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PHYSIOLOGY OF SLEEP AND CLINICAL ASPECTS OF SLEE
Part I

by

Dr. Rudolf Baumann

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From the [redacted]an

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PHYSIOLOGY OF SLEEP AND CLINICAL ASPECTS OF SLEEP THERAPY

Original Title: Physiologie des Schlafes und Klinik der Schlaftherapie

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Introduction

Recent Soviet scientific literature acclaims sleep therapy as new therapeutic method. This therapy was pioneered by the eminent physiologist Pavlov and is based on his research work. Many Sovie clinicians have since become interested in this therapy and applie it to treat a variety of diseases. Bykov, Pavlov's outstanding disciple, investigated the correlation of the cerebrum and the internal organs. His experiments opened new vistas regarding the mechanics of conditioned reflexes, regulatory activity of the cerebral cortex and the function of corticovisceral regulations. His findings served to broaden the scope of sleep therapy applicat

With this book, the author intends to present a general revi of the physiology of sleep, in the light of Pavlov's and Bykov's doctrines, and to explain the clinical application of sleep theraj based on his own observations. When Part I was started in 1949, translations into German from Russian originals were scarce and difficult to obtain. Part II deals primarily with internal disea treated with sleep therapy (approximately 200 cases).

It is not my intention to make final statements yet, but rat to evaluate working hypotheses derived from our observations (mai in regard to indications for and effects of sleep therapy). My m concern is to provide insight into the physiological laws of the sleep process and to define indications for sleep therapy and met of application. Many questions and problems, mainly pertaining t the mechanics of cortical regulatory impulses, have arisen out of our clinical experience with sleep therapy. The influence of the latter on the various metabolic processes is of great interest, b not yet fully understood. Some connections are only intimated an much needs to be clarified, but the twilight already starts to li If this book succeeds in directing clinical and experimental rese toward this new and promising therapeutic method, it will have se its purpose.

Berlin, Spring 1953 Rudolf Baumann

Contents

Part I - Physiology of Sleep

Preface to English Translation ii

Introduction iii

I Sleep and Internal Inhibition. 1

II Is There a Sleep Center? 18

III The Importance of Cortical and Cortico-autonomic Regulation in Sleep. 22

IV Acquired Conditioned Sleep Reflexes and Foci of Arousal. 28

V Foci of Arousal and Dreaming. 29

VI Foci of Arousal and Hypnosis. 33

VII Sleep Theories. 36

VIII Mineral Metabolism and Electrobiologic Processes in Fatigue or Sleep. 41

IX The EEG in Sleep and Wakefulness. 48

X Cortico-autonomic Regulation in Sleep and Wakefulness. 55

XI Sleep and its Connection with Corticovisceral Regulation. 59

XII "Psychosomatic" Medicine. 65

XIII Therapeutic Use of Protracted Sleep. 68

Chapter I

Sleep and Internal Inhibition

by

Rudolf Baumann

The research of I. P. Pavlov, the great Russian physiologist, : at the beginning of the 20th century to revolutionary changes in me(science. In recognizing lawful relationships between living creatu: and their environment, Pavlov laid the foundation of modern medicin(and biology. The theory of higher nervous activity is regarded as l greatest achievement. By means of his dialectic-materialistic meth(based on a synthetic, holistic view of nature, he led physiology an(biology out of the blind alley of strictly analytic methodology. Fr: Engels commented in the "Anti-Dühring" on the analysis-synthesis re: tionship: "The process of thinking consists of both reducing consci(content into separate elements and grouping elements that belong to(into a whole".[1]

Pavlov studied the processes that take place in normal, untrau tized living organisms. His countless experiments and observations which he conducted with greatest accuracy and acumen, revealed that all reactions, or body functions, are determined by environmental influences, that is, by nature surrounding the body. The classic Pavlovian definition reads: "An animal's body is a highly complex s: composed of an infinite number of parts which are not only intercon: but also related as a whole to the environment".[2]

According to Pavlov, an animal's behavior and reactions to env: mental factors depend on the nervous system, the central and domina: role of which he established. After his studies on blood circulati(and digestion, Pavlov turned his attention to the activity of the m(differentiated and complex organ—the brain.

Pavlov himself clearly expressed the goal of his research on h:

[1] Dietz Edition, Berlin 1953, p. 49
[2] Collected Works, Vol. II, p. 452

nervous activity:

"The aim of synthesis is to evaluate the importance of every organ according to its actual function and to show its place and limitations.[3]

"Having worked for several years on the digestive glands, studying their activities carefully and in detail, naturally I could not overlook the so-called psychic stimulation of the salivary glands. It is true for men and hungry animals alike that the sight of food, conversing or even thinking about it causes salivary secretion. This was especially interesting to me since I myself had determined precisely the psychic activation of the gastric glands. I began to investigate the salivary glands with my co-workers. One of them--it was Snarski--took over the task of analyzing the internal mechanism of salivary activation. He used a subjective approach. He assumed that dogs, like humans, have an inner self...and took into consideration their thoughts, feelings and desires. Our understandings of this world differed completely... After long thought, after a spiritual struggle that was not easy, I decided, even on the question of psychic stimulation, to maintain the viewpoint of a true physiologist, that is, of an objective unbiased observer and experimenter whose task is to deal exclusively with external events and their relations."[4]

