and the most delicate reactions of the animal organism. Thus, life as a whole, from the simplest to the most complex organisms, including man, of course, is a long series of equilibrations with the environment—equilibrations which reach the highest degree of complexity. And the time will come, distant or not, when mathematical analysis based on natural science will express in majestic formulae of equation all these equilibrations, including, in the final analysis, itself.

But in stating all this, I should like to avoid any misunderstanding in relation to myself. I do not deny psychology as the knowledge of the inner world of the human being. Even less am I inclined to deny anything which concerns the deepest aspirations of the human spirit. Here I now simply uphold and assert the absolute and incontestable right of natural science to operate wherever and whenever it is *able* to display its power. And who knows the limits to this!

In conclusion allow me to say something about the practical side of this new field of research.

The researcher who has resolved to register *all* the influences of the external environment on the animal organism requires exceptional equipment for his investigations. He must have in his hands all the external influences. That is why he needs an absolutely new, hitherto unprecedented, type of laboratory, where there are no accidental sounds, no sudden fluctuations of light, no abruptly changing air draughts, etc.; in short, it must be a laboratory with the maximum evenness, where the investigator has at his disposal the drives of generators producing all kinds of energy, and the widest range of corresponding analysers and measuring instruments. Here, there must be real competition between the modern technique of the physical instruments and the perfection of the animal analysers. This combination will result in a close alliance between physiology and physics, which, it can be assumed, will greatly benefit physics.

At present, because of existing laboratory conditions, the work in question is often not only restricted, contrary to our will, but almost always entails considerable difficulties for the experimenter. He may have spent weeks preparing for his experiment, and at the very last moment, when he is patiently waiting for positive results, a sudden vibration of the building, a noise from the street, etc., destroys his hopes and delays the desired answer indefinitely.

The right kind of laboratory for this investigation is, in itself, of great scientific importance, and since our country has laid the foundations for this kind of research I would like to see it build the first appropriate laboratory so that this, as it seems to me, highly important scientific establishment should redound solely to our honour and credit. This, of course, can be achieved with the help of public interest and initiative. In conclusion I must confess that this speech has been prompted and encouraged predominantly and mainly by the hope that public interest will be shown here, in Moscow, in this home of Russian glory.

"PURE PHYSIOLOGY" OF THE BRAIN[50]

I have been invited by the President of the Organizing Committee of this congress to read a paper before the Psychology Section on the cerebral activity based on the work of the laboratories of which I am in charge. I have readily accepted the invitation since I feel that an exchange of views between representatives of psychology on this vital problem is an urgent necessity.

Some years ago our esteemed president wrote the following words: "When the physiologists succeed in creating alongside psychology a physiology of the brain—I have in mind *pure physiology*, and not the psychological imitation appearing under this name, a physiology capable of speaking for itself, without psychology prompting it word by word what it ought to say—then we shall see whether or not it would be useful to abolish human psychology and, consequently, comparative psychology. But we have not yet reached that stage."[51]

One cannot but admit the justness of this criticism of the situation as it then was, and that the general formulation of the question is most helpful.

Basing myself on the facts acquired over the years jointly with about a hundred colleagues, and also on the facts accumulated by other investigators, I make bold to state with full conviction that physiology of the cerebral hemispheres (and a "real" physiology at that, in the sense of Prof. Claparède) has made its appearance and is rapidly developing; in studying the normal and pathological activity of the cerebral hemispheres in animals it uses exclusively physiological concepts and has no need whatever to resort to psychological concepts and terminology. Its research rests on the solid foundation of facts, in the same way as the other natural sciences, with the result that exact material is being accumulated at a truly irrepressible rate and the horizon of investigation is constantly widening.

I shall give now only the barest general outline of the fundamental concepts and facts of this physiology of the brain in order to dwell later in detail on one of its points which seems to me particularly appropriate and of special interest for our present meeting.

The basic functions of the higher part of the central nervous system are the coupling of new and temporary connections between the external phenomena and the work of the different organs, and the decomposing by the organism of the complex of the external environment into its separate elements, that is, functions of coupling and analysing mechanisms.

By means of these activities there are established finer and more delicate adjustments of the animal organism to the environment, or, in other words, a more complete equilibration of the system of matter and energy which constitute the animal organism, with the matter and energy of the environment.

The constant connection between certain phenomena and the function of the organs has long been studied by physiologists as the activity of the lower part of the central nervous system and has been called by them reflexes. The function of the higher part of the central nervous system consists in forming new, temporary reflexes; this means that the nervous system is not only a conducting, but a coupling apparatus. Thus, modern physiology distinguishes two kinds of reflexes—constant and temporary (inborn and acquired, reflexes of species and those of the individual). From the purely practical point of view, we call the first reflex unconditioned and the second—conditioned. It is highly probable (and there are indications to this effect) that newly formed reflexes, given the same conditions of life in the course of successive generations, invariably become constant reflexes. Consequently, this must be one of the acting mechanisms in the evolution of the animal organism.

Similarly, elementary analysis is effected by the lower part of the central nervous system, but this, too, like the inborn reflex, has been studied by physiology for a long time already. When, for example, different physiological effects are produced in a decapitated organism by skin stimuli of different quality and location, we have before us the activity of the lower analysing apparatus. In the higher levels of the central nervous system there are the endings of the most delicate and infinitely diverse analysers; the smallest elements of the external world, which are isolated by them, constantly make new connections with the organism and form conditioned reflexes, whereas in the lower parts relatively fewer and more complex agents of the external world participate in the formation of constant reflexes.

As is known, the entire route along which the nervous excitation in an inborn unconditioned reflex travels, is called the reflex arc. Three parts of this arc are rightly distinguished in the lower central nervous system: the receptor (receiving apparatus), the conductor (conducting apparatus) and the effector (apparatus effecting the action). If we add to "receptor" the word "analyser" (the decomposing apparatus) and to "conductor" the word "contactor" (the coupling apparatus), we have a similar anatomical substratum for the two basic functions of the higher part of the central nervous system.

As has long been established by numerous investigators, the conditioned reflex is invariably formed in the presence of a small number of definite conditions; hence, there are no grounds whatever for regarding its formation as an especially complex process. When a certain indifferent stimulus coincides in time with the action of another stimulus producing a definite reflex, after one or several such coincidences this indifferent stimulus itself invariably evokes the same reflex.

In our experiments on dogs we always used two unconditioned reflexes for the elaboration of new conditioned reflexes—the reflex evoked by food and the reflex evoked by introducing acid into the mouth; we measured the secretory reaction of the salivary glands and only occasionally noted motor reactions—positive in the first case and negative in the second. A conditioned reflex can be elaborated in a similar way with the help of an old conditioned reflex. It can be formed also from a stimulus already firmly connected with a certain reflex, even a stable one. Such a conditioned reflex was obtained by us in the case of a destructive stimulus. If the skin of the dog is stimulated by a more or less strong electric current, there is, naturally, a defensive reaction on the part of the animal. By combining this stimulus with repeated feeding of the dog we can make the same current, or even a current of greater strength, as well as any other mechanical or thermal destruction of the skin, produce not a defensive, but a strong alimentary reaction without any signs of the former (the dog turns towards the food and an abundant secretion of saliva begins). A highly essential detail in the elaboration of the conditioned reflex is that the supposed conditioned stimulus should not exactly synchronize with the stimulus of the old reflex, but precede the latter somewhat (by a few seconds).

I shall omit many details relating to the elaboration of conditioned reflexes, their systematization, general characteristics, etc.

As to the activity of the analysers, the first thing to be observed is that in the initial phase all stimuli enter into the new reflex in their general form and only afterwards do they gradually become specialized. If, for example, we elaborate a conditioned stimulus from a given tone, then at first other tones and even other sounds (beats and noises) also produce the same reflex; later, when the conditioned stimulus has been repeated frequently, the range of stimulating sounds becomes smaller and smaller until only the selected tone, and even a certain part of it, evokes the conditioned reflex. In this way the limits of the activity of the analysers are defined; in some analysers of the animal on which we experimented this activity was of incredible delicacy and had possibilities of wide development. A greater or lesser destruction of the brain end of the analyser is respectively reflected in a greater or lesser decline of the degree of analysis.

Again I shall omit many particulars relating to these facts.

Both the conditioned reflex and the process of analysis are subject to constant fluctuations during the normal course of life. I shall not touch now on their chronic changes, but both of them manifest rapid variations, now stronger, now weaker. Up to the present time we have studied most thoroughly the phenomenon of rapid diminution of the activity of the conditioned reflexes. The term "inhibition," generally accepted in physiology, is used by us to denote this phenomenon; we have all the grounds for distinguishing three kinds of this inhibition: external, internal and sleep inhibition.

External inhibition fully reproduces the inhibition which physiology long ago recognized in the lower part of the central nervous system, when the new additional reflex inhibits the one already existing and active. Evidently, this is the expression of constant, non-stop competition between different external and internal stimulations for a relatively predominant role in the organism at the given moment. External inhibition, in its turn, is subdivided into several types.

Internal inhibition has its origin in the mutual relations between the new reflex and the old one with the help of which it was formed; it always develops when the conditioned reflex temporarily or constantly (in the latter case only under a definite new condition) is not accompanied by the stimulus with the aid of which it was elaborated. So far we have studied four kinds of such inhibition. For the sake of brevity I shall dwell only on one of them, the earliest investigated by us. This is the so-called extinction of the conditioned reflex. If an elaborated conditioned stimulus is repeated several times at definite short intervals (two, three, five minutes and more) without being accompanied by the old stimulus with the help of which it was formed, then it gradually weakens and, finally, becomes wholly ineffective. This, however, does not signify destruction of the conditioned reflex, but only its temporary inhibition, since after some time it is completely restored in a spontaneous way. I would like you to keep in mind this kind of internal inhibition since I shall revert to it later in connection with the most important point in my paper.

All kinds of internal inhibition may be disturbed, suppressed and, so to speak, inhibited themselves, i.e., the reflexes inhibited by them become liberated, disinhibited, if external inhibiting agents of moderate strength act on the animal. That is why the study of the phenomena of internal inhibition calls for a specially equipped laboratory, otherwise all accidental agents, and more frequently, of course, acoustic phenomena, may constantly interfere with the experiments.

Finally, the last kind of inhibition is the sleep inhibition, which regulates the proper chemical metabolism of the entire organism, and especially the nervous system. It assumes the form of normal sleep or of hypnotic state.

When describing the nervous activity it is necessary always to take into account the absolute and relative strength of the various stimuli and the duration of their latent traces. Both phenomena clearly manifest themselves in the course of our experiments and can be studied and measured without difficulty. Moreover, one can say that here the most striking phenomenon is the predominance of the law of force and measure; and involuntarily the thought comes to mind that it is not at all accidental that mathematics—the teaching on the relations of numbers—had its origin wholly and solely in the human brain.

The separate features of the nervous systems of different animals were manifested in our experiments with particular force, and can be expressed in exact figures. An example will be given below.

In the course of our investigation of the two basic cerebral functions we gradually disclosed the fundamental properties of the brain mass. One of these is a peculiar movement of the nervous processes in this mass. On the basis of our latest experiments I am in a position to submit to you now, in truly striking form, the fundamental law of the higher nervous activity. This is the law of irradiation and subsequent concentration of the nervous process. This law applies both to excitation and inhibition. It has been frequently and with particular thoroughness investigated by us in the phenomena of internal inhibition. I take the liberty of directing your attention to these experiments.

Before us is a dog, on which by means of the action of acid in the oral cavity as an unconditioned stimulus, a mechanical irritation of more than twenty places on the skin has been made the conditioned stimulus of the acid reaction, i.e., mechanical irritation of these places (effected by a special device) evokes, each time, secretion of a definite quantity of saliva and a corresponding motor reaction. The effect obtained from the stimulation of any of these places on the skin is equal. Now for the experiment itself. Let us apply the mechanical irritation to a certain point of the skin for a definite period, say thirty seconds. We obtain a salivary reflex which is strictly measurable in certain units. This time, to the conditioned stimulus we do not add the introduction of acid into the mouth as an unconditioned stimulus, and after a certain interval, say two minutes, we repeat the application of the conditioned stimulus. In this way we get a decreased reflex. We continue to repeat the application of the conditioned stimulus until the conditioned reflex is reduced to zero. This is what we have termed the extinction of the conditioned reflex, one of the kinds of internal inhibition. We have thus evoked the process of inhibition in a certain point of the brain end of the cutaneous analyser, i.e., in the area of the cerebral hemispheres connected with the skin. Let us now follow the development of this process. Immediately after obtaining the zero effect on the repeatedly stimulated point of the skin (primary extinction) we begin to stimulate, without interruption, a new point 20 or 30 cm. distant from the first (our dog being of average size). We obtain here a normal effect equal to, say, thirty divisions on the tube with which we measure the quantity of the secreted saliva. We repeat this experiment (in one day, in two days, etc.) in the following way: we stimulate a new, distant part of the skin not immediately after obtaining the zero effect on the place of primary extinction, but five seconds later. Now the secretion of saliva is reduced to, say, twenty divisions (secondary extinction). With the next repetition of the experiment, but after an interval of fifteen seconds, the secretory effect is reduced to five divisions. After an interval of twenty seconds it falls to zero. Let us continue. After an interval of thirty seconds, a secretory effect reappears equalling three or five divisions. After an interval of forty seconds we get from fifteen to twenty divisions, after fifty seconds—from twenty to twenty-five divisions, and after sixty seconds—the customary effect is fully restored. Throughout this period (sixty seconds and even much longer) all attempts to irritate the point of the primary extinction have no effect whatsoever. We obtain the same series of figures, no matter which two points of the skin we choose for primary and secondary extinction, provided the distance between them remains the same. If the distance between the stimulated points is decreased, then the difference is as follows: the decrease of the secretory effect and the zero effect at the point of the secondary extinction appear earlier, the zero effect persists longer and the return to normal takes place later.

These experiments, provided, of course, that all the necessary precautions are observed, proceed with marvellous exactitude. These experiments, carried out by two experimenters on five dogs, were observed by me in the course of one year. Their stereotype character was astonishing, and I can say without exaggeration that for a long time I could not believe my eyes.

If we compare these facts with other similar facts and exclude various other hypotheses, we arrive at the following natural and simple conclusion. Regarding the skin as the projection of a definite area of the brain, we must assume that the process of internal inhibition arising in a certain point of this area first spreads, irradiates over the entire area, and immediately afterwards begins to concentrate around the point of origin. It is worth noting that this movement in both directions proceeds very slowly. Also of interest is the fact that this speed, which greatly varies in different animals (in the relation of 1 : 5 and even more) remains for any given animal highly stable, one might even say, invariable.

As we see, the law of irradiation and concentration of the nervous process is of great importance. It can establish the relation between many, seemingly quite different, phenomena, for instance, the generalized character of each individual stimulus when it first becomes a conditioned stimulus, the mechanism of external inhibition; and the formation of the conditioned reflex itself, which can be understood as a phenomenon of concentrated stimulation. However, I shall not now go into detailed consideration of the significance of this law; I shall simply avail myself of the foregoing experiment, which illustrates this law, for some special purpose.

During thirteen years' work jointly with my colleagues on conditioned reflexes, I have always had the impression that the psychological concepts and the systematization of subjective phenomena by the psychologists must profoundly differ from physiological concepts and physiological classification of the phenomena of the higher nervous activity; that the reproduction of the nervous processes in the subjective world is very peculiar, is, so to speak, many times refracted, with the result that the entire psychological concept of the nervous activity is highly conventional and approximate. And it is from this point of view that the above-mentioned experiment deserves special attention.

When we first established the fact of extinction of the conditioned reflex, many people used to say: "There is nothing unusual in this. The explanation is quite simple. The dog notices that the signal no longer corresponds to reality and, therefore, begins to react more and more weakly, until, finally, there is no reaction at all."

I believe that many of you who uphold the scientific validity of zoopsychology would say the same thing. Be that as it may. But then, gentlemen, it seems to me that you are obliged to interpret psychologically the experiment described above in detail and in all its phases. I have suggested this many times to men of different specialities (naturalists and sociologists). The result was most definite: each gave his own interpretation, i.e., fancied in his own way one or another internal state of the animal; however, it proved impossible in most cases to harmonize or reconcile their explanations. The zoopsychologists spoke of the ability of the animal to make distinctions, to remember things, to draw conclusions, to experience confusion, disappointment, and other similar qualities in a variety of combinations. In reality there took place in the nervous mass only irradiation and subsequent concentration of the inhibitory process, and this knowledge made possible an absolutely exact prediction (in figures) of the phenomena.

What can you say in reply, gentlemen? I await your answer with the greatest interest.

Here I conclude the part of my paper which deals with facts. Allow me to make a few supplementary remarks. All parts of the higher nervous activity of the experimental animals are gradually involved in our investigation of the conditioned reflexes; one can see this even from a rough, approximate comparison between the external facts under our observation, and the psychological classification of such subjective phenomena, as consciousness, thought, will, affect, etc. The meaning of some of these facts became clear to us in the course of our objective study of animals with damaged cerebral hemispheres. Finally, the general condition of the brain, in its active state and at rest, was revealed more and more clearly.

So far the entire field of research opening before us comprises our concept of the two basic activities of the cerebrum—the coupling and the analysing functions—and a few fundamental properties of the brain mass. Life will show whether this is sufficient, since, naturally, our general knowledge of the brain and also of its general properties is bound to be extended and deepened.

And so, as mentioned above, the horizon of strictly objective investigation of the higher nervous activity is steadily widening. Why, then, should physiology strive to penetrate into the hypothetical fantastic internal world of the animal? In thirteen years of research I have never had success with psychological concepts. The physiology of the animal brain must not for a single moment leave the ground of natural science, which every day proves its absolute solidity and extreme fruitfulness. We can rest assured that along the path taken by the strict physiology of the animal brain, astonishing discoveries await science and, together with them, extraordinary power over the higher nervous system—discoveries and power not a whit inferior to other achievements of natural science.

I greatly appreciate the contribution of the old and the new psychologists, but it seems to me, and it can hardly be doubted, that this work is being done in an extremely inefficient way, and I am fully convinced that the pure physiology of the animal brain will greatly facilitate, and, moreover, enrich the Herculean labours of those who have devoted their lives to the study of the subjective states of man.

RELATION BETWEEN EXCITATION AND INHIBITION, DELIMITATION BETWEEN EXCITATION AND INHIBITION, EXPERIMENTAL NEUROSES IN DOGS[52]

Dedicated to the memory of my best friend, Professor Robert Tigerstedt, to whom phisiology owes so much for his investigations and for his work in promoting physiological knowledge and physiological research

All the factual material which follows relates to the work of the cerebral hemispheres and has been obtained by the method of conditioned reflexes, i.e., reflexes formed in the course of the animal's individual life. Since the concept of conditioned reflexes is not yet generally known and recognized among physiologists I shall, for the purpose of avoiding repetition, refer the reader to my articles recently published in these archives[53] (1923).

Proceeding from the big difference between the phenomena, we had to distinguish two kinds of inhibition in the work of the cerebral hemispheres—external and internal—according to our terminology. The former appears in our conditioned reflexes at once; the latter develops with the passage of time and is elaborated gradually. The first is an exact repetition of the well-known inhibition in the physiology of the lower part of the central nervous system, which appears when stimuli acting on the various centres and evoking different nervous activities, meet; the second can be inherent only in the cerebral hemispheres. It may be, however, that the difference between these kinds of inhibition is connected only with the conditions of their emergence and not with the essence of the process itself. This question is still being investigated by us. The present article deals only with internal inhibition; further, I shall call it simply inhibition, without the adjective, although each time implying internal inhibition.

There are two conditions, or to be more precise, one condition, the presence or absence of which determines whether the impulse brought into the cells of the cerebral hemispheres from the outside chronically provokes a process of excitation or a process of inhibition. In other words, the impulse will in one case become positive and in the other negative. This fundamental condition consists in the following: if the stimulation coming to a cerebral cell coincides with another extensive stimulation of the cerebral hemispheres, or of a definite lower part of the brain, then it will always remain positive; given the reverse condition it will, sooner or later, become a negative, inhibitory stimulus. Of course this indubitable fact gives rise to the question: why is this so? But so far there has been no answer to this question. Thus, we must proceed from this fact without having analysed it. Such is the first basic relation between excitation and inhibition.

Physiologists have long been aware of the irradiation of the excitatory process. The study of the higher nervous activity led us to the conclusion that the inhibitory process, too, spreads, under certain conditions, from the point where it is originated. The facts underlying this conclusion are perfectly plain and obvious. Now, if the excitatory process spreads from one point, and the inhibitory process from another, they limit each other and confine each other to a definite area and within definite bounds. In this way a very delicate functional delimitation of separate points of the cerebral hemispheres can be obtained. When these separate points are subjected to excitation under corresponding conditions, it can be easily explained by the scheme of the cellular construction. But this interpretation meets with certain difficulties when there is an excitatory or inhibitory process related to various intensities or other similar variations (for example, to different frequencies of the metronome beats) of one and the same elementary external stimulating agent. In order to explain this on the basis of the same simple cellular scheme, it would be necessary to assume as a point of application of this agent not a single cell but a group of cells. In any case, it is actually possible to associate the excitatory process with one intensity of a certain elementary agent and the inhibitory process with another. Thus, the second general relation between excitation and inhibition consists in their mutual spatial limitation, in their delimitation. A clear demonstration of this is obtained by the experiments with mechanical stimulation of various points of the surface of the skin.

Thus, we have to assume that a certain conflict takes place between two opposing processes which normally ends in the establishment of a definite equilibrium between them, in a definite balance. This struggle and this equilibration confront the nervous system with a difficult task. We have seen this from the very outset of our research, and we are seeing it now. This difficulty is often manifested in the animal in the form of motor excitation, whining and dyspnoea. But in most cases equilibrium finally sets in; each process is allotted its place and time, and the animal becomes perfectly quiet, reacting to respective stimuli now by the excitatory, now by the inhibitory process.

Only under certain conditions does this conflict end in disturbance of the normal nervous activity; then a pathological state sets in which lasts for days, weeks, months and perhaps even years, and either gradually returns to the normal of itself after the experiments have been discontinued for a time and the animal has been allowed rest, or it must be eliminated by definite treatment.

These special cases at first emerged spontaneously, unexpectedly, but later they were deliberately produced by us for research purposes. We describe them here in chronological order.

The first of these cases was obtained by us a long time ago (experiments of Dr. Yerofeeva). It consisted in the following. The conditioned alimentary reflex was elaborated in the dog not from an indifferent agent, but from a destructive one, provoking an inborn defensive reflex. The animal's skin was irritated by an electric current, and at the same time the animal was fed, at first even forcibly. In the initial phase a weak current was applied, but later it was increased to the maximum. The experiment ended thus: the strongest current, as well as the severe burning and mechanical destruction of the skin, provoked only an alimentary reaction (a corresponding motor reaction and a secretion of saliva) without any sign of a defensive reaction, or even of any change in respiration and heartbeat—the usual accompaniments of this reaction. Evidently this result was obtained by transferring the external excitation to the food centre and simultaneous inhibition of the centre of the defensive reaction. This specific conditioned reflex persisted for months, and probably would have remained unchanged under the given conditions had we not begun to modify it, systematically transferring the electric irritation to new points of the skin. When the number of these points became considerable, the picture suddenly and abruptly changed in one of our dogs. Now only a very strong defensive reaction manifested itself everywhere, even in the first location of the skin stimulus and under the action of the weakest current; there was no trace of the alimentary reaction.

The old result could not be reproduced. The dog which had previously been quiet became greatly excited. In another dog a similar result was obtained only when—notwithstanding the large number of points on the skin from which we could produce only an alimentary reaction under the application of a strong current—we frequently and quickly, in the course of one and the same experiment, transferred the irritation from one place to another. We had to allow rest to the dogs for several months, and only in one of them were we able, acting slowly and cautiously, to restore the conditioned alimentary reflex to the destructive agent.

The second case of a similar character was observed somewhat later (experiment of Dr. N. R. Shenger-Krestovnikova). A conditioned alimentary reflex was brought about in a dog by a circle of light projected on a screen placed in front of the animal. We then began to elaborate a differentiation of the circle from an ellipse of the same size and intensity of light, i.e., the appearance of the circle was accompanied each time by feeding, whereas that of the ellipse was not. In this way the differentiation was obtained. The circle evoked an alimentary reaction, but the ellipse remained ineffective, which, as we know, is a result of development of inhibition. The ellipse which was applied first greatly differed in form from the circle (the proportion of its axes was 2:1). Then the form of the ellipse was brought closer and closer to that of the circle, i.e., the axes of the ellipse were gradually equalized, and thus sooner or later we were able to obtain an increasingly delicate differentiation. But when we applied an ellipse whose axes were as 9:8, the picture abruptly changed. The new delicate differentiation, which always remained incomplete, persisted for two or three weeks, after which it not only disappeared itself, but caused the loss of all earlier, even the least delicate, differentiations. The dog, which previously behaved quietly in the stand, was now constantly moving about and whining. All differentiations had to be elaborated anew, and the crudest one now demanded much more time than at first. When the final differentiation was reached, the same story was repeated—all the differentiations vanished, and the dog again became excited.

Some time after these observations and experiments we set ourselves the task of investigating this phenomenon more systematically and in more detail (experiments of Dr. M. K. Petrova). Since it was possible to conclude from the above-mentioned facts that the derangement of normal relations was caused by a difficult collision between the excitatory and inhibitory processes, we carried out on two dogs of different types—one very lively and the other inactive and quiet—experiments first of all with various inhibitors and their combinations. Together with the conditioned reflexes, delayed for three minutes, i.e., when the unconditioned stimulus was added to the conditioned only three minutes after the beginning of the latter, owing to which the positive effect of the conditioned reflex appeared only after a preliminary inhibitory period of one or two minutes, other kinds of inhibition were applied (differentiation, etc.). But this task was accomplished by the different nervous systems without any derangement of the normal relations, although with a different degree of difficulty. Then we added the alimentary reflex formed by means of a destructive agent. Now it was sufficient, having evoked this reflex, to repeat it for a certain period of time even on one and the same part of the skin, in order to obtain an acute pathological state. This deviation from the normal occurred in the two dogs in opposite directions. In the lively dog the elaborated inhibitions either suffered to a considerable degree or wholly disappeared and turned into positive agents; in the quiet dog it was the positive salivary conditioned reflexes that either weakened or completely vanished. And these states persisted for months without any spontaneous change. In the lively dog with the weakened inhibitory process a quick and lasting return to the normal was obtained in a few days by means of rectal injections of potassium bromide. It is worth noting that with the appearance of normal inhibition the strength of the positive conditioned action, far from decreasing, was even somewhat increased; consequently, on the basis of this experiment we can assume that the action of bromide does not consist in diminution of nervous excitability, but in regulating nervous activity. In another dog permanent and more or less considerable salivary reflexes could not be restored despite the different means applied for this purpose.

Shortly after these experiments similar results, and even with more instructive details, were obtained with a dog subjected to experimental investigation for quite a different purpose (experiments of Dr. I. P. Razenkov). Many positive conditioned reflexes were elaborated on the animal from various receptors, or several reflexes from one and the same receptor by a certain stimulating agent of varying intensity. Among others there was obtained a reflex to a definite frequency of mechanical stimulation of a certain point on the skin. We then began to elaborate a differentiation from the same place on the skin by means of a mechanical stimulation of another frequency. This differentiation was also obtained without difficulty, and no change in nervous activity was observed. But when, after application of a completely inhibited rhythm of mechanical skin stimulation, we tried without any interval to effect stimulation by a positively-acting rhythm, a peculiar disturbance was manifested in the dog, lasting for five weeks and only gradually ending in a return to the normal, perhaps somewhat accelerated by our special measures. A few days after the collision of the nervous processes occurred, all the positive conditioned reflexes disappeared. This lasted for ten days, after which the reflexes began to reappear, but in a peculiar way: contrary to normal, the strong stimuli remained ineffective or produced the minimum effect; considerable effect was shown only by the weak stimuli. This state persisted for fourteen days and was again superseded by a peculiar phase. Now all the stimuli acted equally, approximately, with the same force as strong stimuli under normal conditions. This lasted seven days, and then came the last period before the return to the normal; this phase was characterized by the fact that the stimuli of average strength greatly exceeded those in the normal state, the strong stimuli became somewhat weaker than in the normal and the weak stimuli lost their action altogether. This, too, lasted for seven days, and then, finally, came the return to the normal. Repetition of the same procedure which was responsible for the disturbance described above, i.e., repetition of direct, without any interval, transition from the inhibitory mechanical stimulation of the skin to the positively-acting stimulation, resulted in the same disturbance with the same variation in phases, but of considerably shorter duration. With further repetition the disturbance became more and more fleeting, until the same procedure no longer evoked any derangement. The decline of the pathological disturbance was manifested not only in the shortened duration of the abnormal state, but also in a reduction in the number of phases, and in the disappearance of the more abnormal phases.

Thus, the difficult collision between the excitatory and inhibitory processes leads now to a predominance of the excitatory process disturbing the inhibition, or, one may say, to a prolonged increase of the tonus of the excitation, and now to a predominance of the inhibitory process, with its preliminary phases, disturbing the excitation, and increasing the tonus of the inhibition.

But then we witnessed the same phenomena also under other conditions, besides those mentioned above.

Under the action of extraordinary, directly inhibiting stimuli on the animal a chronic predominance of inhibition takes place. This manifested itself with particular force in a number of dogs after the unusual flood that occurred in Leningrad on September 23, 1924, when our experimental animals were rescued with great difficulty and under exceptional conditions. The conditioned reflexes disappeared for some time and only slowly reappeared. For a considerable period after rehabilitation any more or less strong stimulus, which earlier would have been regarded as a very strong conditioned stimulus, as well as the application of a previously elaborated and thoroughly concentrated inhibition, again provoked this chronic state of inhibition either in the form of complete inhibition or of its above-mentioned preliminary phases (experiment of Dr. A. D. Speransky and Dr. V. V. Rickman). To a lesser degree and for a shorter time the same thing is often observed in more normal conditions, such as transferring the animals to a new environment, to a new experimenter, etc.

On the other hand, a slight change in the application of a well-elaborated positive conditioned reflex, namely, an unconditioned stimulus administered directly, without any interval, after the conditioned stimulus, increases the tonus of the excitation to such a degree that the elaborated inhibitions, now under investigation, either fully disappear, or greatly lose in constancy and regularity. And often a frequent interchange of positive and inhibitory reflexes brings the dogs, especially the lively ones, to the highest pitch of general excitation (experiments of Dr. M. K. Petrova and Dr. E. M. Kreps).

However, what has been said above does not exhaust all our facts concerning the relation between excitation and inhibition. In the course of our work we encountered other peculiar cases of the same kind.

We frequently noticed that a distortion of the action of conditioned stimuli took place in certain phases of drowsiness in normal animals.

The positive stimuli lost their effect, while the negative inhibitory ones assumed a positive character (for example, in the experiments carried out by Dr. A. A. Shishlo). In the light of this relation we can explain the frequently recurring fact that in the drowsy state of the animal there begins as it were a voluntary secretion of saliva not observed in the waking state. The explanation is that at the beginning of the elaboration of the conditioned reflexes in a given animal the entire mass of accessory stimuli, one can say, the entire laboratory surroundings, enter into conditioned connection with the food centre, but later all these stimuli become inhibited owing to the specialization of the conditioned stimulus applied by us. It can be assumed that in a state of drowsiness these inhibited agents temporarily recover their original effect.

The temporary transformation of the elaborated inhibitory stimulus into a positive one is also observed in pathological states of the cerebral cortex in intervals between the convulsive fits caused by post-operative cicatrization in the cortex. It is interesting to note that along with this elaborated inhibitory stimulus, only the weakest of all the positive conditioned stimuli, viz., light, acts, also positively, during this time, whereas all other moderate and strong positive conditioned stimuli remain ineffective (experiments of Dr. I. P. Razenkov).

Related to this is the fact, frequently reproduced by us, that accessory stimuli evoking certain reflexes of moderate strength transform in the course of their action the inhibitory reflexes into positive ones (we call it disinhibition).

On the contrary, during disturbance of the cortex, caused by extirpation, the positive conditioned stimuli belonging to the disturbed part of the cortex become inhibitory, a point mentioned in my last article on sleep. This phenomenon is particularly manifest and has been best studied in the cutaneous region of the cerebral hemispheres. (Earlier experiments of Dr. N. I. Krasnogorsky and recent experiments of Dr. I. P. Razenkov.) If the lesion is insignificant the effect produced by the previous positive conditioned mechanical stimulation of the skin is less than normal, and if repeated during one and the same experiment soon becomes inhibitory; being added to other effective stimuli it weakens their effect and when applied alone induces a state of sleepiness in the animal. If the lesion is more severe, it does not, in normal conditions, produce any positive effect, being of a purely inhibitory nature; its application leads to the disappearance of all positive conditioned reflexes in the other parts of the cerebral hemispheres.

But this agent, now inhibitory, may, in certain circumstances, manifest a positive effect. If the animal becomes sleepy of itself, this stimulus, as well as the elaborated inhibitory agent, as mentioned above, produces a slight positive effect. But afterwards this effect can be obtained by other methods. If we repeatedly apply this stimulus several times with a brief intermission, for example, of five seconds instead of the usual thirty (i.e., if the unconditioned stimulus is added five seconds instead of thirty seconds after the beginning of the conditioned stimulus), then, upon delaying it again for thirty seconds, we may obtain a positive effect, although a fleeting one. Setting in very soon after the beginning of the stimulation, it quickly diminishes in the course of stimulation and finally disappears altogether (pure excitatory weakness). A similar transitory effect can be obtained by means of a preliminary injection of caffeine and by other measures (experiments of Dr. I. P. Razenkov).

Of a somewhat different character, but still related to our subject, are the following facts. Given a very weak general excitability of the cortex, as observed in aged animals (Dr. L. A. Andreyev's experiments) or in animals with removed thyroid glands (experiments of Dr. A. V. Valkov), as well as in certain states brought on in the animals by convulsions during post-operative scarring in the cortex (experiments of Dr. I. P. Razenkov), the inhibitory process either becomes impossible or is greatly weakened.

In such cases only an increase of the tonus of cortical excitability, achieved by application of stronger unconditioned stimuli, can sometimes provoke an inhibitory process.

The phenomenon of reciprocal induction, mentioned by me in the previous, above-mentioned articles (experiments of D. S. Fursikov, V. V. Stroganov, E. M. Kreps, M. P. Kalmykov, I. R. Prorokov and others), is also related to our subject. Finally, the last fact: if separate points of the cortex are reinforced for a prolonged period by a corresponding procedure, some of them as points of excitation and others as points of inhibition, they become highly resistant to attacks, to the influence exerted by opposite processes, and at times call for exceptional measures in order to change their functions (experiments of Dr. B. N. Bierman and Dr. Y. P. Frolov).

All the foregoing facts allow us, it seems to me, to systematize the states to which the cortex is subjected under different influences in a definite consecutive order. At one pole there is the state of excitation, an exceptional increase of the tonus of excitation, when an inhibitory process becomes impossible or is greatly impeded. Next comes the normal, wakeful state, the state of equilibrium between the excitatory and inhibitory processes. This is followed by a long, but also consecutive, series of states transitory to inhibition; the most typical of these are: the equalization state when in contrast to the wakeful state all stimuli, irrespective of their intensity, act with an absolutely equal force; the paradoxical state, when only the weak stimuli act, or when the strong stimuli act, too, but produce a barely noticeable effect; and finally, the ultra-paradoxical state when only the previously elaborated inhibitory agents produce a positive effect—a state followed by complete inhibition. There is yet no clear explanation of the state when excitability is so low that inhibition is utterly impossible or greatly impeded, just as in the case of the state of excitation.

At present, among other things, we are engaged in the experimental solution of the following question (for which we now have some clues): are there not in evidence the transitory states so sharply expressed in pathological cases also in all cases of normal transition from an active state to a state of inhibition, such as the process of falling asleep, the process of elaborating inhibitory reflexes, etc.?

Should this be so, then only the retardation, certain isolation and fixation of the states which normally develop and change quickly, or almost imperceptibly, bear a pathological character.

The above facts open the way to an understanding of numerous phenomena relating both to the normal and pathological higher nervous activity. I shall give some examples.

I have already shown in previous articles how normal behaviour is based on the elaborated delimitation of the points of excitation and inhibition, on their grandiose mosaic in the cortex, and how sleep represents irradiated inhibition. We are now in a position to give some details showing how certain variations of normal sleep, as well as separate symptoms of the hypnotic state, can be easily understood when regarded as different degrees of extensiveness and intensiveness of the inhibitory process.

Cases of sleep setting in while walking or riding horseback are not unknown. This means that the inhibition is confined only to the cerebral hemispheres and does not spread to the lower centres established by Magnus.[54] We know also of sleep accompanied by partial wakefulness in relation to definite stimuli, for instance, the sleep of the miller who wakes when the noise of the mill stops, the sleep of the mother awakening at the faintest sound coming from her sick child, but who is not disturbed by other and much stronger stimuli, i. e., in general a sleep with easily excitable points on guard. Catalepsy in hypnosis is, apparently, an isolated inhibition only of the motor region of the cortex, not affecting all the other parts of the cortex and not spreading to the centres of equilibrium of the body. Suggestion in hypnosis can be rightly interpreted as such a phase of inhibition when weak conditioned stimuli (words) produce a greater effect, evidently, than the stronger direct and real external stimuli. The symptom established by Pierre Janet[55]—loss of the sense of reality during sleep lasting for many years, can be explained as chronic inhibition of the cortex which is interrupted only for a short time and only under weak stimuli (usually at night); this inhibition particularly concerns the cutaneous and motor regions which are most important for the influence of the external world on the organism, on the one hand, and for the real action of the organism on the external world, on the other. Senile talkativeness and dementia are easily explained by the extreme weakening of inhibition in cases of very low excitability of the cortex. Finally, our experiments on dogs entitle us to regard chronic deviations of the higher nervous activity from the normal, produced in the animals by us, as pure neurosis; to a degree they also explain the mechanism of the origin of these deviations. Similarly the action of exceedingly strong, extraordinary stimuli (for example, unusual flood) on dogs with a weak nervous system and a predominance of the inhibitory process under normal conditions, in other words, with a constantly increased tonus of inhibition, reproduces the aetiology of a special traumatic neurosis.

As for a theory that would cover and generally substantiate all these phenomena, it is obvious that the time has not yet come for it, although many hypotheses have been advanced, each one of them justified to a degree. It seems to me that as things are at present it is possible to make use of the different concepts which actually systematize the factual material and advance new and detailed problems. In our experiments so far we think of different phases, from extreme excitation to deep inhibition, which develop in the nervous cells of the cortex under the influence of effective stimuli, and which depend on the intensity and duration of these stimuli and on the conditions under which the latter are formed. We incline to this view because of the obvious analogy between the changes observed in the activity of the cerebral cortex and the changes taking place in the nerve fibre under various strong influences, which have been described in the well-known work of N. E. Wedensky—*Excitation, Inhibition and Narcosis.*[56] We do not share his theory, but we have grounds for relating all the observed transitions from excitation to inhibition to one and the same elements—to the nerve cells—just as Wedensky rightly did in the case of the nerve fibre.

One can hardly doubt that only the study of the physicochemical process taking place in the nerve fibre will provide us with a real theory of all nervous phenomena, and that the phases of this process will give us an exhaustive explanation of all external manifestations of the nervous activity, of their sequence and interconnections.