With this, Pavlov turned away from the prevailing subjective and speculative method of psychology. He was the first man in the history of medicine and biology to study the brain on a purely physiologic basis. In short, his research demonstrated that the organ of "psychic activity" operates on a reflex principle and that the central nervous system with all its subdivisions is one functional unit. The cerebral cortex has a dominant role. An animal interacts with its environment by means of the conditioned reflex, which Pavlov called a "temporary connection". (Tr. quotes)

He said: "A permanent connection between an external agent and the response activity of the animal should rightly be called an unconditioned reflex; a temporary connection, on the other hand, a conditioned reflex"

[3] Pavlov: Collected Works, 1951, Vol. I, p. 574
[4] Pavlov: Collected Works, 1951, Vol. III, p. 13-14

The principle of temporary connections, i.e. of conditioned reflexes, proved to be, as K. M. Bykov put it, a rigorous scientific criterion in analyzing all physiologic processes that take place under normal as well as pathologic conditions. Pavlov became more and more interested in clinical problems toward the end of his research career. Especially while studying neurosis, he became convinced that not only external environmental factors are responsible for behavior or the function of higher nervous activity, but internal factors as well. In a paper, "Physiology of the Hypnotic State in Dogs," he wrote: "Besides the impressive representation of the external world ...there is also a strong representation of the internal world; that is, of the general state and function of organs and tissues, of all internal processes in the body."[6]

Bykov, Pavlov's outstanding pupil, succeeded in proving that temporary connections (conditioned reflexes) are established by means of interoceptors between the viscera and the cortex. The state of the internal organs can therefore govern an organism's behavior in the environment."

Thanks to Pavlov's basic research, we were able to "describe speci nerve structures that assume also the role of sensory organs. These internal 'sensory organs,' like the external sensory organs, work as receptors and analyzers to establish contact between the cortex and the entire internal environment" (Bykov).

Naturally, the deeper Pavlov penetrated the corticovisceral relationship, the more convinced he became that the localistic organo-pathologic theory which had prevailed in medicine since Virchow could not explain pathophysiologic processes. His synthetic approach to physiologic processes and their dependence upon the environment led him to use the same approach with pathologic disturbances as well, especially those of higher nervous functions. His observations and experiments gave him much insight into these disturbances. During his last years of creative work, Pavlov transferred the experience he had gained in the laboratory on the mechanism of neurosis to disturbances of the human nervous system. In addition, he tackled the analysis of neuroses and psychoses (neurasthenia, hysteria, catatonia, schizophrenia et al). Mostly he tried to use, in appropriate doses and

[5] Pavlov: Twenty years of experience, Moscow, Medgiz, 1951, p. 450
[6] Pavlov: Collected Works, Vol III, p. 417

combinations, certain drugs which he had tested on animals with nervous disorders. But he also worked with another new method of treating these disturbances and organic disorders of nervous origin--artificial sleep, or sleep therapy.

Since the purpose of this paper is to study the physiology of sleep and the therapeutic use of the sleep cure in the light of Pavlov's investigations, our first task is to examine the physiologic problems of sleep.

While studying conditioned reflexes, Pavlov solved the "mystery" of sleep, a problem which had preoccupied many research workers before him and which led to many different theories concerning the origin of sleep (to which we shall return later).

The biologic function of conditioned reflexes is shown by the following: "a small number of external stimuli evoking unconditioned, inherited reflexes can, under certain conditions, temporarily unite with countless environmental stimuli as signals for this stimulation" (Bykov).

How capable an animal is of utilizing these environmental phenomena depends upon the phylogenetic stage of development of the individual species. The more highly developed the animal, the more intricate the nervous system, and the more complex the central regulating mechanism. The ability to establish temporary connections with the outer world, to broaden and adapt it to the varied demands of the environment also depends upon how well developed the central nervous system is. In higher animals the cortex is the highest, most finely differentiated portion of the central nervous system. Temporary connections with the environment are conveyed by impulses to the cortex through the sensory organs (analyzers). The main part of this signaling that is, the mechanism of this activity, is a cortical stimulation process. The degree of stimulation depends upon stimulus intensity as well as biologic importance. And these in turn determine the duration and stability of the temporary connections. Therefore, conditioned reflexes arise only when certain environmental criteria are met and only in response to certain visual, auditory, thermal, tactile or other stimuli. When these conditions are modified (change in intensity or loss of biologic importance), these reflexes extinguish, in contrast to permanent connections, represented by unconditioned reflexes. Pavlov found the key to the sleep riddle in the extinction of conditioned reflexes.

It is necessary to examine these observations in greater detail. We all know Pavlov's famous experiment with the salivary glands of a fistulated dog. Pavlov proved that not only direct contact with food caused salivary secretion, but also visual and auditory stimuli preceding the act of eating and associated with it (such as the sound of the attendant's steps, handling of the dog's bowl, sight of the food, etc.). Pavlov went a step further by presenting the food in combination with certain visual, auditory or electric stimuli and completely excluding all other stimuli. After various repetitions, the animal became accustomed to these combination stimuli so that in later tests salivary secretion occurred in response to visual, auditory and electric stimuli. A conditioned reflex was therefore acquired, a temporary connection established which—through the sensory organs—alerted the cortex to expect the ingestion of food and triggered salivary secretion.