THE CONDITIONED REFLEX[57]

The conditioned reflex is now used as a separate physiological term to denote a certain nervous phenomenon, the detailed study of which has led to the creation of a new branch in the physiology of animals—the physiology of the higher nervous activity, as the first chapter in the physiology of the higher parts of the central nervous system. For many years empirical and scientific observations have been accumulated which show that a mechanical lesion or a disease of the brain, and especially of the cerebral hemispheres, causes a disturbance in the higher, most complex behaviour of the animal and man, usually referred to as psychical activity. At present hardly anyone with a medical education would doubt that our neuroses and psychoses are connected with the weakening or disappearance of the normal physiological properties of the brain, or with its greater or lesser destruction. But the following persistent, fundamental questions arise: what is the connection between the brain and the higher activity of the animal and man? With what and how must we begin the study of this activity? It would seem that psychical activity is the result of the physiological activity of a certain mass of the brain and that physiology should investigate it in exactly the same way as the activity of all other parts of the organism is now being successfully investigated. However, this has not been done for a long time. Psychical activity has long (for thousands of years) been the object of study by a special branch of science—psychology. But physiology, strange as it may seem, only recently—in 1870—obtained with the help of its usual method of artificial stimulation the first precise facts relating to a certain (motor) physiological function of the cerebral hemispheres; with the help of its other usual method of partial destruction it acquired additional facts relating to the establishment of connections between other parts of the cerebral hemispheres and the most important receptors of the organism—the eye, the ear, etc. This raised hopes among physiologists, as well as psychologists, that close connection would be established between physiology and psychology. On the one hand, the psychologists used to begin text-books on psychology with a preliminary exposition of the theory of the central nervous system, and especially of the cerebral hemispheres (sense organs). On the other hand, the physiologists when experimenting with the destruction of various parts of the hemispheres in animals viewed the results obtained by them psychologically, by analogy with the human internal world (for example, Munk's assertion that the animal "sees," but "does not understand").[58] However, both camps soon became disappointed. The physiology of the cerebral hemispheres perceptibly stopped at these first experiments and made no further substantial advance. In the meantime many resolute psychologists again took up the cudgels saying that psychological research should be fully independent of physiological. At the same time there were other attempts to link the triumphant natural science with psychology through the method of numerical measurement of psychical phenomena. At one time an attempt was made to create in physiology a special branch of psychophysics on the basis of the fortunate discovery by Weber and Fechner of the law[59] (named after them) which establishes a certain numerical relation between the intensity of an external stimulus and the strength of a sensation. But the new branch failed to go beyond this single law. More successful was the attempt made by Wundt,[60] a physiologist who became a psychologist and philosopher, experimentally to apply the method of numerical measurement to psychical phenomena in the form of the so-called experimental psychology; thus, considerable material has been collected already and more is being accumulated. Mathematical analysis of the numerical material obtained by experimental psychology is called by some people, as Fechner did it, psychophysics. But now even among psychologists and especially psychiatrists, there are many who are bitterly disappointed in the practical application of experimental psychology.

So what is to be done? However, a new method of solving the fundamental question was already on the way. Was it possible to discover an elementary psychical phenomenon which at the same time could be fully and rightly regarded as a purely physiological phenomenon? Was it possible to begin with it, and by a strictly objective study (as generally done in physiology) of the conditions of its emergence, its various complexities and its disappearance, to obtain first of all an objective physiological picture of the entire higher nervous activity in animals, i.e., the normal functioning of the higher part of the brain, instead of the previous experiments involving its artificial irritation and destruction? Fortunately, such a phenomenon had long been observed by a number of researchers; many of them paid attention to it and some even began to study it (special mention should be made of Thorndike[61]), but for some reason or other they stopped the study at the very beginning and did not utilize the knowledge of this phenomenon for the purpose of elaborating a fundamental method of systematic physiological study of the higher activity in the animal organism. This was the phenomenon now termed the "conditioned reflex," thorough study of which has fully justified the previously expressed hope. I shall mention two simple experiments that can be successfully performed by all. We introduce into the mouth of a dog a moderate solution of some acid; the acid produces a usual defensive reaction in the animal: by vigorous movements of the mouth it ejects the solution, and at the same time an abundant quantity of saliva begins to flow first into the mouth and then overflows, diluting the acid and cleansing the mucous membrane of the oral cavity. Now let us turn to the second experiment. Just prior to introducing the same solution into the dog's mouth we repeatedly act on the animal by a certain external agent, say, a definite sound. What happens then? It suffices simply to repeat the sound, and the same reaction is fully reproduced—the same movements of the mouth and the same secretion of saliva.

Both of the above-mentioned facts are equally exact and constant. And both must be designated by one and the same physiological term—"reflex." Both disappear if we sever either the motor nerves of the mouth musculature and the secretory nerves of the salivary glands, i.e., the efferent drives, or the afferent drives going from the mucous membrane of the mouth and from the ear, and finally, if we destroy the central exchange where the nervous current (i.e., the moving process of nervous excitation) passes from the afferent to the efferent drives; for the first reflex this is the medulla oblongata, for the second it is the cerebral hemispheres.

In the light of these facts even the strictest judgement cannot raise any objection to such a physiological conclusion; at the same time, however, there is a manifest difference between the two reflexes. In the first place, their centres, as already mentioned, are different. In the second place, as is clear from the procedure of our experiments, the first reflex was reproduced without any preparation or special condition, while the second was obtained by means of a special method. This means that in the first case there took place a direct passage of the nervous current from one kind of drives to the other, without any special procedure. In the second case the passage demanded a certain preliminary procedure. The next natural assumption is that in the first reflex there was a direct conduction of the nervous current, while in the second it was necessary preliminarily to prepare the way for it; this concept had long been known to physiology and had been termed "Bahnung."[62] Thus, in the central nervous system there are two different central mechanisms—one directly conducting the nervous current and the second—closing and opening it. There is nothing surprising in this conclusion. The nervous system is the most complex and delicate instrument on our planet, by means of which relations, connections are established between the numerous parts of the organism, as well as between the organism, as a highly complex system, and the innumerable, external influences. If the closing and opening of electric current is now regarded as an ordinary technical device, why should there be any objection to the idea that the same principle acts in this wonderful instrument? On this basis the *constant connection between the external agent and the response of the organism, which it evokes, can be rightly called an unconditioned reflex, and the temporary connection—a conditioned reflex.* The animal organism, as a system, exists in surrounding nature thanks only to the continuous equilibration of this system with the environment, i.e., thanks to definite reactions of the living system to stimulations reaching it from without, which in higher animals is effected mainly by means of the nervous system in the shape of reflexes. This equilibration, and consequently, the integrity both of the individual organism and of its species, is ensured first of all by the simplest unconditioned reflexes (such as coughing when foreign substances enter the larynx), as well as by the most complex ones, which are usually known as instincts—alimentary, defensive, sexual and others. The reflexes are caused both by internal agents arising within the organism and by external agents, and this ensures the perfection of the equilibration. But the equilibrium attained by these reflexes is complete only when there is an absolute constancy of the external environment. But since the latter, being highly varied, is always fluctuating, the unconditioned, or constant connections are not sufficient; they must be supplemented by conditioned reflexes, or temporary connections. For example, it is not sufficient for the animal to take the food placed before it—in this case it would often be hungry and die of starvation; the animal must discover the food by its various accidental and temporary symptoms, and the latter are precisely conditioned (signalling) stimuli exciting the animal's movement towards the food which ends in its introduction into the mouth, i.e., in general, they evoke a conditioned alimentary reflex. The same holds for everything of importance for the well-being of the organism and the species both in the positive and in the negative senses, i.e., for everything which the animal must take from the environment and against which it must be on guard. No great power of imagination is needed to realize at once what a truly innumerable quantity of conditioned reflexes are constantly effected by the most complex system of the human being who is placed not only in a very broad natural environment, but often also in a very broad specifically social environment, which, on the overall scale, embraces all mankind. Let us take this alimentary reflex. How many diverse conditioned temporary connections, both generally natural and specifically social, are required by a human being to secure adequate and wholesome food—and all this is, in essence, a conditioned reflex! There is no need to explain this in greater detail. Let us make a leap and turn directly to the question of the so-called tact in life as a specifically social phenomenon. Tact means the ability to create for oneself a favourable standing in society—the quality infrequently met with, of being able to establish with everyone and in any circumstances relations that constantly evoke a generally favourable attitude; it means changing one's attitude towards other people according to their temper, sentiments and the given conditions, i.e., to react to other people depending on the positive or negative results of the previous intercourse with them. True, there is worthy and unworthy tact, the tact which does not violate self-respect and the dignity of other people, and there is the tact which is quite the reverse; but in their physiological essence both are temporary connections, conditioned reflexes. Thus, the temporary nervous connection is the most universal physiological phenomenon both in the animal world and in ourselves. At the same time it is a psychological phenomenon—that which the psychologists call association, whether it be combinations derived from all manner of actions or impressions, or combinations derived from letters, words and thoughts. Are there any grounds for differentiation, for distinguishing between that which the physiologist calls the temporary connection and that which the psychologist terms association? They are fully identical; they merge and absorb each other. Psychologists themselves seem to recognize this, since they (at least, some of them) have stated that the experiments with conditioned reflexes provide a solid foundation for associative psychology, i.e., psychology which regards association as the base of psychical activity. This is all the more true since it is possible to form a new conditioned stimulus with the help of an elaborated conditioned stimulus; and recently it was convincingly proved on a dog that two indifferent stimuli repeated in succession can also become interconnected and provoke each other. The conditioned reflex has become the central phenomenon in physiology; it has made possible a more profound and exact study both of the normal and pathological activity of the cerebral hemispheres. Of course, the results of this study, which so far has yielded an enormous quantity of facts, can be described here only in general outline.

The basic condition for the formation of a conditioned reflex is, generally speaking, a single or repeated coincidence of the indifferent stimulus with the unconditioned one. The formation of the reflex is quickest and meets with least difficulties when the first stimulus directly precedes the second, as shown in the above-mentioned auditory acid reflex.

The conditioned reflex is formed on the basis of all unconditioned reflexes and from various agents of the internal, medium and external environment both in their simplest and most complex forms, but with one limitation: it is formed only from those agents for the reception of which there are receptor elements in the cerebral hemispheres. Thus we have before us a very extensive synthesizing activity effected by this part of the brain.

But this is not enough. The conditioned temporary connection is at the same time highly specialized, reaching the heights of complexity and extending to the most minute fragmentation of the conditioned stimuli as well as of some activities of the organism, particularly such as the skeletal movements and the speech movements. Thus we have before us a highly delicate analysing activity of the same cerebral hemispheres! Hence the enormous breadth and depth of the organism's adaptability, of its equilibration with the surrounding world. The synthesis is, apparently, a phenomenon of nervous coupling. What, then, is the analysis as a nervous phenomenon? Here we have several separate physiological factors. The foundation for the analysis is provided first of all by the peripheral endings of all the afferent nervous conductors of the organism, each one of which is specially adjusted to transform a definite kind of energy (both inside and outside the organism) in the process of nervous excitation; this process is then conducted to special, less numerous, cells of the lower parts of the central nervous system, as well as to the highly numerous special cells of the cerebral hemispheres. From there, however, the process of nervous excitation usually irradiates to various cells over a greater or lesser area. This explains why when the conditioned reflex has been elaborated, say, to one definite tone, not only all the other tones, but even many of the other sounds produce the same conditioned reaction. In the physiology of the higher nervous activity this is known as the generalization of conditioned reflexes. Consequently, here we simultaneously meet with phenomena of coupling and irradiation. But afterwards the irradiation gradually becomes more and more limited; the excitatory process concentrates in the smallest nervous point of the cerebral hemispheres, probably the group of corresponding special cells. This limitation is most rapidly effected by means of another basic nervous process known as inhibition. This is how the process develops. First we elaborate a conditioned generalized reflex to a definite tone. Then we continue our experiment with this reflex, constantly accompanying and reinforcing it with the unconditioned reflex; but along with it we apply other, so to speak, spontaneously acting tones, but without any reinforcement. The latter gradually lose their effect, and, finally, the same thing takes place with the closest tone; for example, a tone of 500 oscillations per second will produce an effect, whereas the tone of 498 oscillations will not, i.e., it will be differentiated. These tones, which have now lost their effect, are inhibited. This is proved in the following way:

If immediately after the application of the inhibited tone we apply the constantly reinforced conditioned tone, the latter will either produce no effect at all or a considerably lesser effect than usual. This signifies that the inhibition which has eliminated the effect of all accessory tones, has acted on this tone as well. But this is a fleeting phenomenon—it is no longer observed if some time passes after the application of the inhibited tones. From this it can be deduced that the inhibitory process irradiates in the same way as the excitatory process. But the more frequently the non-reinforced tones are repeated, the more concentrated becomes the inhibitory process both in space and in time. Consequently the analysis begins with the special activity of the peripheral mechanisms of the afferent conductors and is terminated in the cerebral hemispheres by means of the inhibitory process. The case of inhibition described above is known as differential inhibition. I shall mention other cases. In order to obtain a definite, more or less constant strength of the conditioned effect, usually, after a certain period of action of the conditioned stimulus, the latter is supplemented by an unconditioned stimulus, that is, it is reinforced. Then, depending on the duration of the isolated application of the conditioned stimulus, no effect is observed during the first seconds or minutes of the stimulation, since being premature as a signal of the unconditioned stimulus, it is inhibited. This is the analysis of the different moments of the acting stimulus. Inhibition of this kind is called the inhibition of a delayed reflex. But the conditioned stimulus, as a signalling one, is itself corrected by the inhibition, gradually being reduced to zero, if it is not reinforced during a certain period of time.

This is the extinguishing inhibition. It persists for some time and then disappears of itself. The restoration of the extinguished conditioned effect of the stimulus is accelerated by reinforcement. Thus, there are positive conditioned stimuli, i.e., provoking an excitatory process in the cerebral cortex, and negative ones, provoking an inhibitory process. In the above cases we have a special inhibition of the cerebral hemispheres, the cortical inhibition. It arises under certain conditions at points where previously it was absent, it varies in size and disappears under other conditions; this distinguishes it from a more or less constant and stable inhibition of the lower parts of the central nervous system, and this is why, in contrast to the latter (i.e., to external inhibition), it is called internal inhibition. It would be more correct to call it elaborated, conditioned inhibition. The participation of inhibition in the work of the cerebral hemispheres is as continuous, complex and delicate as that of the excitatory process.

Just as in some cases the stimulations coming into the hemispheres from without enter into connection with definite cerebral points which are in a state of excitation, in other cases similar stimulations can, also on the basis of simultaneity, enter into temporary connection with the inhibitory state of the cortex, if there is any. This follows from the fact that such stimuli have an inhibitory effect, evoke by themselves an inhibitory process in the cortex and are conditioned negative stimuli. In this case, as in the foregoing cases, we have a conversion, under certain conditions, of the excitatory process into the inhibitory. And this can to a degree be explained if we recall that in the peripheral apparatus of the afferent conductors there takes place a constant transformation of various kinds of energy into an excitatory process. Why, then, should there not take place in certain conditions a similar transformation of the energy of the excitatory process into the energy of the inhibitory process, and vice versa?

As we have just seen, both the excitatory and inhibitory processes, arising in the cerebral hemispheres, first spread over them or irradiate, and then concentrate in the point of origin. This is one of the fundamental laws of the entire central nervous system, but here, in the cerebral hemispheres, it manifests itself with the mobility and complexity which are inherent only in them. Among the conditions which determine the onset and course of irradiation and concentration of the processes, the strength of these processes must be considered of prime importance. The facts which have been accumulated up to date entitle us to draw the conclusion that given a weak excitatory process irradiation takes place, given a medium one—concentration, and under a very strong one—again irradiation. Exactly the same thing occurs in the inhibitory process. Cases of irradiation accompanying very strong processes are observed more seldom, and, therefore, have been less investigated, especially under inhibition. The irradiation of a weak excitatory process, being of a temporary character, discloses the latent state of excitation which is caused by another acting stimulus (but too weak to be revealed) or by a stimulus that had acted not long before, and finally by one which was often repeated and resulted in an increased tonus of a certain cortical point. On the other hand, the irradiation eliminates the inhibitory state of other points of the cortex. This phenomenon is known as disinhibition: the irradiation of an accessory weak stimulus transforms the effect of a certain acting negative conditioned stimulus into the opposite, positive effect. When the excitatory process is of medium strength, it concentrates in a definite and limited point and is manifested in certain activity. Under very strong excitation the irradiation evokes the highest tonus of the cortex, and against the background of this excitation all other successive stimulations produce the maximum effect. The irradiation of a weak inhibitory process is what we call hypnosis; under alimentary conditioned reflexes it manifests itself in both the secretory and motor components. When, in the above-mentioned conditions there arises inhibition (differential and others), the development of peculiar states of the cerebral hemispheres is the most common fact. At first, contrary to the rule of a more or less parallel change in the size of the salivary effect of the conditioned alimentary reflexes, corresponding to the physical intensity of the stimuli, all stimuli become equal in effect (the equalization phase). Then the weak stimuli provoke a more abundant secretion of saliva than the strong (the paradoxical phase). And finally there takes place a distortion of the effects: the conditioned positive stimulus remains fully ineffective, whereas the negative stimulus produces a secretion of saliva (the ultra-paradoxical phase). The same thing occurs with the motor reaction: when, for example, food is offered to the dog (i.e., when natural conditioned stimuli begin to act), the dog turns away from it; on the contrary, when the food is being removed, taken away, the dog reaches for it. Besides, in the state of hypnosis, in the case of alimentary conditioned reflexes, it is sometimes possible clearly to observe a gradual irradiation of inhibition over the motor region of the cortex. First the tongue and the masticatory muscles become paralyzed, then the inhibition of the cervical muscles follows, and, finally, of all muscles of the body. Given a further downward irradiation of the inhibition along the brain a state of catalepsy is sometimes observed, and finally general sleep sets in. The hypnotic state, being of an inhibitory nature, enters quite easily, on the basis of simultaneity, into temporary conditioned connection with the numerous external agents.

When the inhibitory process is intensified, it becomes concentrated. This leads to delimitation between the cortical point which is in a state of excitation and the points in a state of inhibition. And since there is a multitude of diverse points in the cortex, excitatory and inhibitory, relating both to the external world (visual, auditory and others) and to the internal world (motor, etc.), it represents a grandiose mosaic of intermittent points of various properties and various degrees of strength of the excitatory and inhibitory states. Thus, the alert working state of an animal or of a human being is a mobile and at the same time localized process of fragmentation of the excitatory and inhibitory states of the cortex, now in large, now in very small parts; it contrasts with the state of sleep when inhibition at the height of its intensity and extensity is spread evenly over the whole mass of the cerebral hemispheres, as well as down to a certain level. However, even then there may remain separate excitatory points in the cortex—which are, so to speak, on guard or on duty. Consequently, in the alert state both processes are in permanent mobile equilibration, as if struggling with each other. If the mass of external or internal stimulations falls off at once, a marked predominance of the inhibitory process takes place over the excitatory. Some dogs, in which the peripheral basic external receptors (visual, auditory and olfactory) are damaged, sleep twenty-three hours a day.

Along with the law of irradiation and concentration of the nervous processes, there is another permanently operating fundamental law—the law of reciprocal induction. According to this law, the effect of the positive conditioned stimulus becomes stronger when the latter is applied immediately or shortly after the concentrated inhibitory stimulus, just as the effect of the inhibitory stimulus proves to be more exact and profound after the concentrated positive stimulus. The reciprocal induction manifests itself both in the circumference of the point of excitation or inhibition simultaneously with their action, and in the point itself after the termination of the processes. It is clear that the law of irradiation and concentration and the law of reciprocal induction are closely interconnected, mutually limiting, balancing and reinforcing each other, and thereby determining the exact correlation between the activity of the organism and the conditions of the external environment. Both laws operate in all parts of the central nervous system, but in the cerebral hemispheres they manifest themselves in newly arising points of excitation and inhibition, and in the lower parts of the central nervous system—in more or less permanent points. In the theory of conditioned reflexes, negative induction, i.e., the emergence or intensification of inhibition in the circumference of a point of excitation, was previously called external inhibition, when the given conditioned reflex diminished and disappeared as a result of the action on the animal of an accessory, accidental stimulus, more often evoking an orienting reflex. It was this that gave the occasion to group all the cases of inhibition described above (extinguishing and others), occurring without the interference of outside stimulation, under the common name of internal inhibition. Besides these two different cases of inhibition in the cerebral hemispheres, there is a third one. When the conditioned stimuli are physically very strong, the rule of direct proportionality between the strength of the effect produced by these stimuli and their physical intensity is violated; their effect becomes not stronger but weaker than that of moderate stimuli; this is the so-called transmarginal inhibition. This inhibition arises both under the action of a very strong conditioned stimulus and in the case of summation of separate and not very strong stimuli. It is natural to regard transmarginal inhibition as a kind of reflex inhibition. If we systematize the cases of inhibition more exactly, we shall have either permanent, unconditioned inhibition (inhibition of negative induction and transmarginal inhibition), or temporary, conditioned inhibition (extinguishing, differential and retarding). However, from the point of view of their physicochemical foundation, there is every reason to regard all these kinds of inhibition as one and the same process, but arising under different conditions.

The entire establishment and distribution in the cortex of excitatory and inhibitory states, taking place in a certain period under the action of external and internal stimuli, become more and more fixed under uniform, recurring conditions and are effected with ever-increasing ease and automatism. Thus, there appears a dynamic stereotype (systematization) in the cortex, the maintenance of which becomes an increasingly less difficult nervous task; but the stereotype becomes inert, little susceptible to change and resistant to new conditions and new stimulations. Any initial elaboration of a stereotype is, depending on the complexity of the system of stimuli, a difficult and often an extraordinary task.

The study of conditioned reflexes in numerous dogs gradually led to the idea of different nervous systems in different animals, until, finally, sufficient data were obtained to systematize the nervous systems according to some of their basic properties. There proved to be three such properties: the strength of the basic nervous processes (excitatory and inhibitory), their equilibrium and their mobility. Actual combinations of these three properties produce four more or less strongly-pronounced types of nervous system. According to the strength, the animals are divided into strong and weak types; according to the equilibrium of the nervous processes, the strong animals are divided into equilibrated and unequilibrated; and the equilibrated strong animals are divided into labile and inert. This, approximately, coincides with the classical systematization of temperaments. Thus, there are strong but unequilibrated animals in which both nervous processes are strong, the excitatory process, however, predominating over the inhibitory; this is the excitable, impetuous type, or choleric, according to Hippocrates. Further, there are strong, quite equilibrated but inert animals; this is the inert, slothful type, or phlegmatic, according to Hippocrates' classification. Then come the strong, quite equilibrated, but labile animals; this is the lively, active type, or sanguine, according to Hippocrates. And finally, there is the weak type, which is closest to Hippocrates' melancholic type; the predominant and common feature of this type is quick inhibitability due to internal inhibition which is always weak and easily irradiates, and especially to external inhibition under the action of various, even inconsiderable, accessory external stimuli. In other respects it is less uniform than all other types; it includes various animals: those in which both nervous processes are equally weak; those in which the inhibitory process is predominantly very weak; fussy animals, constantly glancing around, and, on the contrary, animals constantly halting, as if becoming petrified. The cause of this non-uniformity lies, of course, in the fact that animals of the weak type, as well as those of the strong type, differ in other features, apart from the strength of the nervous processes. But the predominant and extreme weakness now of the inhibitory process, now of both processes, abolishes the vital significance of the variations of all other features. Constant and strong inhibitability makes all these animals equally disabled.

Thus, type is a congenital, constitutional form of the nervous activity of the animal—the genotype. But since the animal is exposed from the very day of its birth to the most varied influences of the environment, to which it must inevitably respond by definite actions which often become more and more fixed and, finally, established for life, the ultimate nervous activity of the animal (phenotype, character) is an alloy of the characteristics of type and the changes produced by the external environment. All that has been said above, obviously, represents indubitable physiological material, i.e., the objectively reproduced normal physiological activity of the higher part of the central nervous system; and it is precisely with this activity that the study of every part of the animal organism must begin and actually does begin. However, this does not prevent certain physiologists from regarding the above facts as having no relation to physiology. A case of conservatism not infrequent in science!

It is not difficult to bring this physiological activity of the higher part of the animal brain into natural and direct connection with numerous manifestations of our subjective world.

As already mentioned, a conditioned connection is, apparently, what we call association by simultaneity. The generalization of a conditioned connection corresponds to what is called association by likeness. The synthesis and analysis of conditioned reflexes (associations) are, in essence, the same as the basic processes of our mental activity. When we are absorbed in our thoughts or carried away by certain work, we do not see and hear what is going on around us; this is obvious negative induction. Who would separate in the unconditioned highly complex reflexes (instincts) the physiological, the somatic from the psychical, i.e., from the powerful emotions of hunger, sexual attraction, anger, etc.? Our sense of pleasure, displeasure, composure, difficulty, joy, pain, triumph, despair, etc., is connected now with the conversion of very strong instincts and of their stimuli into corresponding effector acts, now with their inhibition; they are connected with all the variations of an easy or difficult course of development of the nervous processes in the cerebral hemispheres, as is observed in dogs which are able or unable to cope with nervous tasks of varying degrees of difficulty. Our contrasting emotions are, of course, phenomena of reciprocal induction. The irradiation of excitation makes us speak and act in a manner that would not be admitted by us in a state of calm. Obviously, the wave of excitation transforms the inhibition of certain points into a positive process. A drastic weakening of the memory for the near past —a normal phenomenon in old age—signifies a senile decrease of the mobility of the excitatory process, its inertness, and so on.

When the developing animal world reached the stage of man, an extremely important addition was made to the mechanisms of the nervous activity. In the animal, reality is signalized almost exclusively by stimulations and by the traces they leave in the cerebral hemispheres, which come directly to the special cells of the visual, auditory or other receptors of the organism. This is what we, too, possess as impressions, sensations and notions of the world around us, both the natural and the social—with the exception of the words heard or seen. This is the first system of signals of reality common to man and animals. But speech constitutes a second signalling system of reality which is peculiarly ours, being the signal of the first signals. On the one hand, numerous speech stimulations have removed us from reality, and we must always remember this in order not to distort our attitude to reality. On the other hand, it is precisely speech which has made us human, a subject on which I need not dwell in detail here. However, it cannot be doubted that the fundamental laws governing the activity of the first signalling system must also govern that of the second, because it, too, is activity of the same nervous tissue.

The most convincing proof that the study of the conditioned reflexes has brought the investigation of the higher part of the brain on to the right trail and that the functions of this part of the brain and the phenomena of our subjective world have finally become united and identical, is provided by the further experiments with conditioned reflexes on animals reproducing pathological states of the human nervous system—neuroses and certain psychotic symptoms; in many cases it is also possible to attain a rational deliberate return to the normal—recovery—i.e., a truly scientific mastery of the subject. Normal nervous activity is a balance of all the above-described processes participating in this activity. Derangement of the balance is a pathological state, a disease; and often there is a certain disequilibrium even in the so-called normal, or to be more precise, in the relative normal. Hence the probability of nervous illness is manifestly connected with the type of nervous system. Under the influence of difficult experimental conditions those of our dogs are quickly and easily susceptible to nervous disorders which belong to the extreme—excitable and weak—types. Of course, even in the strong equilibrated types the equilibrium can be deranged by applying very strong, extraordinary measures. The difficult conditions, which chronically violate the nervous equilibrium, include: overstrain of the excitatory process, overstrain of the inhibitory process and a direct collision of both opposite processes, in other words, overstrain of the mobility of these processes. We have a dog with a system of conditioned reflexes to stimuli of different physical intensity, positive and negative reflexes which are called forth stereotypically in one and the same order and at the same intervals. We sometimes apply exceptionally strong conditioned stimuli, sometimes we greatly prolong the duration of the inhibitory stimuli; we now elaborate a very delicate differentiation, now increase the quantity of inhibitory stimuli in the system of reflexes; finally, we either make the opposing processes follow each other immediately, or even simultaneously apply opposite conditioned stimuli, or at once change the dynamic stereotype, i.e., convert the established system of conditioned stimuli into an opposite series of stimuli. And we see that in all these cases the above-mentioned extreme types fall with particular ease into chronic pathological states differently manifesting themselves in these types. In the excitable type the neurosis is expressed in the following way. The inhibitory process, which even in a normal state constantly lags behind the excitatory process in relation to strength, now becomes very weak, almost disappearing: the elaborated, although not absolute, differentiations become fully disinhibited; the extinction assumes an extremely protracted character, the delayed reflex is converted into a short-delayed one, etc. In general, the animal becomes highly unrestrained and nervous during the experiments in the stand: it either behaves violently, or—which is much less frequent—falls into a state of sleep; this had not been observed before. In the weak type the neurosis is almost exclusively of a depressive character. The conditioned reflex activity becomes highly confused, and more often completely vanishes; in the course of the experiment the animal is in an almost continuous hypnotic state, manifesting its various phases (there are no conditioned reflexes at all, the animal even refuses food).

Experimental neuroses in most cases assume a lingering character lasting for months and even years. Some therapeutic remedies have been successfully tested in protracted neuroses. Already long ago bromide was applied in the study of the conditioned reflexes when certain experimental animals could not cope with the tasks of inhibition. And it was of essential help to these animals. A prolonged and diverse series of experiments with conditioned reflexes on animals proved beyond all doubt that bromide bears no special relation to the excitatory process and does not decrease the latter, as was generally believed, but influences the inhibitory process, intensifying and tonifying it. It is a powerful remedy, regulating and rehabilitating the disturbed nervous activity, on the indispensable and essential condition, however, that it is exactly dosed according to the types and states of the nervous system. In the case of a strong type and when the state of the dog's nervous system is still strong enough, large doses of bromide are to be administered—from two to five grammes a day; for the weak type the dose must be reduced to centigrammes and milligrammes. Such bromization for a period of two or three weeks sometimes proves sufficient to cure a chronic experimental neurosis. Recent experiments have shown even a greater therapeutic effect, especially in very severe cases, of a combination of bromide and caffeine, but again subject to very precise dosage of both substances Sometimes recovery was also attained in animals, though not so quickly and fully, exclusively by means of a regular prolonged or short rest from laboratory work in general, or by the abolition of the difficult tasks in the system of conditioned reflexes.

The described neuroses in animals can best be compared with neurasthenia in human beings, especially since some neuropathologists insist on two forms of neurasthenia—excitatory and depressive. Besides, certain traumatic neuroses may correspond to them, as well as other reactive pathological states. It may be assumed that recognition of two signalling systems of reality in man will lead specially to an understanding of the mechanisms of two human neuroses—hysteria and psychasthenia. If, on the basis of the predominance of one system over the other, people can be divided into a predominantly thinking type and a predominantly artistic type, then it is clear that in pathological cases of a general disequilibrium of the nervous system, the former will become psychasthenics and the latter hysterics.

Along with elucidation of the mechanisms of neuroses, the physiological study of the higher nervous activity provides a clue to an understanding of certain aspects and phenomena in the pictures of psychoses. We shall dwell first of all on some forms of delusion, namely, on the variation of the persecution delusion, on what Pierre Janet[63] calls "senses of possession," as well as on Kretschmer's[64] "inversion." The patient is persecuted precisely by that which he particularly wants to avoid; he desires to have his own secret thoughts, but he is certain that they are constantly being disclosed and made known by others; he wishes to be alone, but he is tormented by the persistent sensation that someone else is in the room, although there is nobody there except himself, etc.; according to Janet, these are senses of possession. Kretschmer refers to two girls who, having entered the period of puberty, and being sexually attracted by certain males, for some reason suppressed this attraction. As a result, they were first seized with an obsessive idea; to their great grief, it seemed to them that their countenance betrayed their sexual excitation and that everybody noticed this; at the same time they greatly valued their chastity, their virginity. Afterwards one of the girls suddenly began to imagine and even to sense that the sexual tempter—the serpent which had seduced Eve in the Garden of Eden—was inside her and was even reaching towards her mouth. The other girl imagined that she was pregnant. It is this latter phenomenon that Kretschmer terms inversion. In respect of its mechanism it is obviously identical with the sense of possession. This pathological subjective experience can, without undue strain, be interpreted as a physiological phenomenon of the ultra-paradoxical phase. The idea of sexual inviolability, being a very strong positive stimulus, on the background of the state of inhibition or depression in which both girls found themselves, turned into an equally strong opposite negative idea, reaching the level of sensation; in one girl it was the idea of a sexual tempter existing inside her body, in the other—the idea of pregnancy as a result of sexual intercourse. Exactly the same thing is experienced by the patient with the sense of possession. The strong positive idea "I am alone" turned, under the same conditions, into a similar negative idea—"there is always someone near me!"

In the course of experiments with conditioned reflexes in various difficult and pathological states of the nervous system it is often observed that temporary inhibition leads to a temporary improvement in these states; in one dog there was twice observed a patent catatonic state,[65] which resulted in a marked decline of a chronic and persistent nervous disorder, almost in a return to the normal for several days in succession. In general, it should be pointed out that in experimental disorders of the nervous system almost always separate phenomena of hypnosis are observed, which gives the right to assume that this is a normal physiological remedy against morbific agents. Hence, the catatonic form or phase of schizophrenia[66] entirely consisting of hypnotic symptoms, can be regarded as physiological protective inhibition, limiting or fully excluding the work of the disordered brain which, owing to the action of a certain, still unknown, noxious agent, has been threatened by serious disturbances or complete destruction. Medicine knows very well that the first therapeutic measure, which must be applied in the treatment of almost every illness is to ensure a state of rest for the diseased organ. That such a concept of the mechanism of catatonia in schizophrenia conforms to reality, is convincingly proved by the fact that only this form of schizophrenia shows a considerable rate of recovery, despite the protracted character of the catatonic state, which sometimes persists for years (twenty years). From this point of view any attempt to act on catatonics by means of stimulating methods and remedies is definitely injurious. On the contrary, a very considerable increase in the rate of recovery can be expected when physiological rest (inhibition) is supplemented with deliberate external rest for such patients, when they are kept away from the action of constant and strong stimuli emanating from the surroundings, kept away from other, restless patients.

In the course of the study of conditioned reflexes, along with general disorders of the cortex, there were frequently observed extremely interesting cases of disorders experimentally and functionally produced in very small points of the cortex. Let us take a dog with a system of various reflexes and among them conditioned reflexes to different sounds—a tone, a noise, the beat of a metronome, the sound of a bell, etc.; it is possible to induce a disorder only at one of the points of application of these conditioned stimuli, while all other points remain normal. The pathological state of an isolated cortical point is produced by the methods described above as morbific. The disorder manifests itself in different forms and degrees. The mildest change effected at this point is expressed in its chronic hypnotic state: instead of the normal relation between the strength of the effect induced by the stimulation and the physical intensity of the stimulus, the equalization and paradoxical phases develop at this point. Proceeding from the above, this, too, can be interpreted as a physiological preventive measure under a difficult state of a cortical point. When the pathological state develops further, the stimulus in some cases has no positive effect at all, provoking only inhibition. In other cases the opposite occurs. The positive reflex becomes unusually stable: its extinction proceeds more slowly than that of the normal reflexes; it is less susceptible to successive inhibition by other, inhibitory conditioned stimuli; it often stands out in bold relief for its strength among all other conditioned reflexes, which was not observed prior to the disorder. This signifies that the excitatory process at the given point has become chronically and pathologically inert. The stimulation of the pathological point sometimes remains indifferent to the points of other stimuli, and sometimes it is impossible to touch this point with its stimulus without deranging in one way or another the entire system of reflexes. There are grounds for assuming that in the case of disorder of isolated points, when now the inhibitory, now the excitatory processes predominate at the diseased point, the mechanism of the pathological state consists precisely in the derangement of equilibrium between the opposed processes: there takes place a considerable and predominant decrease now of one process, now of the other. In the case of pathological inertness of the excitatory process bromide (which reinforces the inhibitory process) often fully eliminates the inertness.

The following conclusion can hardly be considered fantastic. If stereotypy, iteration and perseveration, as is perfectly obvious, have their natural origin in the pathological inertness of the excitatory process of the different motor cells, then obsessional neurosis and paranoia must also have the same mechanism. This is simply a matter of other cells or of groups of cells connected with our sensations and notions. Thus, only one series of sensations and notions connected with the diseased cells becomes abnormally stable and resistant to the inhibitory influence of other numerous sensations and notions, which to a greater degree conform with reality because of the normal state of their cells. Another phenomenon, frequently observed in the study of pathological conditioned reflexes and having a direct bearing on human neuroses and psychoses, is circularity in the nervous activity.[67] The disturbed nervous activity manifested more or less regular fluctuations. There was observed at first a period of extremely weakened activity (the conditioned reflexes were of a chaotic character, often fully disappeared or declined to the minimum); then, after several weeks or months, as if spontaneously, without any visible reason, there took place a greater or lesser, and even complete, return to the normal, which was again superseded by a period of pathological activity. Sometimes periods of weakened activity and abnormally increased activity alternated in this circularity. It is impossible not to see in these fluctuations an analogy with cyclothymia[68] and the manicdepressive psychosis.[69] The simplest way would be to ascribe this pathological periodicity to the derangement of normal relations between the excitatory and inhibitory processes, as far as their interaction is concerned. Since the opposite processes did not limit each other in due time and in the proper measure, but acted independently of each other and excessively, the result of their activity reached its maximum—and only then was one process superseded by the other. Thus, there developed a different, namely, exaggerated, periodicity, lasting a week or a month, instead of the short and very easy periodicity of one day. Finally, it is impossible not to mention a phenomenon which so far has manifested itself with exceptional force only in one dog. This is the extreme explosiveness of the excitatory process. Certain individual stimuli or all the conditioned stimuli produced an extremely violent and excessive effect (both motor and secretory), which, however, abruptly disappeared already during the action of the stimulus—when the alimentary reflex was reinforced, the dog did not take the food. Obviously, this was because of the high pathological lability of the excitatory process, which corresponds to the excitatory weakness of the human clinic. In certain conditions a weak form of this phenomenon is often observed in dogs.

All the pathological nervous symptoms described above are manifested in corresponding conditions both in normal dogs, i.e., not subjected to surgical operation, and (especially some of these symptoms, for example, circularity) in castrated animals, being, consequently, of an organic pathological nature. Numerous experiments have shown that the most fundamental property of the nervous activity in castrated animals is a considerable and predominant decline of the inhibitory process, which in the strong type, however, is greatly levelled out with the passage of time.

To sum up, we must emphasize once more that when we compare the ultra-paradoxical phase with the sense of possession and with inversion, and the pathological inertness of the excitatory process with obsessional neurosis and paranoia, we see how closely the physiological phenomena and the experiences of the subjective world are interconnected and how they merge.

PHYSIOLOGY OF THE HIGHER NERVOUS ACTIVITY[70]

Since this, I suppose, is my last opportunity to address a general meeting of my colleagues, I shall take the liberty of calling your attention to the general, most systematized and summarized results of my recent work, which I have carried out jointly with my esteemed fellow-workers and which comprises a full half of my entire physiological activity; naturally, I shall repeat many of the already published facts. I pass on to you the results of our work, passionately dreaming of the majestic, ever-widening horizon opening up before our science, and of the ever-growing influence exerted by science on human nature and human destiny.

For the anatomist and histologist the cerebral hemispheres have always been as accessible and tangible as any other organ or any other tissue, i.e., that they possess similar workability and are susceptible of investigation, but, of course, commensurately with their specific properties and construction. Quite different was the position of the physiologist. Every organ of the animal body, the general role of which in the organism is known, its actual function, and the conditions and mechanism of this function, are objects of study. As to the cerebral hemispheres, their role is well known—they effect the organism's most complex relations with the environment; but the physiologist did not engage in a further study of their activity. For him the study of the cerebral hemispheres did not begin with the concrete reproduction of their activity, only after which the gradual analysis of the conditions and mechanism of this activity is possible. The physiologist possessed many facts relating to the cerebral hemispheres, but these facts were not manifestly and closely connected with their usual normal activity.

Today, after thirty years of diligent and ceaseless work jointly with my numerous collaborators, I make bold to say that the situation has radically changed, that while remaining physiologists, i.e., the same objective observers as in all other branches of physiology, we are studying at present the normal activity of the cerebral hemispheres and at the same time constantly analysing it in ever-increasing measure. The generally-recognized criteria for every true scientific activity, namely, precise prevision and control over phenomena, testify to the serious character of this study, which is irrepressibly advancing, overcoming all obstacles. An ever-growing number of relations which constitute the most complex external activity of the higher animal organism, unfolds before us.