During these experiments Pavlov noticed something strange. It often happened that the animals became drowsy or even fell asleep. This behavior always occurred when a conditioned reflex was well established, but the unconditioned stimulus (ingestion of food through the act of eating) did not follow or was delayed. Thereupon, the experiment was revised, and food was given to the animal at certain fixed intervals after the conditioned stimulus. If an animal was then regimented to a 15-30 second interval between the conditioned and the unconditioned stimulus and always received food at the same time, the drowsiness or sleep disappeared. But if the schedule was changed and reinforcement was not provided within the stated interval (the food was presented later), the animal became drowsy and often fell into such a deep sleep that it was difficult to awaken it again. The animal ate reluctantly even though it was 24 hours since the last feeding. If this procedure was repeated (for several days he was fed later than he was originally), the conditioned reactions disappeared gradually, inhibition developed, and in each experiment the animal fell asleep immediately after testing started. This "internal inhibition" set in every time the conditioned stimulus was not followed by the unconditioned stimulus.

At this point I feel it is important to quote Pavlov's own observations:

"Three facts struck us very early. First, some conditioned stimuli are particularly conducive to drowsiness and sleep. Chief among these are: thermal stimuli, application of heat as well as cold

on the skin, mechanical stimuli: light touching or scratching of the skin, etc., and finally, all weak stimuli. The second factor is the period of time the conditioned stimulus is continued before the unconditioned stimulus is applied. Let's assume we are experimenting with a dog which regularly receives food or acid as reinforcement ten seconds after the beginning of the conditioned stimulus. During these ten seconds an extremely strong motor as well as secretory reaction takes place. It is amazing how radically the situation changes if we depart ever so slightly from this procedure. If, for example, the unconditioned stimulus is applied instead of ten, thirty seconds or a minute after the conditioned stimulus, the animal begins to get drowsy during the conditionned stimulus and the conditioned reactions disappear. Whereas the dog had never fallen asleep before in the experimental booth, he does so now every time such a conditioned reflex is first solicited. Thirdly, the development of drowsiness and sleep under these conditions undoubtedly depends on the individual animal, on the type of nervous system.

In the beginning, we approached the problem of sleep from a purely practical viewpoint. It appeared as something hindering our experiments with conditioned reflexes. This led to a most amusing error on our part. Since we endeavored to have in our tests animals in which sleep would be no problem, we selected dogs which were very lively and active by nature, which investigated and reacted to everything. We achieved, however, exactly the opposite result. These dogs fell asleep more readily under the above described conditions. Dogs, on the other hand, which we regarded as "stable" (quiet and not easily distracted) proved to be better suited for our studies because they were able to resist sleep for a very long time.

These sleep-producing conditions led us to raise some scientific questions. What is sleep? What are its characteristics and conditions? What role does it play in our experiments? These problems occupied us theoretically and practically for more than ten years. We tested five or six different hypotheses before finally concluding, as the situation now stands, that sleep and inhibition (which we regard as a stepping stone to a better understanding of the conditioned reflex), "internal" inhibition (in our terminology), are one and the same process... The basic concept is as follows: every more or less protracted stimulation of certain cells in the cerebral hemispheres, regardless of its biologic importance but moreso in the absence of such importance, howsoever strong the stimulus may be, leads sooner or later to drowsiness or sleep. This, however, occurs only when the stimulus is not accompanied by simultaneous stimulation of other cells or is not interchanged

with other stimuli... The conditioned stimulus, impinging on certain cells in the cerebrum, may even be associated with food--and hence with the chief biologic urge--and still lead to sleep, provided it continues for a time, perhaps only a few seconds, alone, without the other simultaneous stimuli accompanying the act of eating. Even an extremely strong electric shock, serving as the conditioned stimulus in this case, is no exception to this rule... Every long, monotonous stimulation leads to drowsiness and sleep...

While continuing this research, we also became interested in another phenomenon. Whenever a new stimulus appears in the animal's environment, whenever any change takes place, in other words, the animal reacts in a general way by turning the receptor organs in that direction (looks up, pricks up its ears, etc.), provided the specific stimulus does not call for a specific reaction. We call this general reaction an orientation or exploratory reflex. If this stimulation is repeated at short intervals or allowed to continue over a long period of time, the exploratory reflex gradually becomes weaker ('process of becoming accustomed,' author) and finally disappears completely. In the absence of other distracting stimuli, the animal gets drowsy and eventually falls asleep. (See note below.)

By repeating this procedure several times, one can produce the induction of sleep with the same accuracy as, for example, the reaction of an alert and hungry dog to a piece of meat... A single, protracted stimulation of certain cells invariably leads to drowsiness and sleep. Most likely, the mechanism underlying this phenomenon, according to what we know about living tissue, can be explained on the basis of exhaustion, especially since normal periodic sleep occurs as a result of exhaustion..."[7]

Author's Note: B. Roth made a similar observation with patients suffering from narcolepsy. As it is known, these patients fall asleep very often even at work. Roth noticed that these patients would temporarily lose their desire to sleep whenever there was a change in environment and they were brought into new surroundings. But once they became accustomed to their new environment (by means of the orientation and exploratory reflexes described by Pavlov), the orientation reflex gradually became weaker and, owing to a lack of new stimuli, the patient succumbed to sleep as before.

(B. Roth: Concerning some general properties of vegetative regulatory functions, with special regard to sleep.) Czech Medical Journal, Vol. XC 1, No. 19

Exhaustion of given cells of the hemispheres arises, as Pavlov explained, from protracted, monotonous stimulation which is not interrupted or replaced by new stimulation. This state of exhaustion, which can therefore lead to fatigue, drowsiness and sleep, should be equated with internal inhibition. It is necessary to define the concepts of inhibition and sleep in greater detail. Pavlov believed[8] that the activity of the cerebral hemispheres, of the entire central nervous system with its excitatory and inhibitory processes, is governed by two basic laws: 1) "the law of irradiation and concentration of each of these processes and 2) the law of reciprocal induction". In cases of simple stimulation these processes spread out from the point of origin With heavier demands, they concentrate and when overstressed, they irradiate again. If the processes concentrate, then "they induce the reverse process in outlying areas during the action as well as at the site of the action after it has terminated"..." If an excitatory process concentrates within the central nervous system, then inhibition is seen as part of the induction process. In negative induction, the focus of concentration of excitation is surrounded to a larger or smaller extent by an inhibitory process. Negative induction occurs with conditioned as well as unconditioned reflexes." The process of positive induction means that the inhibition of the ganglion cell Y, for example,

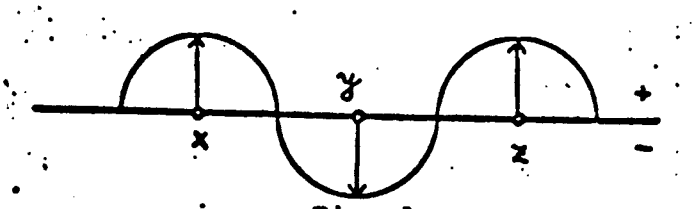


Fig. 1

results in increased excitability of the neighboring ganglion cells X and Z (Fig. 1). Conversely, excitation of one cortical area causes increased inhibition in neighboring areas. This is known as negative induction (Fig. 2).

[7] Pavlov: "Internal Inhibition" of conditioned reflexes and sleep—one and the same process, in I. P. Pavlov Three Treatises on the Activity of the Cerebral Hemispheres from the Years 1922, 1923 and 1925. VEB Verlag Volk und Gesundheit, 1952.

[8] Pavlov: Attempted Physiologic Interpretation of the Symptomatology of Hysteria, Selected Works, 1951, pp. 423-428, Russia.

Pavlov further established that inhibition due to negative induction takes place immediately and is active not only for the duration of the excitation which occasions this negative induction, but may continue for a certain period of time after the excitation has died down.

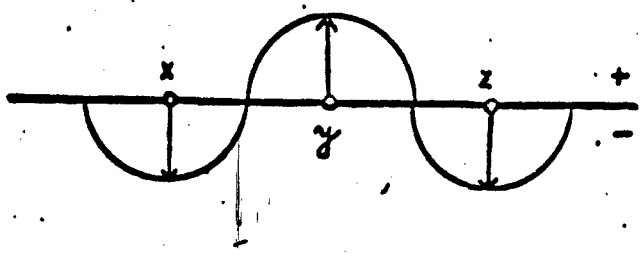


Fig. 2

By the law of negative induction, inhibition is especially dee seated and prolonged when the degree of excitation is related inver to the positive tonus of cortical areas in proximity. Therefore, the stronger the excitatory stimulus and the lower the positive ton of surrounding areas, the more intensive is the role of the inhibit process in negative induction. Pavlov called this inhibition exter passive unconditioned, as opposed to internal active, conditioned inhibition. The purpose of active internal inhibition is to consta update conditioned reflexes, especially "when the conditioned stimu as a signal is not accompanied by the reinforcing stimulus, in some cases temporarily and in others with considerable delay, thereby ho up the whole stimulation process," (when, for example, eating does follow the conditioned stimulus at the usual time, is delayed or is even absent altogether. The author.) This active internal inhibit also appears "when positive conditioned agents are completely cut o segregated and differentiated from the countless negative agents cl by. It arises spontaneously under the conditions just described, increases and grows stronger continuously. It can be reinforced an perfected by training. This inhibition can also form an associatio with any indifferent external stimulus whenever its action coincide with the presence of inhibition in the cortex. This stimulus then begins by itself to trigger an inhibitory process in the cortex. T special cortical inhibition functions along with the conditioned re in adapting the organism to the external environment by constantly analyzing stimuli emanating from this environment."

Pavlov also describes a third form of inhibition. He says the following about it: "All conditions being equal, the effect of the conditoned stimulus is, as a rule, proportional to its intensity, but only up to a certain maximum level (and probably also to a certain minimum). Above this maximum, the effect does not become stronger and may sometimes even become weaker. We say that at this maximum level such a stimulus stops producing excitation and begins to produce inhibition. We view all these phenomena in light of the fact that a given cortical cell has a limited working capacity (that is, of harmless and easily compensated functional destruction)*. With stimuli that might exceed the allowable maximum, this limit is preserved by the rise of inhibition. The higher the stimulus above the allowable maximum, the stronger the inhibition. In this case the effect of stimulation either remains at an acceptable maximum, which is most often the case, or decreases somewhat if the stimulus is too intense. This inhibition could be called above-the-maximum."