The central physiological phenomenon in the normal work of the cerebral hemispheres is that which we have termed the *conditioned reflex*. This is a temporary nervous connection between numberless agents in the animal's external environment, which are received by the receptors of the given animal, and the definite activities of the organism. This phenomenon is called by psychologists *association*. The fundamental physiological significance of this connection is as follows: in the higher animal, for example, in the dog which was the object of our investigations, the basic, most complex correlations established between the organism and the environment in order to preserve the individual and the species, are determined first of all by the activities of the subcortex which is nearest to the cerebral hemispheres; this was demonstrated long ago in Goltz's[71] experiment with the extirpation of the cerebral hemispheres in a dog. These activities include the search for food, or the alimentary activity; the avoidance of injurious factors, or the defensive activity, etc. They are usually called instincts or inclinations; psychologists term them *emotions*, but we designate them by the physiological term *most complex unconditioned reflexes*. They exist from the very day of birth and are indispensably called forth by definite, though very limited in number, stimuli which are sufficient only in early childhood, under the conditions of parental care. It is this latter circumstance that makes an animal with extirpated cerebral hemispheres disabled, incapable of a self-dependent existence. The basic physiological function of the cerebral hemispheres throughout the subsequent individual life consists in a constant addition of numberless signalling conditioned stimuli to the limited number of the initial, inborn unconditioned stimuli, in other words, in constantly supplementing the unconditioned reflexes by conditioned ones. Thus, the objects of the instincts exert an influence on the organism in ever-widening regions of nature and by means of more and more diverse signs or signals, both simple and more complex; consequently, the instincts are more and more fully and perfectly satisfied, i.e., the organism is more reliably preserved in the surrounding nature.

The basic condition for the formation of a conditioned reflex is a single or repeated coincidence in time of indifferent stimuli with unconditioned reflexes. This is the same principle of coincidence in time, on the basis of which groups of various agents or elements of nature, both simultaneous and consecutive, are synthesized by the animal into units. In this way the *synthesis* is effected in general.

But owing to the complexity of the permanent movement and variation of the natural phenomena, the conditioned reflex must, of course, also undergo certain changes, i.e., be constantly corrected. If for some reason or other the conditioned stimulus in the given conditions is not accompanied by its unconditioned stimulus, then, when repeated, it quickly loses its effect, however, temporarily, being restored spontaneously, after a certain lapse of time. If the conditioned stimulus constantly and greatly precedes in time the moment when the unconditioned stimulus is added, then its distant part, which is, so to speak, premature and violates the principle of economy, proves ineffective. When the conditioned stimulus, connected with another indifferent one, is permanently not accompanied by an unconditioned stimulus, it remains, in this combination, ineffective. Finally, if agents closely akin to the given elaborated conditioned stimulus (for example, close tones, other spots of the skin, etc.) are usually effective immediately after the elaboration of the first one, they gradually lose their effect when repeated later on without the accompaniment of the unconditioned stimulus, or, in our usual terminology, without reinforcement. All this ensures the differentiation, the *analysis* of the surrounding world with all of its elements and moments.

In the long run, the cerebral hemispheres of the dog constantly effect in the most varying degrees both the *analysis* and *synthesis* of stimuli coming to them, and this can and must be termed *elementary, concrete thinking*. And it follows that this thinking is responsible for the perfect adaptation of the organism, for its more delicate equilibration with the environment.

This real activity of the cerebral hemispheres and of the nearest subcortex, just described in general outline, the activity which ensures normal complex relations between the organism as a whole and the external world, must be rightly considered and denoted as the *higher nervous activity*, the external behaviour of the animal, instead of "psychical" as it was termed previously; it should be distinguished from the activity of other parts of the brain and of the spinal cord which are mainly in charge of the correlations and integration of separate parts of the organism; this activity should be termed the *lower nervous activity*.

Now the following questions arise: what intrinsic processes and laws govern the higher nervous activity? What has it in common with, and how does it differ from, the lower nervous activity which until now has been the predominant object of physiological study?

The basic processes of the entire central nervous activity are, obviously, always the same, namely, the excitatory and inhibitory processes. There are sufficient grounds for assuming that the fundamental laws governing these processes are also of a constant nature—irradiation and concentration of the processes and their reciprocal induction.

It seems to me that experiments with conditioned reflexes on the cerebral hemispheres, given normal conditions, permit a more complete and exact formulation of these laws than was possible on the basis of experiments performed mainly on the lower parts of the central nervous system, and which, in most cases, were acute experiments.

Concerning the cerebral hemispheres we can say that the following phenomenon is observed in them: when the excitatory and inhibitory processes are weak, then, under the action of corresponding stimuli there takes place irradiation, diffusion of the processes from the point of origin; when they are of medium strength, a concentration of the processes occurs at the point of application of the stimulus, and when they are very strong irradiation is again in evidence.

In the entire central nervous system, on the basis of irradiation of the excitatory process, a summation reflex sets in, i.e., a summation of the spreading wave of excitation with a local manifest or latent excitation; in the latter case the latent tonus becomes revealed—a phenomenon already known for a long time. While in the cerebral hemispheres the confluence of waves irradiating from various points leads to a quick delevopment of a temporary connection, to an association of these points, it bears a momentary, transient character in the remaining part of the central nervous system. This connection in the cerebral hemispheres probably owes its emergence to their extremely high reactivity and ability to impress, and is a permanent and inherent property of this part of the central nervous system. Moreover, in the cerebral hemispheres the irradiation of the excitatory process instantly and for a short period of time eliminates, washes off the inhibition from the inhibitory, negative points of the hemispheres, converting these points for the same period of time into positive ones. This phenomenon is called disinhibition.

Under the irradiation of the inhibitory process there is observed a decline or complete disappearance of the effect of the positive points and an increased effect of the negative points.

When the excitatory and inhibitory processes are concentrated, they induce the opposite processes (both at the periphery during their action and in the place of action upon its termination); this is the law of reciprocal induction.

In the entire central nervous system when there is a concentration of the excitatory process, we meet with phenomena of inhibition. The point of concentration of the excitation is encircled to a greater or lesser extent by the inhibitory process; this is the phenomenon of negative induction. This phenomenon manifests itself in all reflexes, develops at once and in full measure, persists for some time after the termination of excitation and exists both between the small points and the large parts of the brain. We call this external, passive, unconditioned inhibition. This phenomenon, which has also been known for a long time, was sometimes called the conflict of centres.

There are in the cerebral hemispheres also other kinds or cases of inhibition, in all probability, having one and the same physicochemical substratum. This is, in the first place, the inhibition effecting the correction of the conditioned reflexes, already mentioned and arising when the conditioned stimulus in the above-indicated conditions is not accompanied by its unconditioned stimulus; it gradually grows, becomes stronger and can be trained and perfected; this, too, is due to the exceptional reactivity of the cortical cells, and hence to the particular lability of inhibition in them. We call this inhibition internal, active, conditioned. The stimuli, which are thus converted into permanent agents of inhibition in the points of the cerebral hemispheres, are called by us inhibitory, negative. Similar inhibitory stimuli can be also obtained in another way—if we repeatedly apply indifferent stimuli during the inhibitory state of the cerebral hemispheres (experiments of Prof. Volborth). As is known, the initial inhibitory reflexes are also developed in the lower parts of the brain and in the spinal cord; but here they appear at once in a finished and stereotyped form, while the same inhibitory reflexes of the cerebral hemispheres arise gradually and are always observed by us in the process of formation.

There is one more case of inhibition in the cerebral hemispheres. All other conditions being equal, the effect of conditioned stimulation, as a rule, is proportionate to the intensity of the physical strength of the stimulus, but to a certain maximum (and probably to a certain minimum, too). Beyond this limit the effect does not increase; it either remains unchanged or declines. We have grounds for assuming that beyond this margin the stimulus together with the excitatory process evoke also an inhibitory process. We interpret this fact in the following way. The cortical cell possesses a certain limit of efficiency, and beyond this point there arises inhibition which prevents an excessive functional exhaustion of the cell. The limit of efficiency is not constant; it undergoes both acute and chronic changes—in cases of inanition, hypnosis, disease and in old age. This inhibition, which can be called transmarginal, arises sometimes instantaneously and sometimes manifests itself only when the super-powerful stimuli are repeated. It can be assumed that analogical inhibition also exists in the lower parts of the central nervous system.

Peculiar internal inhibition could also be considered as transmarginal inhibition, in which case the intensity of excitation is, as it were, replaced by its long duration.

Any inhibition irradiates in the same way as excitation, but the irradiation of internal inhibition is particularly distinct in the cerebral hemispheres where it is very easily observed in various forms and degrees.

There is no doubt that inhibition, when spreading and deepening, calls forth different degrees of a hypnotic state, and when irradiating to the utmost from the cerebral hemispheres down the brain, produces normal sleep. Particularly manifest, even in our dogs, is the diversity and multiplicity of the stages of hypnosis, which at first hardly differs from the wakeful state. In respect of intensity of inhibition the following stages are worth mentioning: the so-called equalization, paradoxical and ultra-paradoxical phases. Now conditioned stimuli of different physical strength produce either an equal, or even an inversely proportional effect; in rare cases only the inhibitory stimuli act positively, and the positive stimuli are converted into inhibitory ones. In respect of extensity of inhibition, functional dissociations in the cortex itself are observed, as well as between the cortex and the lower parts of the brain. In the cortex the motor region is particularly often isolated from other regions, and even within this region a distinct functional dissociation sometimes comes to the fore.

Unfortunately, the rivalry of what the clinicians and some experimenters designate "the centre of sleep" prevents these facts from being generally recognized and properly utilized for an understanding of the multitude of physiological and pathological phenomena. However, it is not difficult to reconcile and combine these facts. Sleep can be originated in two ways—either by irradiation of inhibition from the cortex, or by limiting the stimulations reaching the higher parts of the brain both from without and from within the organism. Strümpel long ago produced sleep in a patient by means of drastic limitation of external stimulations.[72] Recently Prof. Speransky and Galkin by means of a peripheral destruction of the olfactory, auditory and visual receptors in dogs obtained a very profound and chronic sleep (lasting weeks and months). Similarly, as a result of a pathological or experimental exclusion of stimulations, constantly reaching the higher part of the brain there sets in due to the vegetative activity of the organism an exaggerated and more or less profound and chronic sleep. It can be recognized that in some of these cases too, sleep, in the final stage, is produced by similar inhibition which becomes predominant when the number of stimuli is limited.

The law of reciprocal induction begins to operate when there is a concentration of the inhibitory process, just as it does when there is a concentration of the excitatory process. The point of concentration of the inhibition is to a greater or lesser extent encircled by the process of heightened excitability; this is the phenomenon of positive induction. The heightened excitability arises either instantly or gradually and persists not only during the action of inhibition, but for some time after, and in some cases even for a quite considerable length of time. The positive induction manifests itself between the small points of the cortex, when the inhibition is fragmentary, as well as between the large parts of the brain, when it is more diffused.

The permanent operation of the above-mentioned laws helps us to understand the mechanism of the origin of the numerous separate phenomena (among which are many peculiar, at first sight enigmatic, phenomena) of the higher nervous activity; however, I cannot dwell on them here. I shall refer only to one of a series of similar cases which for a long time completely baffled comprehension. It relates to the complex influence of accessory stimuli on the delayed conditioned reflex (experiments performed a long time ago by our colleague Zavadsky).

Let us suppose that a delayed conditioned reflex is being elaborated, the conditioned stimulation constantly lasting three minutes before the unconditioned stimulus is added to it. When such a reflex has been elaborated, the conditioned stimulus does not produce any effect during the first minute. Half-way through or towards the end of the second minute the stimulus begins to produce a certain effect, and maximum effect is attained only during the third minute Thus, the conditioned reflex consists of two external phases—ineffective and effective. Special experiments, however, have established that the first phase is not a zero phase, but an inhibitory one.

Now, if simultaneously with the conditioned stimulus there are applied accessory stimuli of different intensity calling forth only an orienting reaction, a number of changes are observed in the delayed reflex. When the stimulation is weak the ineffective phase becomes effective, that is, the special effect of the conditioned stimulus is manifested; the effect of the second phase either remains unchanged or is slightly increased.

When the stimulation is more intense the same thing occurs with the first phase, but the effect of the second phase drastically declines. Under the strongest stimulation the first phase again remains ineffective, while the effect of the second completely disappears. At present, on the basis of the latest, not yet published, experiments carried out by our colleague Rickman, we interpret all these phenomena as a result of the operation of the following four laws: 1) irradiation of the excitatory process, 2) negative induction, 3) summation, and 4) the law of maximum. Given a weak orienting reflex the spreading wave of excitation eliminates the inhibition of the first phase; this reflex, which soon all but disappears when the same stimulation is continued, either does not influence the second phase at all, or, owing to a slight summation, somewhat intensifies it. With a more considerable orienting reflex the effect persists longer; consequently, along with the disinhibition of the first phase, due to a considerable summation of the effective phase of the conditioned reflex with the irradiated wave of excitation of the orienting reflex, transmarginal inhibition takes place during the last minute of the delayed reflex. Finally, given a very strong orienting reflex there takes place a complete concentration of excitation accompanied by a strong negative induction which merges with the inhibition of the first phase and abolishes the effective phase.

Despite the fact that a multitude of particular relations between the excitatory and inhibitory processes have been studied by us, the general law of the interconnection of these processes cannot, as yet, be exactly formulated. As for the profound mechanism of both processes, many of our experimental facts incline us to the point of view that the inhibitory process is probably connected with assimilation, just as the excitatory process is naturally connected with dissimilation.

As for the so-called *voluntary volitional movements*, in this field, too, we have accumulated some material. In keeping with earlier investigations we have shown that the motor region of the cortex is first of all a receptor one, like all its other regions—visual, auditory, etc., since the animal's passive movements, i.e., the kinesthetic stimuli of this region can be transformed by us into conditioned stimuli in the same way as all external stimuli. Another ordinary phenomenon, reproduced by us also in the laboratory, is the temporary connection established between various external stimuli and passive movements which in response to certain signals evokes definite active movements of the animal. However, it is still not clear whether the connection between the kinesthetic stimulus and the corresponding motor action is of an unconditioned or of a conditioned character. Beyond this extreme point the *entire mechanism of volitional movement is a conditioned associative process* which obeys all the above-mentioned laws of the higher nervous activity.

The cerebral hemispheres are continually receiving countless stimuli both from the external world and the internal medium of the organism itself. These stimuli are conducted from the periphery along definite and numerous paths and, consequently, they first of all come to definite points and areas in the mass of the brain. Thus we have before us in the first place a highly complex structure, a mosaic. Countless and varied positive processes enter the cortex along the conductor paths, and in the cortex itself they are joined by inhibitory processes. From each of the separate states of the cortical cells (and there is an infinite number of such states) a specific conditioned stimulus may arise, as constantly observed by us in the course of our investigation of the conditioned reflexes. All these meet, collide, must come together and be systematized. Thus, in the second place, we have a vast dynamic system. We observe and study in the conditioned reflexes of our normal dogs this continual systematization of the processes, this, one may say, constant tendency towards a dynamic stereotype. Here is a most illustrative fact. If we elaborate in an animal a number of conditioned positive as well as inhibitory reflexes from stimuli of different intensity, and apply them during a certain period of time from day to day at regular intervals between the stimuli and always in a definite order, we establish thereby a stereotype of processes in the cerebral hemispheres. This can be easily demonstrated. If we now repeatedly apply throughout the experiment at equal intervals only one of the positive conditioned stimuli (better, one of the weak stimuli), it will reproduce in the proper sequence the fluctuations in the strength of the effects, as they were represented by the entire system of the various acting stimuli.

Not only the establishment, but a more or less lasting maintenance of the dynamic stereotype, is a nervous task of considerable difficulty, the degree of which depends on the complexity of the stereotype and on the individuality of the animal. There are, of course, nervous tasks the solution of which requires even from animals of the strong nervous type painful efforts. Other animals react to any simple change in the system of conditioned reflexes, such as the introduction of a new stimulus, or even to a certain transposition of the old stimuli, by complete loss of the conditioned reflex activity, sometimes lasting for a considerable period. Some animals can retain the proper system only if there are recesses in the experiments, i.e., if they are allowed certain rest. And finally, some animals show regular work only under a very simplified system of reflexes, consisting, for example, of two stimuli, both of them positive and of equal intensity.

It can be assumed that the *nervous processes in the cerebral hemispheres, when establishing and maintaining a dynamic stereotype,*[73] are what we usually call *senses* in their two categories—positive and negative, and their extensive gradation of intensity. The processes of establishing a stereotype, of fully accomplishing it, of its maintenance and derangement are subjectively different positive and negative senses, and that has always been manifested in the motor reactions of the animals.

Our entire work gradually enabled us to establish various types of nervous system in our animals. Since the cerebral hemispheres are the most reactive and supreme part of the central nervous system, their individual properties, naturally, must determine to a great extent the principal nature of the general activity of each animal. Our systematization of types coincides with the ancient classification of the so-called temperaments. There is the type with a strong excitatory process, but a relatively weak inhibitory process. Animals belonging to this type are aggressive and unrestrained. We call them strong and excitable or choleric. Next comes the type of strong and at the same time equilibrated animals, in which both processes are of equal strength. This is an easily disciplined and highly practical type which is met in two variations—quiet, sedate animals and active, lively ones. We name them respectively phlegmatic and sanguine. And finally, there is the weak inhibitable type, in which both processes are weak. We call such animals weak and also inhibitable since they are highly susceptible to external inhibition. They are cowardly and fussy and can be also characterized as melancholic, since everything constantly upsets them.

That our investigation of the higher nervous activity has taken the right road, and our definition of its phenomena, as well as our analysis of its mechanism are correct, is most convincingly proved by the fact that at present we are able in many cases to produce with great exactitude its functional chronic disturbances, and at the same time subsequently to obtain a return to the normal at will. We know which type of our animals can be easily turned into neurotics, we know how to achieve this, and the kind of disorder that will set in. The strong, but unequilibrated, excitable and weak inhibitable types prove to be the best objects for the elaboration of experimental neuroses. If an excitable animal is persistently offered such tasks, the solution of which requires strong inhibition, then it loses it completely and is deprived of the ability to correct the conditioned reflexes, i.e., ceases to analyse, to distinguish the stimuli reaching it as well as the intervals of time. Stimulations produced by the strongest agents have no noxious pathological influence on them. With equal ease the weak inhibitable type becomes ill both under a slightly strained inhibition and under the action of very strong stimuli; it either fully loses its conditioned reflex activity under our experimental conditions, or manifests it in a chaotic way. As for the animals of the equilibrated type, we did not succeed in inducing nervous disorders in them even by colliding the opposite processes, which is a particularly morbific method.

Bromide proved to be the most reliable remedy against neuroses, just as it is in the human clinic; as shown by our numerous and in many respects instructive experiments, it has a special bearing on the inhibitory process, greatly tonifying it. However, very strict dosage is essential; for the weak type the dose of bromide must be from five to eight times smaller than that for the strong type. Rest, i.e., a recess in the experiments, often produces good results.

Among animals of the weak type there are frequent instances of natural neurotics.

We already have and we can even produce certain symptoms of psychotics: stereotypy, negativism and circularity.

Last year I specially acquainted myself with the clinic of human hysteria, which is regarded as being entirely or predominantly a mental disease, as a psychogenic reaction to the surroundings; as a result, I have become convinced that its symptomatology can, without any hesitation, be interpreted physiologically, from the point of view of the described physiology of the higher nervous activity, and I have expressed this conviction in the press.[74] However, some particulars of this symptomatology made us guess the existence of an addition which should be taken into consideration in order to get a general idea of the human nervous activity as well. This addition relates to the speech function, which signifies a new principle in the activity of the cerebral hemispheres. If our sensations and notions caused by the surrounding world are for us the first signals of reality, concrete signals, then speech, especially and primarily the kinesthetic stimuli which proceed from the speech organs to the cortex, constitute a second set of signals, the signals of signals. They represent an abstraction from reality and make possible the forming of generalizations; this constitutes our extra, *specially human, higher mentality* creating an empiricism general to all men and then, in the end, science, the instrument of the higher orientation of man in the surrounding world and in himself. The extreme fantasticism, the twilight states of hysterical persons, and the dreams of all men, are nothing more than the vitalization of the imaginative and concrete first signals, as well as of the emotions; the oncoming hypnotic state first of all switches off the organ of the system of the second signals—the most reactive part of the brain, which always predominantly functions in the wakeful state, and which regulates, and at the same time to a certain degree inhibits, both the first signals and emotional activity.