If we study the role of these three different kinds of inhibition in the onset of sleep, we find it is not always possible to determine exactly which type of inhibition predominates. Let us review the example which Pavlov gives in connection with sleep induction in dogs: The dog always fell asleep when the unconditioned stimulus did not follow the conditioned stimulus or if the interval for the unconditioned stimulus he was accustomed to was delayed or prolonged. Pavlov pointed out that the conditioned reflex extinguished here because it lost its biologic importance. When the experiment was repeated, only a few seconds of delay were sufficient to cause the animal to fall asleep. The salivary reflex was extinguished as a result of inhibition. At the same time, Pavlov showed that a single, monotonous stimulus which is not interrupted or replaced by new stimuli always produces exhaustion of the stimulated cortical area (inhibition), in this case by means of the metronome, a light or uniform cutaneous, tactile and thermal stimuli, so long as a new stimulus, as represented by the act of eating, does not check or interrupt inhibition. This is an example of active internal conditioned inhibition. Another factor often enters the picture here—negative induction, which appears when a strong excitatory stimulus encounters surrounding cortical regions of weak positive tonus. Whenever a single, protracted stimulus impinges on cortex which has a low positive tonus, in accordance with [the law of] negative induction inhibition arises (external passive unconditioned inhibition). This type of inhibition, still speaking of Pavlov's dog experiments, also depends on

*Trans. Note: i.e., "loss of ability to function" or "deactivation."

the type of nervous system the animal possesses. Pavlov found that highly active, restless dogs with weak nervous systems fall asleep sooner than quiet, well-behaved dogs. The weak nervous system of the former is characterized by the predominance of low positive tonus in the cortex. Pavlov showed that lability and restless, lively behavior actually serve as a defense mechanism to adapt thes animals to their environment. This mechanism prevents the cortex f becoming exhausted too rapidly through high receptivity to constant changing stimuli. The dogs exhibit, therefore, lively, excited, st: reactions. External passive unconditioned inhibition also plays an important part in reaction time while the inhibitory process is for

The third type of inhibition responsible for the onset of slee depends on the working capacity of stimulated cortical cells. In o words, supermaximal stimuli can produce inhibition. This occurs, f example, when the cortex is overtaxed. When working capacity is li this inhibition protects the cortical cell from functional destruct: and thus is able, according to the law of irradiation, to spread fu: over the brain. Another factor which is important for the producti of inhibition or sleep lies in the types of agents which serve as c ditioned stimuli. Thermal and tactile stimuli as well as stimuli w are generally weak and monotonous have a sleep-inducing effect.

In summary, the following factors all play an important role i producing inhibition or sleep:

(1) The conditioned reflex becomes extinct because its biolog: importance is lost;

(2) A single, protracted weak stimulus; (Factors 1) and 2) = active internal inhibition)

(3) Cortical tonus (type of nervous system) when the excitato process concentrates as a result of negative induction; (passive external inhibition)

(4) A supermaximal stimulus which goes beyond the limit of th working capacity [of cortical cells];

(5) The type of agents responsible for inhibition.

Which of the three types of inhibition Pavlov described domina during the onset of sleep is not always clear. On the basis of many

experiments and studies, Pavlov concluded that active internal inhibition plays the chief role in inducing sleep.

Concerning this problem and in particular how active internal inhibition and inhibition created by supermaximal stimulation of a cortical cell of limited working capacity compare to passive external inhibition, Pavlov says:

"The following problem remains unsolved: what is the relation between the latter two types of inhibition and the first universal case of negative induction? If in reality they are only a special variation of the first case, what is this variation and how does it take place in relation to the special properties of the cortex? Probably inhibition which transcends the working capacity limit is closer to external passive inhibition than to internal active inhibition since it, too, arises spontaneously without having to be elaborated and cannot be trained like internal inhibition. Both these cortical inhibitions move and spread over the brain. Many different experiments on the movement of internal inhibition, in fact, have been carried out... While spreading and deepening, internal inhibition no doubt develops various degrees of a hypnotic state. When it spreads downward from the cerebral hemispheres over the brain, it represents normal sleep."

But every internal inhibition does not correspond to sleep as we think of it. Pavlov distinguishes between a partial inhibitory process localized to one or several points (this, if one may say so, represents a sleep process within several restricted areas of the hemisphere) and generalized inhibition which spreads over vast cortico-subcortical areas and through the lower portions of the central nervous system and which is analogous to deep sleep. Partial inhibition arises under the same conditions as generalized inhibition; namely, to repeat it once more, monotonous stimulation that is not relieved or interrupted by new stimulation. However, partial inhibition does not pass immediately into generalized inhibition because, as the law of induction states, every inhibition of one portion of the cortex is accompanied by increased excitation of the surrounding hemisphere.