The frontal lobes, in all probability, represent the organ of this additional purely human mentality, but it can be assumed that it is subordinated to the same general laws of the higher nervous activity.

The foregoing facts, as well as the considerations based on them, are bound to lead to the closest connection between physiology and psychology—a development particularly observed in American psychology. In the 1931 Address of Walter Hunter, President of the American Psychological Association, despite strenuous efforts on the part of the speaker—who is a psychologist-behaviourist—to detach physiology from his psychology, it is absolutely impossible to see any difference between them. But even psychologists not belonging to the camp of behaviourists admit that our experiments with the conditioned reflexes have been of great help to the association theory of the psychologists. Other facts of a like nature could be cited.

I am convinced that an important stage in the development of human thought is approaching, a stage when the physiological and the psychological, the objective and the subjective, will really merge, when the painful contradiction between our mind and our body and their contraposition will either *actually* be solved or disappear in a natural way. Indeed, when the objective study of the higher animals, for example, the dog, reaches the level when the physiologist is able to foresee with absolute exactitude the behaviour of this animal under any conditions (and this level will be reached), then what will be left to prove the independent, separate existence of the subjective state, which the animal, of course, possesses but which is as peculiar as our own? When that occurs will not the activity of any living thing, man included, be indispensably regarded by us as a single, indivisible whole?

VI

THEORY OF ANALYSERS, LOCALIZATION OF FUNCTIONS AND MECHANISM OF VOLUNTARY MOVEMENTS

SUMMARY OF RESULTS OF THE EXPERIMENTS WITH EXTIRPATION OF DIFFERENT PARTS OF THE CEREBRAL HEMISPHERES BY THE METHOD OF CONDITIONED REFLEXES[75]

When I was confronted with the question of a subject for my report today I was uncertain for a time what to do—whether to take a small part of the subject, to review and discuss the results of a single series of experiments, or to make a general review of a considerable part of our work. I chose the latter course. It seems to me that a general review will be more instructive for my audience, and at the same time quite useful for ourselves. It is always of great value to review and summarize the work carried out over a period of years, to weigh its results, thoroughly to consider them, to define more distinctly our shortcomings and to fix our goal and tasks for the future.

In my laboratory we have been occupied for seven years now with the partial and complete extirpation of the cerebral hemispheres; scores of dogs have been used for this purpose, and this has provided ample data which must be thoroughly summarized. To this I shall now proceed.

As most of the audience knows, we, many years ago, expressed our special point of view regarding the higher nervous activity, as manifested in the higher animals. In the study of this activity we rejected the subjective, psychological conceptions and chose the external, objective point of view—the method employed by naturalists in studying the material of their sciences. From this point of view the entire complex nervous system, previously interpreted as psychical, appears to us as the expression of two chief mechanisms—the mechanism of the formation of temporary connections between the agents of the external world and the activities of the organism, i.e., according to our usual terminology, the mechanism of conditioned reflexes, and the mechanism of the analysers, i.e., of an apparatus whose purpose is to analyse the complexity of the external world, to decompose it into separate elements and moments. At least until now all the results obtained by us fit into these concepts. This, however, does not exclude the possibility of a further extension of our concepts relative to this subject.

As the audience is also aware, the study of the complex nervous activity is carried out by us on an organ of minor physiological importance—the salivary gland; nevertheless, the two mechanisms governing the work of the cerebral hemispheres, which I have mentioned above, are very clearly manifested in the activity of this organ.

I shall, naturally, submit my material not in chronological order, that is, not in the order in which the facts were obtained by us, but in their logical sequence, arranging the material in such a way as to clarify the essence of the matter.

The first question to be decided here is the relation of the cerebral hemispheres to the above-mentioned mechanisms—to the mechanism of the formation of conditioned reflexes and to the mechanism of the analysers. The fundamental fact which in the course of the seven years was constantly observed and established by us and our numerous colleagues in a large number of animals is that the cerebral hemispheres are the seat of conditioned temporary reflexes, that one of the most important functions of the cerebral hemispheres consists precisely in the formation of conditioned reflexes, of temporary connections. We have very many facts testifying to this, although, of course, our subject is of such a character that every additional proof is always helpful. When fully extirpating the cerebral hemispheres, or removing certain parts of them, the experimenters observed the disappearance either of all the conditioned reflexes or only of certain groups of them. Various measures were taken to obtain the most precise and pure facts, and the results were always the same. Under certain conditions all the conditioned reflexes, or only some of them, invariably disappeared. We were most persevering in this experimental work; in some cases we tried for years to restore a reflex before deciding that it was impossible. In the case of one dog, we even went so far as to accompany the feeding—not only in the experimental chamber, but at all times—with a certain sound, by means of which we expected finally to form, if it was at all possible to do so, a conditioned reflex. However, since the organ of the given conditioned stimulus was destroyed, the reflex could not be formed. In view of these, so to speak, stubborn facts, it had to be admitted that the cerebral hemispheres are, in effect, the organ of temporary connections, the birthplace of the conditioned reflexes. Certainly, one might categorically ask the following question: can these conditioned, temporary connections be formed also outside the cerebral hemispheres? But it seems to me that there are no grounds for considering this question. The facts already obtained by us inevitably lead to the conclusion that the temporary connections owe their emergence to the cerebral hemispheres and that they disappear with the extirpation of the latter. But, of course, it is possible that sometimes, in certain specific conditions, conditioned reflexes may arise also outside the cerebral hemispheres, in another part of the brain. In this respect one cannot be too rigid, since all our classifications and laws are always of a more or less conditional character and are valid only for the given time, under the given methods and within the limits of the given available material. Still fresh in all our minds is the recent example—the indivisibility of the chemical elements, long regarded as a scientific axiom.

Thus, I repeat, in the course of various experiments many investigators constantly found that the temporary connections developed only in the presence of the whole or part of the cerebral hemispheres. In view of this, we can now admit without any hesitation that one of the essential functions of the cerebral hemispheres is precisely the elaboration of conditioned reflexes, just as the most important function of the lower parts of the nervous system is connected with the simple reflexes, or in our terminology, unconditioned constant reflexes.

The second mechanism related to the cerebral hemispheres is the mechanism of the so-called analysers. In this respect we proceeded from the old facts, but somewhat modified their interpretation. We define an analyser as an apparatus whose purpose is to decompose the complexity of the external world into separate elements; for example, the eye analyser consists of the peripheral part—the retina, of the optic nerve and, finally, of the cerebral cells in which this nerve ends. The union of all these parts into a single mechanism, which is called analyser, is justified by the fact that so far physiology does not possess any data for an exact division of the entire analysing activity. So far we cannot say which part of it is performed by the peripheral section and which by the central one.

Thus, the cerebral hemispheres, according to our understanding, consist of a number of analysers—the eye, ear, skin, nose and mouth analysers. Study of these analysers led us to the conclusion that their number must be increased, that in addition to the above-mentioned analysers relating to the external world, the existence of special analysers in the cerebral hemispheres must be recognized, whose function is to decompose the enormous complexity of the internal phenomena arising within the organism itself. Undoubtedly, not only an analysis of the external world is of importance to the organism; it also needs a signalling upwards and an analysis of everything taking place inside the organism itself. In a word, in addition to the external analysers already mentioned, there must be internal analysers, the most important of which is the motor analyser, the analyser of movement. We know that from all parts of the motor apparatus—from the joint capsules and surfaces of the joints, tendons, etc., there stretch centripetal nerves which signalize every moment the slightest detail of the act of movement. All these nerves unite at the supreme points—in the cerebral cells. The various peripheral endings of these nerves, the nerves themselves, as well as the nerve cells, in which they end, in the cerebral hemispheres, constitute a special analyser which decomposes the motor act with its enormous complexity into a large number of the most delicate elements; this ensures the enormous variety and the precision of our skeletal movements.

The concept of such an analyser is of particular interest in the physiology of the cerebral hemispheres. As you know, in 1870 (the year when fruitful scientific study of the cerebral hemispheres began) the Germans Fritsch and Hitzig demonstrated that stimulation of definite parts of the cortex in the anterior half of the cerebral hemispheres by means of an electric current evoked a contraction of certain groups of muscles. This discovery supplied the grounds for recognizing the existence of special motor centres in these places. But then the question arose as to how these parts of the cerebral hemispheres should be pictured. Are they motor centres in the full sense of the term, i.e., cells from which impulses proceed direct to the muscles, or are they sensory cells to which the peripheral stimulations come and from which the latter are merely transmitted to the active motor centres, the motor cells, where the motor nerves going direct to the muscles originate? This controversy, started by Schiff, is still in progress.

We also had to take part in deciding this question and this is how we did it. We had long inclined to the view that the places in the cerebral cortex, stimulation of which results in certain movements, represent aggregations of sensory cells, or brain endings of the centripetal nerves going from the motor apparatus. But how to obtain more or less convincing proofs of the correctness of this view? In addition to the old-established facts already utilized by the adherents of this view, we succeeded in finding fresh proof which, in our opinion, is most convincing.

If the so-called motor region is really the motor analyser, fully analogous to any other analyser—the ear, the eye, etc.—then the stimulation brought to this analyser can be directed along any centrifugal path, i.e., the stimulation can, at our will, be connected with any activity. In other words, in this case a conditioned reflex can be elaborated from a motor act. And we did elaborate it. Dr. Krasnogorsky, applying, on the one hand, our usual stimuli, for example, acid, and, on the other hand, flexing a certain joint, formed a conditioned reflex, a temporary connection between the flexion and the work of the salivary gland. Definite movements produced the same secretion of saliva as was the case with conditioned stimuli from the eye, ear, etc. Then the question arose, how correct is the interpretation of this fact, and is it really a reflex proceeding from flexion, in other words, from the motor act, or a reflex from the skin? In this respect, too, Dr. Krasnogorsky was fortunate enough to round off his proof, one can say, to the point where it was beyond reproach. When he formed a cutaneous reflex on one of the legs of the dog, and a flexion reflex on another, and then extirpated different parts of the cerebral hemispheres, the following phenomena were observed. If the g. sigmoideus was removed, the flexion reflex disappeared, but the cutaneous reflex persisted and could be elaborated. On the contrary, when the gg. coronarius and ectosylvius[76] were removed, the cutaneous reflex disappeared, while the flexion reflex remained. Thus, it was established beyond doubt that the cutaneous and motor analysers are different and that the motor analyser is located in the motor region of the brain.

It seems to me that all these experiments give us the right scientifically to speak of the motor analyser in exactly the same way as we do in respect of the eye, ear and other analysers.

It remains for us to explain why movement is provoked by electrical stimulation of those areas in the cerebral hemispheres where, as some investigators believe, the special motor centres are located. Since, in our opinion, it is the sensory cells of the motor analyser that are located here, and consequently, from here throughout lifetime stimulations normally and constantly stream out to definite motor centres, it is clear that with such well-beaten paths and with electrical stimulation of these areas, a usual effect arises, i.e., the stimulation proceeds from here along the customary path to the muscles.

Thus, on the basis of all our experiments we can say that the cerebral hemispheres constitute a combination of analysers, having the function, on the one hand, of analysing the external world, for example, the eye and ear analysers, and on the other hand, of analysing the internal phenomena, for example, the motor analyser. As for all the possible internal analysers, it is clear that the analysis of any other internal phenomena must be much more limited. So far, apart from the motor analyser, no other analysers of this kind have been revealed by the method of conditioned reflexes. There is no doubt, however, that sooner or later, these phenomena, too, will enter into the physiology of the conditioned reflexes.

Now let us pass to a thorough consideration of the analysers. What functions do they perform? As indicated by their name, their purpose is to decompose complex phenomena into separate elements. But what else do we know about their functions, and what have our experiments, based on the method of conditioned reflexes, shown us in this respect? I think that here the objective point of view has been of great service to us. The general facts relating to the work of the analysers have been known for a long time. The research carried out by Ferrier and Munk provided a number of facts which have a bearing on the work of the analysers. But these facts were elucidated from a very confused and unscientific point of view. You probably remember that when Munk extirpated the occipital and temporal lobes of the cerebral hemispheres, he observed certain abnormalities of hearing and sight in the dog subjected to the operation. He termed the peculiar attitude of the animal towards the external world which resulted from these abnormalities of hearing and sight, "psychical deafness" and "psychical blindness." But what did this mean? Let us consider psychical blindness. This meant that after the removal of the occipital lobes the dog did not lose the ability to see; it avoided objects met on its way, distinguished between light and dark, but at the same time no longer recognized its master whom formerly it had known very well; it completely failed to react to him; if he existed at all for the dog, it was only as an optical stimulus. The dog displayed the same attitude to all other objects. Munk and others assert that the dog "sees" but "does not understand." But what does this mean—he "understands" and "does not understand"? These words express nothing definite; they, too, must be explained.

Only the method of conditioned reflexes, excluding all psychological concepts ensured a solid foundation to the matter and fully clarified it. From the objective point of view the destruction of a certain part of the cerebral hemispheres was regarded as complete removal or partial destruction of one or another analyser. If the given analyser remained intact and its cerebral end undamaged, the dog, by means of this analyser, could differentiate both separate elementary phenomena and their definite combinations, i.e., it behaved normally. But when the analyser was destroyed, or damaged to a greater or lesser degree, then the dog could no longer differentiate delicately the corresponding phenomena of the external world. And the more the analyser is destroyed, the greater the decline of analysis. If the analyser is completely destroyed no trace remains of analysis even of the simplest phenomena. If, however, some fragments of the analyser remain, if a certain part has escaped destruction, then the correlation between the organism and the environment in respect of the given phenomena also remains, although in a very general form. Further, the larger the part of the analyser remaining intact, the more of it that remains uninjured, the better and the more delicate is the analysis it can effect. In brief, since the damage of the analyser is regarded as damage of a mechanism, it is clear that the greater the scale of the damage, the poorer is its capacity for work. This concept makes the subject quite clear and paves the way for further investigation, while the psychological point of view brings the subject into a blind alley and cannot add anything to the words "understands" and "does not understand."

Now let us consider Munk's experiments from our standpoint. We destroy the occipital lobes of the animal, i.e., the cerebral end of the eye analyser. If after this operation a minimal part of the analyser remains undamaged, the animal is still capable of a very crude analysis; it can distinguish only between light and dark. In such animals it is impossible to elaborate conditioned reflexes to the form of objects or to their movement. At the same time, however, a reflex to light or darkness is easily formed in them. If, for example, during the feeding of the animal you repeatedly produce an intensive light, then afterwards, as soon as the light appears, the animal begins to show a secretion of saliva; this means that only the small part of the analyser left after the extirpation of the occipital lobes continues to function. This explains why Munk's dog did not stumble against objects in its way; it could distinguish between dark and light, and thus avoided objects. In this limited way the eye analyser functioned very well. But when a more delicate analysis was required, when it was necessary to distinguish between various combinations of light and shade, as well as between different forms, the power of analysis proved insufficient and the damaged analyser did not function. It is understandable, therefore, that a dog in this state cannot recognize its master—it cannot distinguish him from other objects. The point is absolutely clear, and there is no need for vague formulations. Instead of saying that the dog no longer understands, we say that its analyser is injured, with the result that it has lost the ability to form conditioned reflexes to more delicate and more complex visual stimuli. And now our big task is to investigate this analyser step by step, to study its action when fully intact and to see what disappears gradually from its activity when damaged to one or another degree.

We already have precise and convincing data in this respect. If after extirpation an insignificant part of the eye analyser of the dog is left, then in such an animal a conditioned reflex can be evoked only by intensity of light, and nothing else. If the analyser is injured to a lesser degree, a reflex can be elaborated also to the movement of an object, later to its form, etc., up to the point of normal activity.

The same is true for the ear analyser. If a small part of it is left undamaged or if its activity is temporarily inhibited to a similar degree, then the animal distinguishes only between silence and sound. For an animal in this state different sounds are identical—for it all sounds, noises and tones, both high and low, are the same; it reacts only to the intensity of the sounds, but does not discern their detailed properties. If the damage to the analyser is less and a larger part of it is left, then it is possible to form reflexes to noises and tones separately; this means that here we have also a qualitative analysis, although a crude one. When the damage is still less, a reflex can be formed to separate tones and different varieties can be observed: the less the injury, the more delicate is the analysis of tone. When the analyser is severely damaged, the animal distinguishes only between big intervals of pitch, for instance, octaves; if the damage is moderate, it distinguishes first between tone, and then between fractions of a tone ($^1/_2$, $^1/_4$ of a tone). Thus there takes place a gradation from complete inability to analyse to perfectly normal activity of the ear analyser.

Now I shall dwell on the highly interesting experiments carried out by Dr. Babkin. One of his dogs lived for three years after extirpation of the posterior part of its cerebral hemispheres; thus it can be said that the condition of the dog became stationary. The dog distinguished perfectly not only between noise and sound, but also between different tones. To one tone there was a definite reflex, while to another—a close tone—no reflex at all, which shows that in this respect the dog was quite normal. But it suffered from an irreparable defect: it could not distinguish between more complex sound combinations. For example, you elaborate in the dog a conditioned stimulus from a series of ascending tones—*do, re, mi, fa* After some time you obtain a corresponding conditioned reflex. Now you reverse the tone sequence to *fa, mi, re, do.* A normal dog distinguishes the change very well, but this animal is unable to make such an analysis, and the change means nothing to it; it cannot differentiate between the sequence of sounds. Try as you may, no differentiation will be obtained. The damage to the analyser is so great that the dog is unable to perform this work. Closely linked with this fact is another, old one, to which the words "understands" and "does not understand" have also been applied: it relates to dogs which, because of damage to the ear analyser, failed to respond to their names. The just mentioned dog was named "Ruslan," but after the operation the name, even if repeated a thousand times, produced no effect whatever. Obviously the ear analyser of this animal was in such a state that it could not distinguish one combination of sounds from another. If the dog is unable to distinguish between the group of tones *do, re, mi, fa* and the same group in a reverse order—*fa, mi, re, do*—then, of course, it cannot recognize its name, since the word "Ruslan" is an even more complex sound combination. Such an analysis is beyond the ability and power of its damaged ear analyser.

I wish to stress once more the great merit of the objective method, the method of conditioned reflexes, in studying the function of the analysers. This method has completely stripped all mystery from the subject, discarded the meaningless words "understands" and "does not understand," and has replaced them with a clear and effective programme for the study of the analysers.

The task of the investigator is to define exactly the functions of the analysing apparatus, to investigate all the variations in its operation in cases of destruction of its different parts. And from the mass of facts so obtained it will be possible to attempt to reproduce the structure of the analyser, to establish its parts and discover how these parts interact.

So much for the activity of the analysers. As for the topography of the analysers and their arrangement, it should be pointed out that the view concerning their exact localization, established on the basis of earlier facts, cannot be regarded as satisfactory. Even in the past many objections to this view had been raised. Our experiments have also shown that the formerly established limits of the analysers are incorrect, that actually they are much wider, not so distinctly separated, but intermingled and interwoven one with another. Of course, it is a very difficult matter to define exactly the localization of the analysers in the cerebral hemispheres and to establish how and why they are interlaced.

Thus, from the point of view of the conditioned reflexes the cerebral hemispheres appear as a complex of analysers, whose purpose is to decompose the complexity of the internal and external worlds into separate elements and moments, and then to connect all these with the manifold activity of the organism.

Now another question arises, closely connected with the method of conditioned salivary reflexes, a question which in all probability cannot be decided or even strictly formulated without this method. Here it is: is the activity of the cerebral hemispheres confined to the mechanism of the formation of temporary connections and to the mechanism of the analysers, or are there not other, higher mechanisms which so far have not been designated by names? This is not a far-fetched question, but one which is advanced by life, by experimental practice. If you extirpate the entire posterior part of the cerebral hemispheres in a dog, i.e., just behind the gyrus sigmoideus and then along the fissura Sylvii, you will have a generally normal animal; it will recognize you and the food, as well as all other objects on its way, with the help of its nose and skin. It will wag its tail when you stroke it, evince joy upon recognizing you by sniffing, etc. But this animal will not react to you if you are at a distance, i.e., it does not use its sight in the normal manner. Nor will it react if you call it by name. You are bound to conclude that this dog uses its eyes and ears only very little, but in other respects it is absolutely normal.

But, if you remove the anterior part of the cerebral hemispheres along the same line as in the above-mentioned operation with the removal of the posterior part, you will, to all appearances, get a completely abnormal animal; its attitude to you, to other dogs, and to food (which it will be unable even to detect), and generally to all the surrounding objects, will be abnormal; it will be a completely mangled animal, obviously with no trace of proper behaviour left. Thus, there is a big difference between the two animals—the one without the anterior, and the other without the posterior part of the cerebral hemispheres. With regard to the first animal you would say that it is blind or deaf, but otherwise normal, about the other that it is a confirmed invalid and a helpless imbecile.

Such are the facts. An important and perfectly lawful question arises: Is there not something special in the anterior parts of the cerebral hemispheres, and are they not called upon to fulfil higher functions than the posterior parts? Perhaps here, in the anterior parts, there is concentrated the most essential activity of the cerebral hemispheres?

I believe that the method of conditioned salivary reflexes provides a clear answer to this question, an answer that cannot be obtained by any other method of investigation. Is it really the case that an animal with the anterior parts of the cerebral hemispheres extirpated differs essentially from a normal animal and shows no trace of normal higher nervous activity? If you adhere to the old methods of investigation, if you observe only the work of the skeletal muscles, then you will reply to this question in the affirmative. But if you turn to the salivary gland with its conditioned reflexes, the picture will be entirely different. This is not only the merit of the method of conditioned reflexes; it is also due to the fact that precisely the salivary gland was selected for the study of these reflexes. If you observe the work of the salivary gland in such an animal, which at first sight seems completely disabled, you will be surprised at the high degree the gland maintains its complex nervous relations. You will not observe even the slightest disorder in the function of the gland. On the basis of this gland you can elaborate in such an animal temporary connections, inhibit and disinhibit them, etc. In short, the salivary gland displays the whole complex of the relations observed in the normal animal. You can see clearly an unexpected discrepancy between the work of the skeletal musculature and that of the salivary gland. While the work of the former is abnormal and deranged, the latter functions perfectly well.

What does all this mean? First of all it is quite obvious that there are no mechanisms in the anterior lobes dominating the entire cerebral hemispheres. If such mechanisms existed, then the removal of the anterior lobes would destroy the entire delicate and complex work of the salivary gland. However, everything proceeds here quite normally. Evidently, we must admit that all the abnormalities which we observe in this dog are phenomena which relate only to the skeletal muscles. And our task boils down to revealing the causes of this disturbance in the work of the skeletal muscles. The existence of any general mechanism in the anterior lobes is out of the question. Obviously, the latter do not contain any particularly vital arrangement that could be regarded as establishing the highest perfection of the nervous activity.

Here is a simple explanation of this peculiar disturbance in the work of the skeletal musculature. At any given moment this work greatly depends on the cutaneous analyser and on the motor analyser. Thanks to these the animal's movements are constantly co-ordinated and adapted to the surrounding world. Since in the given dog both the cutaneous and the motor analyser are destroyed, the general activity of its skeletal musculature is, naturally, profoundly disturbed. Consequently, when the anterior lobes are destroyed we actually get a partial defect, just as in the case of the damage to the eye analyser, but not a general defect which might ensue from the abolition of the work of a hypothetical higher mechanism of the cerebral hemispheres situated in the anterior lobes.

In view of the importance of this question, a series of corresponding experiments were carried out by Drs. V. A. Demidov, N. M. Saturnov, and S. P. Kurayev. The experiments were so conducted that first the entire anterior parts together with the olfactory lobes were removed from the dog. In this dog it proved possible to elaborate a conditioned salivary reflex only from the mouth cavity by using water; when acid was repeatedly poured into the dog's mouth as an unconditioned stimulus of the salivary gland, then the subsequent introduction of water, which formerly had been absolutely indifferent to the gland, also caused a secretion of saliva, thus acting as a conditioned stimulus. However, since this water reflex might be regarded as being doubtful, it was necessary to prove the existence in such a dog of other conditioned reflexes. Therefore, Dr. Saturnov extirpated the anterior lobes but left the olfactory ones. Then, after the operation, it was possible to obtain in this dog a conditioned reflex from the olfactory nerves.

After these experiments we regarded the subject as being sufficiently clarified, and we reached the final conclusion that a dog deprived of the anterior parts of the cerebral hemispheres loses only particular mechanisms, i.e., some of the analysers, but by no means any general mechanisms.

Thus, the study of the activity of the cerebral hemispheres by the method of conditioned reflexes provides an absolutely definite answer. Basing ourselves on precise facts, we can state that the cerebral hemispheres represent a system of analysers, which decompose the complexity of the external and internal worlds into separate elements and moments and then connect the phenomena thus analysed with one or another activity of the organism.

Can we be satisfied with the results obtained? Of course, we can, and chiefly because they have paved the way for further fruitful study of the subject. At the same time, however, it is clear that this study has just been started, and that the most complicated, the most essential part of this study is still ahead of us. In outlining the further course of research, we must pay attention first of all to our present method of dismembering the apparatus under investigation into separate parts. It is an awful method! The more we experiment with extirpation of the cerebral hemispheres, the more we are surprised at the successful results achieved by former investigators by means of this method. Because of extirpation we hardly ever obtain stable conditions; they bear a fluctuating, changeable character. You place your heavy hands on the brain, and damage it by removing certain of its parts. The damage irritates the brain and this irritation persists for some time, spreading to uncertain limits. You never know when its action will end. That such irritation really exists is proved by many well-known experiments on which I shall not dwell here. But finally the desired moment comes—the irritation evoked by the damage passes, and the wound begins to heal. Then a new irritation appears—the scar. And it may be that there are only a few days at your disposal during which you can work with the assurance that all the changes observed depend only upon the absence of the removed parts of the cerebrum. Then the following phenomena begin to develop. At first the phenomena of depression appear, and you know that it follows from the action of the scar. This state lasts for days, and then convulsions set in. After this, after the excitation, there comes a new period of subsequent depression, or an entirely new, peculiar state of the animal develops. After the convulsions a drastic change takes place in the dog and you cannot recognize it: it becomes much more disturbed than was the case immediately after the operation. Obviously the scar not only irritates, but exerts pressure on the tissues, strains and wrenches them, i.e., causes fresh damage.

I must add that this effect of the scar never ends, at least I have never seen it end. Sometimes it persists for months and years. Convulsions usually appear after a month or a month and a half, and then recur. We have operated on scores and scores of dogs, and I can state categorically that not one of them escaped convulsions and recurring fits of them provided it survived the first attack.

Just try under these unfavourable conditions to analyse successfully such complex activity as that of the cerebral hemispheres. Without a shadow of doubt the present-day investigator of the cerebral hemispheres must, above all, attend to the question of how to adapt the whole procedure of his investigation to the brain. This is a highly important matter, since the present method of investigation entails a tremendous waste of human labour and a great loss of animals. Endeavours have already been made to reduce this waste. A German experimenter (Trendelenburg) has attempted local cooling of the brain. In our laboratory this method is employed by Dr. L. A. Orbeli. The near future will show whether this method will be suitable and bring us good results.

Such are our achievements, our aspirations, our complaints and hopes.

PHYSIOLOGICAL MECHANISM OF THE SO-CALLED VOLUNTARY MOVEMENTS[77]

In the physiological laboratory of the Military Medical Academy Dr. Krasnogorsky (1911) definitely established the undoubtedly afferent nature of the motor region of the cortex by forming from the kinesthetic stimulation[78] of the skeletal musculature a conditioned food stimulus just as it is formed from all other stimulations entering the cortex through the external receptors—the eye, the ear, etc. In other words, he showed that any passive skeletal movement could be made a signal of a positive unconditioned alimentary reflex, that is, a conditioned alimentary stimulus. Y. M. Konorsky and S. M. Miller, who had obtained their basic experimental facts in Warsaw and who are going ahead with their elaboration in the Physiological Department of the Institute of Experimental Medicine, afterwards applied successfully kinesthetic stimulation (passive movements) as signals of unconditioned negative reflexes (a painful stimulation of the ear, the introduction of acids, etc.) and as conditioned inhibitors for both groups of unconditioned reflexes. In this way many facts were obtained relating to the highest important physiological problem of the mechanism of voluntary movements, i.e., movements proceeding from the cerebral cortex.

First of all we must recognize as an established fact that a definite movement corresponds to the stimulation of definite kinesthetic cells in the cortex, and, on the contrary, a passive reproduction of a definite movement, in its turn, evokes impulses in the kinesthetic cerebral cells, the stimulation of which actively produces this movement. This can be proved in the following way. The first part of the above proposition is a constant physiological fact of long standing: when definite points of the surface of the motor region in the cerebral cortex are stimulated by means of a weak electric current, mechanically or chemically, strictly definite skeletal movements arise. As for the second part of the proposition, it is proved by the simplest facts relating to the training of domestic animals, for example, dogs. You lift the dog's paw saying "give me the paw," or simply "paw," and then give the dog something to eat. After repetition of this procedure the dog itself offers its paw at these words; it does so even without any word of command when it has a keen appetite, i.e., when it experiences alimentary excitation. The physiological conclusions from this well-known and constant fact are both obvious and many-sided. It is clear, in the first place, that the kinesthetic cell, stimulated by a definite passive movement, produces the same movement when it is stimulated not from the periphery, but from the centre; in the second place, that the kinesthetic cell establishes a connection both with the auditory cell and the cell of alimentary excitation, or the gustatory cell, since the stimulations coming from both of these cells evoke an active state of the kinesthetic cell; and in the third place, that in this interconnected system of cells the process of excitation moves in two opposite directions—from the kinesthetic cell to the gustatory, alimentary one (during the establishment of the connection) and from the alimentary to the kinesthetic cell (in the case of alimentary excitation). These conclusions are also confirmed by other facts. It has long been observed and scientifically proved that when you think of a certain movement (i.e., when you have a kinesthetic idea), you involuntarily, without noticing it, produce the movement. The same thing occurs in the well-known trick when a man has to do something of which he has no knowledge: he has to go somewhere and do something with the help of another man who knows how to do the thing, but has neither the intention nor the desire to help. However, to get actual help it suffices for the first man to take the other's hand in his own. In this case the second man involuntarily, without noticing it, gives the first slight pushes towards the goal and keeps him from moving in the opposite direction.[79] The process of learning to play the piano or the violin from music entails an obvious transition of the excitation from the visual to the kinesthetic cell.

Thus, the kinesthetic cells of the cerebral cortex can, and do establish connections with all the cerebral cells which represent the external influences as well as various internal processes of the organism. It is this that constitutes the physiological basis of the so-called voluntariness of movements, i.e., of their dependence on the aggregate activity of the cortex.

Still unsolved in this physiological concept of voluntary movements is the question of the cerebral connection of the kinesthetic cells with the corresponding motor cells, whence the pyramidal efferent paths originate. Is this connection inborn, or is it acquired, elaborated in the course of the post-natal existence? Most probably the latter is the case. If this connection is constantly extended and perfected during the entire lifetime, then it can be assumed that even the first period of the individual existence of higher animals, and especially of man who for months learns to control his first movements, is spent on establishing this connection.

The general physiological law of the work of the skeletal musculature, on the one hand, consists in constant movement towards everything, in grasping everything that preserves and ensures the integrity of the animal organism, that equilibrates it with the surrounding medium; this is a positive reaction, positive movement. On the other hand, it is constant movement from everything, throwing aside and ejecting everything that hinders and threatens the vital process, that violates the equilibration of the organism with the environment; this is a negative reaction, negative movement. A conditioned stimulus is a signal, as it were, a substitute for the unconditioned stimulus. This explains why a dog, for example, reaches for the electric bulb and even licks it, when its flashing acts as a conditioned alimentary stimulus. And on the contrary, under the action of a conditioned acid stimulus, the dog reproduces the movements it makes when acid is introduced into its mouth. The same thing occurs when a kinesthetic stimulation acts as a conditioned stimulus. Thus a passive movement, when it is connected with an alimentary reflex, evokes a positive alimentary reaction, and when it is connected with an acid reflex—a negative, acid reaction.

Now let us consider all the cases in which kinesthetic stimulation (passive movement) has been applied by the researchers in studying conditioned reflex activity.

1. When the flexion of a leg is connected with an alimentary reflex, it is reproduced by the animal, just as any other natural alimentary movement, every time it is in a state of alimentary excitation; this takes place so long as the connection functions, so long as it is not eliminated by a protracted non-reinforcement, or is not abolished temporarily by one or another kind of inhibition.

2. In the case of a conditioned acid reflex, when the flexion of the leg is a signal, a substitute for the acid, a struggle begins against the flexion, just as against the acid itself. The flexion must be eliminated just as the acid must be ejected from the mouth. But flexion can be eliminated by extension, and it is the latter phenomenon which is actually observed. It is a well-known fact that when for some reason the flexion is associated with pain, the animal keeps its leg extended.

3. In the case of flexion, applied as a conditioned inhibitor, i.e., when a passive movement is added to the conditioned alimentary stimulus, but no food is offered, this

movement is a signal of the animal's difficult state caused by inducing but not satisfying the alimentary excitation. Naturally, there must be a struggle against it: it must be eliminated—and this is attained by extension.

4. In the last case, when the flexion of the leg is added to the conditioned acid stimulus as a conditioned inhibitor, without introducing acid, the passive movement is a signal of the elimination of the noxious agent; at the same time it is, as it were, a reliable means of combating this agent, and is, naturally, always repeated by the animal even when it encounters other noxious agents.

But all that has been said above explains the phenomena only from the more general physiological point of view. It is impossible not to see that the mechanism of some particular physiological phenomena still remains to be elucidated. The question arises: how and on what immediate basis does the transition from flexion to extension take place, since physiologically these motor acts are definitely and constantly interconnected? And another question: was there manifested in the third and fourth cases, and if so when and how, the inhibitory process which, in our experiments, inevitably appeared when the combination of a conditioned stimulus with an extraneous one was not reinforced by a corresponding unconditioned stimulus? These questions must be subjected to further experimental analysis, since the available data are insufficient to answer them properly.

VII

THEORY OF TYPES

GENERAL TYPES OF ANIMAL AND HUMAN HIGHER NERVOUS ACTIVITY[80]

The mode and standards of our own behaviour, as well as of the behaviour of the higher animals close to us and with which we are in constant vital relations (for instance, dogs), represent a great, a truly boundless variety, if behaviour is considered as a whole, in its smallest details, especially as manifested in man. But since our behaviour, as well as that of higher animals, is determined and controlled by the nervous system, it is possible to reduce the above-mentioned variety to a more or less limited number of basic properties of this system, with their combinations and gradations. This makes it possible to distinguish between the types of nervous activity, i.e., between these or other complexes of the basic properties of the nervous system.

The observation and study of a large number of dogs, using the method of conditioned reflexes, carried out in our laboratory for many years, have gradually disclosed to us these properties in their vital manifestations and combinations. These properties include: in the first place, the *strength* of the basic nervous processes—excitatory and inhibitory—which always constitute the sum total of nervous activity; in the second place, the *equilibrium* of these processes; and, finally, in the third place, their *mobility*. It is obvious that while all these properties exist and act simultaneously, they provide the highest adaptation of the animal's organism to the surrounding world, or, in other words, the complete equilibration of the organism as a whole with the external environment, i.e., they secure the organism's existence. The significance of the strength of the nervous processes is clearly shown by the fact that in the surrounding medium there arise (more or less often) unusual, extraordinary developments, powerful stimuli, and that, naturally, other external conditions of a similar and even greater force not infrequently necessitate the suppression or retardation of the effects of these stimuli. And the nervous cells must endure this extraordinary tension in their activity. From this also follows the importance of equilibrium between both processes, their equal strength. Since the organism's external environment is constantly—and often powerfully and abruptly—fluctuating, both processes must, so to speak, keep pace with these fluctuations, i.e., they must possess great mobility and be able, in compliance with the demands of the external conditions, rapidly to recede, to give preference to one stimulus, to excitation before inhibition and vice versa.

Leaving aside the gradations and considering only the extreme cases, only the limits of fluctuation, viz., strength and weakness, equality and inequality, lability and inertness in both processes, we obtain eight combinations, eight different complexes of basic properties of the nervous system, eight types of the nervous system. If we also take into account that in the absence of equilibrium the predominance may, generally speaking, be on the side now of the excitatory, now of the inhibitory process, and that in the case of mobility, inertness or lability may also become a property now of one, now of the other process, then the number or possible combinations increases to twenty-four. And finally, if we also take into consideration even the rough gradations of the three basic properties, we shall thereby again greatly augment the number of possible combinations. However, only extensive and thorough observation can establish the presence, frequency and intensity of these or other actual complexes of basic properties, of the actual types of nervous activity.

Since normally our general behaviour, as well as that of higher animals (we imply here healthy organisms), is directed by the higher part of the central nervous system—by the cerebral hemispheres and the adjacent subcortex—the study of this higher nervous activity under normal conditions by the method of conditioned reflexes is bound to lead to knowledge of the actual types of nervous activity and the basic standards of behaviour of human beings and higher animals.

It seems to me that this problem was solved—of course, only in general outline—by the Greek genius in his system of the so-called temperaments, where the basic components of the behaviour of human beings and higher animals were exactly emphasized and advanced, as we shall show in our further exposition.[81]

But before proceeding to our factual material, I must touch on one very substantial and so far almost insurmountable difficulty connected with the definition of the type of nervous activity. Human and animal behaviour is determined not only by congenital properties of the nervous system, but also by the influences to which the organism is continuously subjected during its individual existence; in other words, it depends on constant education and training in the broadest sense of these words. This is due to the fact that along with the above-mentioned properties of the nervous system, another very important property incessantly manifests itself—its high plasticity. Consequently, since this is a question of the natural type of nervous system, we must take into account all the influences to which the organism has been exposed from the day of its birth to the present moment. With regard to our experimental material (i.e., our dogs) in the overwhelming majority of cases the fulfilment of this requirement still remains a passionate desire. We shall be able to fulfil it only when our dogs are born and reared before our eyes, under our unremitting observation. We shall soon have convincing corroboration of the importance of this requirement. So far there is only one way of overcoming the above-mentioned difficulty: it is necessary to increase and to diversify the forms of our diagnostic tests as much as possible in the hope that in this or that case we shall succeed in bringing to light the specific changes in the natural type of nervous system that were determined by the definite influences of the individual existence; in other words, by means of a comparison with all other features of the type we shall reveal both the more or less disguised natural features and the elaborated, acquired ones.

Right from the very beginning of our experiments with dogs based on the method of conditioned reflexes we (like others) were struck by the different behaviour of the bold and the cowardly dogs. The former offered no resistance when led to experimentation; they remained quiet in the new experimental conditions, both when they were placed in the stands mounted on tables, and when certain apparatuses were attached to their skin and even placed in their mouths. When food was given to them by means of an automatic device, they began to eat it at once. Such was the behaviour of bold animals. But the cowardly animals had to be accustomed gradually to the procedure—a process which required days and even weeks. Another difference was observed when we began to elaborate conditioned reflexes in these dogs. In the first case the conditioned reflexes developed rapidly, after the application of two or three combinations; they reached considerable strength and remained constant, no matter how complicated the system of reflexes. In the second case, on the contrary, the conditioned reflexes were formed very slowly, after many repetitions; their strength increased at a very low rate, and they never acquired stability, being sometimes even at zero, no matter how considerably their system was simplified. It was, therefore, natural to assume that in the first dogs the excitatory process was strong, while in the second it was weak. In the bold dogs the excitatory process, which from the biological point of view arises properly and in time, for instance, at the sight of food, constantly resists minor influences, remaining, so to speak, legitimately predominant. In the cowardly dogs the strength of the excitatory process is insufficient to overcome conditions which are less important in the given case and which produce what we term external inhibition; for this reason we say that such dogs are inhibitable. In the bold dogs even physically excessive external stimuli, when conditionally connected with physiologically important functions, continue to serve their purpose without bringing the nerve cell to a pathological state; thus they represent an exact index of the intensity of their excitatory process, of the strength (i.e., working capacity) of their nerve cells.