Consequently, not every inhibition spreads automatically within the hemisphere and continues to involve new cells. This also follows the basic law of nervous activity. Every nervous activity, says Pavlov, is composed of two processes, excitation and inhibition, and life itself consists of the continuous interaction of these indivisible processes. Pavlov proved that excitation as well as inhibition are active,

dynamic processes that can spread, depending on the intensity or pr dominance of either. Following the law of irradiation, the change compared to the norm) in one cortical area spreads to surrounding a provided they are not excited or inhibited by a new stimulus. Let suppose that the uniform, monotonous stimuli which have produced pa inhibition continue undiminished, without any interruption from new or internal stimuli, mainly through the sensory organs. In this ca surrounding areas of the hemisphere will, as a result of increasing tion, fall under this inhibition, and partial inhibition passes int general inhibition. Thus, partial inhibition must always be regard the first stage of general inhibition.

The transition from partial inhibition to general inhibition i gradual. Consequently, there is never an abrupt shift from wakeful to sleep; instead, the phases of fatigue and drowsiness precede actu sleep. We shall discuss the different phases of the sleep state la Pavlov found that sleep is produced by two different mechanisms. H distinguished between active and passive sleep. He says:

"Active sleep originates in the cerebral hemispheres and is ba on a process of active inhibition, arising primarily in the hemisph and spreading from there to the lower portions of the brain. Passi sleep results from the reduction or limitation of stimulating impul which impinge upon the higher parts of the brain (not only the cere hemispheres but also the adjacent subcortical layer). Excitatory impulses can be either external stimuli which reach the brain throu the external receptors or internal stimuli which arise from interna body functions and are relayed to higher parts of the brain from au nomic regulatory centers."

As explained earlier, the sensory organs play a substantial ro in the rise of general inhibition, and therefore of sleep. Speransl and Galkin proved that in a very revealing experiment. These autho totally deprived dogs of their senses of hearing, smell and vision severing the olfactory nerve, the optic nerves and by damaging the cochlea. After this operation the animals fell into a deep sleep which lasted 23 1/2 hours a day, on the average. They woke up only for short periods of time, i.e. when aroused by the need for food, defecation or urination. Only strong stimuli, such as energetic sh produced temporary wakeful states of short duration. However, it w essential in this experiment to operate on all the sensory organs simultaneously. If first one sensory function is removed, another or three months later and the third 2-3 months after that, sleep do not set in. The animal is now, of course, less active and since th loss of sensory organs means he has very little contact with the

environment. When one of the remaining senses, as the sense of touch, for example, is stimulated, the dog becomes immediately more lively. Strümpell reported a similar case of a patient whose sensory organs had been severely injured so that he, as he expressed it, had only two windows to the outer world left; namely, one eye and one ear. When his eye was covered and his ear plugged, the patient inevitably fell asleep. What do the Speranski and Galkin experiments and Strümpell's observation prove? Pavlov commented as follows:

"I think that reasons could be cited which would make it clear that the sleep of dogs, on which the Speranski and Galkin procedure has been performed, is due to inhibition. Moreover, it is an active inhibition that finds itself under extremely favorable conditions since it does not meet any excitatory processes to speak of at this time, any stimuli, in other words. Sleep is greatly facilitated. Why is this so? Because certain areas of the dog's body surface, when the animal is lying down, are continuously stimulated both mechanically and thermally. It is conceivable, therefore, that passive sleep is evoked by continuous, monotonous stimulation of the remaining receptors... The fact must be stressed that there are two kinds of sleep: passive sleep which arises when the majority of stimuli normally reaching the brain are eliminated and active sleep—which, as I understand it, is an inhibitory process since the latter is an active process and not merely a state of inactivity..."

Thus, passive sleep arises, as explained earlier, through extensive exclusion of stimuli from the external environment. It is induced artificially and, unlike active sleep, does not require a state of general physical exhaustion. In the final analysis, of course, in "active" as well as in "passive" sleep active, dynamic processes (as represented by inhibition) are responsible for the sleep process. The key to passive sleep lies, according to Pavlov, in the artificial elimination of external stimuli so that only a few ineffectual monotonous stimuli remain, which then exhaust the hemisphere. "Active" sleep, on the other hand, involves normal exhaustion of the hemisphere. Regarding passive sleep, Pavlov continues:

"We know, and this is a basic fact, that every cell experiencing protracted, monotonous stimulation automatically passes into a state of inhibition. It is therefore possible to regard passive sleep as sleep resulting from inhibition which originates when remaining receptors (let us recall here the dogs deprived of vision, hearing and smell, the Author) are subjected to prolonged, monotonous stimulation. Consequently,

if these dogs are brought into new surroundings, they seem to liven up at first. For example, become wide awake faster, i.e. they remain more alert for a certain length of time.

Here also, as a result of lower tonus and weaker excitatory processes, inhibition present in the hemispheres can spread faster since weak, monotonous stimulations arise and facilitate the inhibitory process."