It is here that the specific difficulty, which I have just mentioned made itself felt. All the dogs which seemed to us cowardly, i.e., which only very slowly became accustomed to our experimental conditions and formed conditioned reflexes with difficulty (since their entire conditioned reflex activity was easily disturbed by insignificant new external influences), were regarded by us, quite groundlessly, as belonging to the weak type of nervous system. This even resulted in a blunder—at one time I regarded these dogs as experts in inhibition, i.e., as being strong in this respect. The first doubts as to the correctness of this diagnosis arose in connection with the external behaviour of these animals in their habitual surroundings. Further, it seemed strange that their conditioned reflex activity, despite its high complexity, should be of a perfectly regular character so long as the surrounding conditions remained strictly uniform. But the final solution was found thanks to a special investigation. We (Virzhikovsky and Mayorov) took a litter of puppies and divided it into two parts: half of the puppies, from the very day of their birth, were kept in the kennel, the others were given complete freedom. All the animals of the first group turned out to be cowardly and susceptible to inhibition given the slightest changes in the surroundings; in the animals of the second group nothing of the kind was observed. It became clear that when the puppies first appeared in the external environment they were provided with a special reflex, sometimes referred to as a panic reflex, but which I suggest should be termed an initial and temporary reflex of natural caution. The moment acquaintance with the new environment begins it is necessary to wait some time for the consequences of any new stimulation, no matter which receptor it affects, i. e., to abstain from any new movement and to repress the existing movement, since it is not known what the new phenomenon promises the organism, whether harmful, useful, or of no consequence at all. And only in the course of the gradual acquaintance with the environment is this reflex replaced, little by little, by a new, special, investigatory reflex, and, depending on its effect, by other corresponding reflexes. The puppy, which is not given the opportunity to gain this practical experience independently, retains the persisting temporary reflex for a very long time, if not for life, and the reflex constantly disguises the real force of the nervous system. What a vital pedagogical fact this is! A sure sign of this unduly persisting feature, apart from the fact that in many respects it contradicts other stable inborn features, is the inhibitory action not so much of the particularly strong stimulations but of the new stimulations—no matter how weak they may be in themselves (Rosenthal, Petrova).

Thus, the strength of the excitatory process was regarded by us as the first property of the type of nervous system. Hence the initial division of all our dogs into strong and weak ones.

Another property of the nervous system, clearly observed by us and according to which the animals are subdivided into new groups, is the equality or inequality of the two opposite nervous processes—excitation and inhibition. We imply here the higher active cortical inhibition (or according to the terminology used in the theory of conditioned reflexes—internal inhibition), which, together with the excitatory process, continuously maintains the equilibration of the organism with the surrounding medium and helps (on the basis of the analysing function of the organism's receptors) to distinguish between the nervous activity corresponding to the given conditions and moments and that which does not (extinction, differentiation and retardation).

The significance of this property was first observed by us in dogs with a very strong excitatory process. We soon noticed that whereas in such dogs positive conditioned reflexes were formed rapidly, inhibitory reflexes, on the contrary, were elaborated very slowly, with obvious difficulty; this was often accompanied by a violent resistance on the part of the animal; it was manifested either in destructive actions and barking, or, on the contrary, in stretching out the forepaws, as if imploring the experimenter to release it from the task (the latter, however, is rarer). At the same time, these reflexes are never fully inhibited; they are often disinhibited, i.e., greatly deteriorate in comparison with the degree of inhibition obtained previously. The following phenomenon is usually observed: when we subject the cortical inhibition in such animals to severe strain by means of very delicate differentiation, or by a frequent or protracted application of difficult inhibitors, their nervous system becomes fully, or almost fully, deprived of the inhibitory function; real neuroses set in, typical and chronic nervous diseases, which must be treated either by allowing the animals a very long rest, i.e., by a complete discontinuance of the experiments, or by giving bromide. Together with such animals, there are others in which both nervous processes are at an equally high level.

Consequently, the strong animals are divided into two groups—equilibrated and unequilibrated. Unequilibrated animals belonging to the category described above are met with quite often. It might seem that there should also be unequilibrated dogs of another kind, namely, with a predominance of the inhibitory process over the excitatory. But so far we have not met with such absolutely incontestable cases, or at least we have not been able to discern them. However, we have had fairly obvious and not infrequent cases when, after a time interval and with the help of gradual and repeated exercises, the initial disequilibrium levelled out to a considerable degree. And this is just another instance when the natural type of nervous system proved to be disguised to a great measure as a result of lifetime training.

Thus, we have a perfect group of strong and equilibrated dogs. However, the animals with this type of nervous system differ greatly, even in appearance. Some are extremely reactive, mobile and lively, i.e., as it were, extremely excitable and alert. Others, on the contrary, are only slightly reactive, sluggish and self-contained, i.e., in general, so to speak, little susceptible to excitation, inert This difference in the general behaviour must, of course, be due to a specific property of the nervous system and may be best accounted for by the mobility of the nervous processes. Like everybody else we long ago observed this external difference between animals, but we lag considerably in elucidating, on the basis of the conditioned reflex activity, its cause—the mobility of the nervous processes. Only now is this mobility being systematically investigated on two dogs—strongly pronounced representatives of the latter group. Strong and equilibrated, these animals differ greatly in external behaviour. On the one hand, we (Petrova) have an exceedingly lively and reactive animal, on the other (Yakovleva)—an extremely inert and indifferent one. The different mobility of the nervous processes in these animals is distinctly manifested in their conditioned reflex activity which, unfortunately, was not investigated in identical experiments.

The first animal ("Boy") even in the course of usual experimentation with conditioned reflexes displays an amazingly rapid transition from extreme excitation at the beginning—when being placed in the stand and equipped with the apparatus—to a state almost of petrifaction, to a statuesque posture, and, at the same time, to a good working state in the course of the experiment. In the intervals between the conditioned alimentary stimuli the animal remains in a very strained posture, evincing no reaction to extraneous accidental stimuli; but under the action of conditioned stimuli a strictly recurring salivary reaction sets in immediately, and the dog gulps the food placed before it. Subsequently, this high mobility of the nervous processes; their rapid interchange, manifested themselves, so to speak, with incredible force also in the course of special experiments. In our "Boy" we long ago elaborated two opposite conditioned reflexes to a metronome; one frequency of the metronome acted as a positive conditioned alimentary stimulus, while the other acted as a negative inhibitory one. We then began to reverse the action of the metronome. The negative stimulus was reinforced, i.e., it had to be transformed into a positive stimulus, while the positive one was no longer accompanied by feeding and had to be converted into an inhibitory stimulus. Next day we were able to observe the onset of this reversal and by the fifth day it had been fully accomplished—a rare case of such rapid transformation. One day later an error was made—the metronomes were applied in accordance with their previous significance, namely, the old positive stimulus was again reinforced, while the old inhibitory stimulus was left without reinforcement; as a result, the old relations were immediately re-established. When the error was corrected, the new relations again quickly reappeared. But this dog presented a truly wonderful, unprecedented example of the formation of a delayed reflex. Generally the elaboration of a delayed reflex, when one and the same stimulus during different periods of its action produces now an inhibitory, now an excitatory effect, is in itself a difficult task. But its elaboration after a long experience of short-delayed reflexes, and even during it, is a truly complicated task, one that cannot be accomplished by the overwhelming majority of dogs and which in successful cases requires much time, even many months. Our dog accomplished this task in the space of few days. What an extraordinary rapid and free use of the two opposite processes!

All that has been said about this dog entitles us to state that it represents the most perfect type, since it ensures strict equilibration with all that is taking place in the external environment, no matter how strong the stimuli are —both those to which the response must be positive activity, and those the effect of which must be inhibited— and no matter how quickly these different stimuli may interchange. It should be added that these extremely difficult tests were endured by the dog after it had been castrated.

The very opposite, in relation to the property of the nervous system under consideration, is the other dog ("Zolotisty," used by Yakovleva), whose general behaviour has been characterized above. Particularly manifest in the study of the conditioned reflex activity of this dog was the impossibility of obtaining a constant and adequate salivary alimentary reflex; it fluctuated chaotically, often falling to zero. What did this signify? If the reflex tended to be strictly related to the moment of reinforcement, i.e., of feeding, why did it fluctuate and not become constant? This could not have been caused by insufficient inhibition, since we knew that the dog could endure protracted inhibition. Besides, the absence of preliminary salivation is by no means a manifestation of perfection; on the contrary, it indicates an obvious defect. Indeed, the importance of this salivation consists in the fact that the food introduced into the mouth immediately meets with the substance it needs. That this interpretation conforms to reality is proved, in the first place, by its universality, and, in the second place, by the fact that the extent of the preliminary salivation, which is biologically indispensable and important, always strictly corresponds to the amount of food. The natural explanation for the peculiarity of our dog must be sought in the fact that the initial inhibition, which exists in each delayed conditioned reflex —the period of retardation (or the latent period, as we called it previously)—although strong, is obviously insufficiently labile to keep within the proper time, and owing to inertness, oversteps the normal limits. None of the measures aimed at obtaining a constant salivary effect was successful.

Since the excitatory and inhibitory processes were strong in the dog, it was offered a very difficult task, one, however, that is satisfactorily solved by some other dogs. Among other elaborated conditioned stimuli, and at different moments of this system of reflexes, a new stimulus was applied four times in the course of the experiment, but it was reinforced only when applied the last time; this was a task which required all the resources of the nervous system, and above all a high mobility of the nervous processes. Our dog did its best to solve this problem in a roundabout way, holding on everything which could be a simple, ordinary signal of the fourth reinforced application of the new stimulus. First of all it made use of the noise produced by the food receptacle which was moving before its eyes; during the first three applications of the new stimulus, when no food was offered and consequently no movement of the food receptacle took place, the dog remained in sitting posture. When, during the intervals between the stimulations, empty food receptacles were placed before it in order to deprive it of the signal connected with the reinforcement, it looked into them to see whether there was any food, and only when this was the case, did it stand up (usually it was sitting). When the receptacle was placed too high so that the dog could not see whether it contained anything, it rejected the food altogether, remaining in sitting posture regardless of the stimulus applied. In the case of a positive stimulus, it was necessary to enter the chamber and show the dog that the receptacle contained food, i.e., to invite it to eat, and only then did it begin to eat. Then both the new stimulus and the presentation of empty receptacles were discontinued. Only the old stimuli were applied, of course accompanied by reinforcement. And only *gradually* did the dog begin to rise under the action of the stimuli and to eat. Again the reflex evoked by the empty receptacle was extinguished. The dog continued to rise under the action of the old conditioned stimuli but—which was the usual thing with it—did not always exhibit any preliminary secretion of saliva. Now the new stimulus was again applied four times, being reinforced only the last time; during the first three applications the food receptacle was not placed before the dog, since, as has just been mentioned, the reflex to it had been extinguished. This time, too, the problem was solved by means of a simple, but new signal, namely, a complex stimulus formed from the new stimulus plus the noise of the moving food receptacle. When the new stimulus was applied for the first three times without the addition of the last stimulation, there was no reaction. But when during these first applications the receptacle was placed before the dog, but with no food in it, i.e., when the complex stimulus was depreciated, the dog, after rising several times in vain, definitely and completely ceased to react to the new stimulus, rising only under the influence of all the other stimuli. Then it was decided to restore the extinguished reflex to the new stimulus, abolishing all other stimuli and reinforcing the new stimulus eight times in succession in the course of the experiment. The rehabilitation of the reflex proceeded *very slowly*. The new stimulus was reinforced in the course of two days, that is, sixteen times, but despite the fact that the experimenter entered the chamber more than once and during the action of the new stimulus showed the food to the dog (only after which it rose to its feet and began to eat) it never stood up by itself under the action of the new stimulus. At first the same thing was observed on the third day; only during the nineteenth application of the new stimulus, when it was prolonged after the expiration of the usual thirty seconds and when new food receptacles were placed at intervals of ten seconds, did the dog, at the fourth presentation of a food receptacle, rise and eat the food. And only later, at first with considerable omissions on the part of the animal, a motor alimentary reflex formed; for the purpose of accelerating its full restoration the dog was more than once left without food for a space of twenty-four hours. Afterwards, on the fifteenth day, there finally developed a full reflex accompanied by a preliminary secretion of saliva, but, inconstant, as usual. On the twentieth day, in order to obtain a constant salivary reflex, the dog was given only half the usual portion of food and this reduced ration was offered for a period of ten days. But the aim was not achieved—the salivary reaction remained inconstant, and even the motor reaction manifested itself either at the end of the action of the conditioned stimulus or only after the presentation of the food receptacle. What striking inertness of the *inhibitory* process! After this, for a period of fourteen days, the dog was given only a quarter of the normal quantity of food, but this, too, hardly changed the picture as far as the reflexes were concerned.

Against this background we began once again to elaborate a new and extremely simplified differentiation: in strict alternation the new stimulus was now reinforced, now not; it was necessary to elaborate reflexes to a single rhythm. In a period of eight days we failed to observe even the slightest trace of a reflex. What striking inertness of the *excitatory* process! Thinking that this phenomenon was partly due to excessive alimentary excitability we increased the quantity of food to half the usual ration. As a result, the difference in the extent of the salivary reaction under reinforced and non-reinforced stimuli now began gradually to manifest itself, and finally a stage was reached when, in the case of reinforced stimuli, the reaction became very considerable, while in the case of non-reinforced stimuli it fell to zero. However, the motor reaction persisted in all cases, although under positive stimuli it appeared quicker. When the experiments were prolonged in order to obtain a complete differentiation also of the motor reaction, the dog began to whine, at first before the experiment and then in the course of it, and tried all the time to escape from the stand. The motor reaction under a non-reinforced stimulus was fully differentiated in some experiments only when it came first in the experiment. The more time passed, the more difficult became the state of the dog; it no longer entered the experimental chamber of its own accord and when taken forcibly would turn back and run away. While in the chamber it kept on howling and barking. Under the action of stimuli the howling and barking became louder. This general behaviour was in striking contrast with the previous behaviour of the animal over a period of three years. In order to help the dog to attain complete differentiation, it was given a full daily ration of food; it gradually calmed down, went to the stand willingly, stopped howling and barking. At the same time a secretion of saliva was observed also under the action of a non-reinforced stimulus; then the salivary secretion induced by the action of the two kinds of stimuli began steadily to diminish until it reached zero. Finally, the motor reaction to a repeated stimulus also fully disappeared. The dog refused to perform its task and lay quietly throughout the experiment, searching for fleas or licking its body. After the experiment it devoured its food with avidity.

Thus, during the long period of the elaboration of a differentiation (the latter being at first difficult, and then quite simple) we observed the extreme inertness both of the excitatory and inhibitory processes. Particularly interesting and clear as to its mechanism was the last period —when a simple differentiation was being elaborated. Owing to a considerably heightened alimentary excitability this differentiation was at last almost completely worked out, but it was accompanied by extreme excitement on the part of the animal; this testified to the difficult state of its nervous system. But when the alimentary excitability declined to the level usually displayed by all the dogs during the experiments, our previous success in keeping the opposite nervous processes within the time limits required by the external conditions was reduced to naught. It proved more difficult for the dog to interchange the excitatory and inhibitory processes at intervals of five minutes, i.e., to maintain the almost elaborated procedure, the already formed nervous stereotype, than to repress the rather strong alimentary excitation, under which all our dogs worked quite satisfactorily during the experiments; this excitation was also in evidence in our dog, as proved by the fact that it eagerly devoured the food placed before it after the experiments. This fact strikingly testifies to the great importance of the normal mobility of the nervous processes, as well as to its obvious and considerable insufficiency in our dog, whose nervous processes, however, possessed great strength.

It is now possible clearly to see how the Greek genius, personified (individually or collectively) by Hippocrates, succeeded in discerning the fundamental features in the multitudinous variations of human behaviour. The singling out of melancholics from the mass of people signified the division of the entire mass of human beings in two groups—the strong and the weak, since the complexity of life must, naturally, tell with particular force on individuals with weak nervous processes and darken their existence. Thus, the paramount *principle of strength* was clearly stressed. In the group of strong individuals the choleric is distinguished by his impetuousness, i.e., inability to repress his temper, to keep it within the proper limits; in other words, he is distinguished by a predominance of the excitatory process over the inhibitory. This, consequently, established the *principle of equilibrium* between opposite processes. Finally, by means of a comparison between phlegmatic and sanguine types the principle of the mobility of the nervous processes was established.

There remains the question whether the number of basic variations of human and animal behaviour is confined to the classical figure "four." After years of observations, and as a result of numerous investigations on dogs, we acknowledge at any rate, for the time being, that this number conforms to reality; at the same time we admit that there are minor variations in the basic types of nervous system, especially in the weak type. In the strong unequilibrated type, for example, the animals with a particularly weak inhibitory process and, at the same time, quite a strong excitatory process, stand out. In the weak type the variations are, above all, based on the same properties which underlie the subdivision of the strong type into equilibrated and unequilibrated, active and inert animals. But in the weak type the feebleness of the excitatory process, so to speak, depreciates the significance of these other properties and actually makes this type, to a greater or lesser degree, an invalid one.

Now I shall dwell in more detail on the methods, on the more or less definite forms of experimentation already mentioned and which clearly disclose the basic properties of the types; I shall also touch on other, less manifest, forms, which are capable of demonstrating the same properties, though not so distinctly, and at the same time reveal to a greater degree the complexity of the type, even its entire outline. It should be added, however, that many forms of our experiments have not yet assumed definite importance in the solution of the problem of types. Of course, were our knowledge of the subject complete, everything observed by us in our animals, everything recorded by us, would find its proper place in this problem. But this is still far from being the case.

We have already mentioned a definite method of ascertaining the strength of the excitatory process, believing that this strength is most inherent in the strong type. It is a physically most powerful external agent which the animal is able to endure and to turn, along with other less powerful ,stimuli, into a certain signal, a conditioned stimulus, which remains active for a long period. For this purpose we usually apply very strong sounds, produced by a special rattle which our ear endures with difficulty. In some dogs this stimulus, when reinforced, could be developed, equally with all others, into a real conditioned stimulus, and even take first place among them by virtue of the law of proportionality between the extent of the effect and the intensity of the external stimulus. In other dogs, in accordance with the law of maximum, its effect declined compared with the other strong conditioned stimuli, however, without interfering with the action of the other stimuli. In still other dogs, when applied, it led to the inhibition of the entire conditioned reflex activity, without becoming a conditioned stimulus. And finally, there were dogs in which one or two applications of this stimulus immediately evoked a chronic nervous disorder—a neurosis which did not disappear of itself and had to be treated.

The second method employed in the case of conditioned alimentary reflexes consists in augmenting alimentary excitability by means of a more or less protracted state of hunger. As a result, in dogs with a strong excitatory process the effects of the strong stimuli, in some cases, are increased; however, there also takes place a relatively greater increase of the effects of weak stimuli, so that they fully or almost fully approximate to the effects of the strong stimuli. In other cases the effects of the strong stimuli remain unchanged, since they have reached their limit and have even somewhat overstepped it; and only the effects of weak stimuli increase, to the degree that they may even exceed the effects of strong stimuli. But in dogs with a weak excitatory process, a heightened alimentary excitability usually leads to a decline in the effects of all stimuli.

The two methods make it possible to determine directly the maximum possible tension of the nerve cell, the limit of working capacity, either directly by the application of extremely strong external stimuli or through the action of stimuli of average strength, provided there is heightened reactivity of the cell, that its state is labile, which is essentially the same thing.

The third method consists in administration of caffeine. In the strong type a definite dose of caffeine increases the effect of the excitatory process; in the weak type it diminishes this effect, causing the cell to overstep the limits of its working capacity.

The weakness of the excitatory process is manifested with particular distinctness, perhaps, in the following experiment; it relates to the course of the excitatory process during the period of the isolated action of the conditioned stimulus; the ascertainment of the effect is facilitated by dividing this period into smaller time units. Three cases are possible: the effect of stimulation may increase regularly and progressively until it is joined by the unconditioned stimulus; it may, on the contrary, be considerable at the beginning and then gradually diminish; and finally, fluctuations of the effect may be observed—now increasing and now declining during the above-indicated period. This fact can be interpreted in the following way. The first case might indicate the presence of a strong excitatory process developing irresistibly under the unceasing action of the external stimulus. The second case, on the contrary, can be interpreted as the manifestation of a weak process for the following reason. In particular cases, for example, after local extirpations of the cerebral cortex, when un-