Why, then, did dogs whose sensory organs were removed one at a time over a long period of time fail to fall into a sleep state? This phenomenon can be explained by the fact that the remaining receptors developed increased sensitivity, as a compensatory reaction, permitting new impulses to reach the cortex again through gradual adaptation to the environment. Sharper orientation and exploratory reflexes due to this increased sensitivity maintained cortical tonus at a level which prevented the animals (although they were less active and less responsive than normal animals) from falling asleep. Impulses relayed by the sensory organs, or exteroceptors, are not solely responsible for the tonic state of the cortex. Impulses transmitted from the inner organs by interoceptors can also influence cortical tonus. After much experimentation, Bykov succeeded in describing the function of the interoreceptors. They, too, are able to form conditioned reflexes. In his writings on higher nervous activity Pavlov explained the interrelationship of cortex and organ systems. He assumed that the inner organs influence cortical tonus and, vice versa cortical tonus influences the inner organs. From this it is obvious that stimuli from the inner organs can disturb, curb and even bring to extinction partial as well as generalized inhibition.

Consequently, first active sleep can set in as a result of normal physiologic exhaustion and fatigue of the hemispheres, which is brough on by the demands placed on and the increase in cortical tonus during work. This state of physiologic exhaustion and fatigue is the result of widely different, complex stimuli which in the wakeful state continuously reach the brain through the exteroceptors of sensory organs and the interoceptors of inner organs. Secondly, passive sleep can develop during the wakeful state without exhaustion in the purely physiologic sense. Whenever stimulation is reduced, mainly from the external environment (sensory organs), the cortex becomes tired and exhausted through protracted, monotonous stimulation of one region, resulting in general (sleep) inhibition. This happens in the absence of physical exhaustion or fatigue. In both cases inhibition arises in the same way. The only difference is that in the first case general physical exhaustion is involved, the type normally experienced after exertion or at the end of the day. In the second case it is specific,

I might add, artificially induced exhaustion, arising from specially controlled stimuli. Naturally, it is impossible to differentiate the physiologic aspect both these exhaustion states for in the case of general exhaustion and fatigue (after the day's activities are over), we usually remove from the environment stimuli which could keep us awake.

When we "go to bed" we darken the room, remove auditory stimuli, and assume a horizontal position in uniform thermal surroundings (warmth of the bed). As we know, inviting sleep is nothing more than subjecting the body to uniform tactile and thermal stimuli. Sleep is more easily induced by protracted, monotonous weak stimuli, such as the sound of falling rain or of a brook, the regular breaking of waves at the seashore, the rustle of trees, the ticking of a clock, quiet, sleepy music or reading a dull book that is not at all stimulating. In addition, there are conditioned reactions that are associated by habit with the onset of sleep, as the customary hour for retiring, the familiar surroundings of a room, one's own bed (as we know, it is usually more difficult to fall asleep in a strange bed), etc.

Pavlov made special studies of the transition from wakefulness to deep sleep. Cortical activity shows definite changes through the various stages of drowsiness to deep sleep. These changes are evident in the conditioned reflexes, or in conditioned stimuli and their dependence upon stages of the inhibitory process. When cortical tonus is normal in the wakeful state, reactions are proportional to stimulus strength, that is, a strong conditioned stimulus causes a relatively strong reaction; a mild conditioned stimulus, on the other hand, produces a mild reaction. In the drowsy state (the first phase of falling asleep), weak and strong conditioned stimuli alike evoke the same reaction. This phase is called the phase of equalization. The next stage is just the reverse. It is characterized by progressive inhibition in which localized inhibition spreads to involve larger areas of the cortex. Under these conditions, Pavlov noticed that a weak conditioned stimulus results in a strong reaction. And a strong conditioned stimulus produces either a mild reaction or none whatsoever. This phase is called the paradoxical phase. New weak stimuli are especially disturbing during this phase of inhibition or sleep. Everyone is familiar with the disturbance caused when someone rustles a newspaper, turns a page or quietly clears his throat, for example. During the paradoxical phase weak auditory stimuli can therefore prevent a person from falling asleep or "chase sleep away" so that it takes a long time to reestablish the transition to sleep. Pavlov also described

the ultra-paradoxical phase, in which a negative conditioned stimulus to which the cortical cells do not react in the wakeful state now produces a reaction. In the narcotic phase the cortex reacts only to relatively strong stimuli. In deepest sleep, on the other hand, there are no responses even to strong conditioned stimuli. Awakening, when not artificially induced, is due to physical unconditioned stimuli which arise during the transition from the assimilatory to the dissimilatory cycle. As we have seen, sleep sets in gradually, which explains why sleep and awakening are not sudden processes. We never fall asleep or wake up suddenly. Instead, these events occur in stages although the speed of falling asleep and awakening differs from individual to individual.

Chapter II

Is There a Sleep Center?

Pavlov's experiments with animals have shown that sleep, as a process related to internal inhibition, depends on the tonus of the cortex, the predominance of inhibitory as opposed to excitatory processes. Ignorance of cortical function and the concept of the absolute autonomy of autonomic centers led most physiologists and clinicians to assume the existence of a regulatory center for sleep and wakefulness. The cortex was believed responsible only for somatic (motor) and psychic functions. This view stemmed mainly from clinical observations of autonomic disturbances accompanying lesions in the mesencephalon and diencephalon. Medical studies of encephalitis epidemica, of which sleep is a well-known symptom, led to the opinion that sleep is regulated by one center most probably located on the border between the mesencephalon and the diencephalon in the retroinfundibular region near the third ventricle. R. W. Hess believed the sleep center to be located in the brain stem because he was able to induce sleep in animals by stimulation of the brain stem with weak electric currents. Morphologic changes in this area also explain the hypersomnia observed in basilar meningitis, tubercular meningitis, syphilis, tumors of the base of the brain and of the mesencephalon and occasionally in multiple sclerosis. Experiments also showed that decerebrate and the anencephalus (Gamper) still undergo periods of sleep and wakefulness.

I regard it necessary to give Pavlov's views of this important question, too. Pavlov states:

"What happens to dogs whose hemispheres have been extirpated? They certainly sleep. This fact is often used as evidence against what I have just said, namely that sleep normally originates in the cerebral hemispheres. But I do not regard this objection as physiologically justified. Since sleep is generalized inhibition and the latter spreads throughout the entire nervous system, it is clear that inhibition has to extend as far as the central nervous system and the nerve fibers themselves. Even after the hemispheres have been removed, why should inhibition not develop in the lower portions of the central nervous system, in either concentrated or irradiated form? This is all the more likely since in dogs some telereceptors are on a lower level—the corpora geniculata (one relating to hearing, and the other to vision)—and since we know that a dog deprived of cerebral hemispheres reacts to visual and auditory stimuli. Conditions are the same, therefore, as

when the hemispheres are intact. Sleep in this case is not exclud but must set in. Since inhibition exists and there is a cell whic becomes exhausted as a result of stimulation and passes over into state of inhibition, then all conditions are present for inhibitio to develop. When the cortex is removed, sleep begins in subcortic regions. Hence we do not see any contradiction here as far as bas facts are concerned, that is, the alternation of excitation and in bition and their concentration and irradiation; since all this can also take place at the lower levels of the central nervous system, why should sleep not develop there as well? I consider these obje tions physiologically unfounded; they do not refute my statement t sleep normally originates in the hemispheres"...

Continuing, Pavlov touches on the subject of encephalitis, th morphologic changes it produces in the hypothalamus, and Hess's experiments.

"Let me say that it is an oversimplification merely to see sl on one hand and hypothalamic changes on the other. This is a very hasty conclusion. I steadfastly maintain that all knowledge we ha to date on cerebral function makes the concept of the hypothalamus as the true sleep center [extremely] doubtful. It is difficult for me to believe that an infectious process within the brain should no have the slightest effect on the most reactive section of the brain the cerebral hemispheres. Surely the toxins do not remain exclusiv in the subcortex without diffusing into the hemispheres. Naturally I realize that bacteria favor certain media and that there are very fine structural differences between such possible regions [in the brain]. It is entirely possible that the process concentrates in the hypothalamus, causing changes in the nerve cells that are visib under the microscope later on. But in the hemispheres these change may be only functional; they may appear simply as decreased excitability of the hemispheres without being microscopically observable. We can assume that pathologico-anatomic changes proceed smoothly from visible changes to purely functional ones and, finally, to invisible ones.*)

*Author's Comment: It is amazing that Pavlov at that time touched upon two extraordinarily important problems in biology:

1) The affinity of certain bacteria for a certain medium,
2) The view, completely inconceivable in those days, that purely functional changes could develop into structural, morphologic changes; these predictions of Pavlov have been confirmed beyor doubt.

"I do not dispute the fact that somnolence occurs in encephalitis and that this condition is related to the hypothalamus; it is, in other words, in conformity with the hypothalamus. But I would interpret this fact in the same way that I did the one Speranski and Galkin brought out... There is no doubt that the hypothalamus is a broad avenue where stimulations from the internal environment, that is, from all our organs, come together. Damage to the hypothalamus robs the cerebral hemispheres of contact with the internal environment, i.e. with the functional state of the organs. This situation is analogous to the one created when the three abovementioned receptors were nullified, i.e. external stimuli were prevented from reaching the hemispheres. Stimuli coming from the internal organs, although we are not aware of them, are responsible for continuous, increased tonus in the hemispheres. The fact that dogs deprived of cerebral hemispheres sleep proves this. Or, let us take a pigeon in which the cerebrum has been removed and which constantly stays motionless and somnolent. As soon as the necessity to eat or to relieve itself occurs, the pigeon wakes up...

"There remains still another very important fact supporting the clinicians in their assumption of a sleep center. I am speaking of Hess's experiments on sleep induction by electric stimulation of certain parts of the brain. I won't deny this fact either. I recognize it and believe it can be demonstrated by repeating Hess' experiments... Hess pointed out that his experiments should settle the issue since the points he used to produce sleep do not coincide with the clinicians' concept of the sleep center. Typical lesions in encephalitis are located in the region of the third ventricle and in its lateral walls, whereas Hess stimulated the lowest part of the brain, near the brain stem. How should we explain this? I must say, there is a difference between the events which take place within the body under normal conditions, as in our case, and events, on the other hand, that take place under pathologic conditions, especially when they are deliberately produced in the laboratory (stimulation of the brain, for example). They are two completely different things. While in the latter case everything can be simplified, in the normal state phenomena become quite complicated. And Hess, who produced a definite state in dogs by stimulating certain points in the brain, admits himself that this could be caused not only by stimulation of cells of an imaginary sleep center but also possibly of centrifugal and centripetal pathways. At the same time he stresses that sleep-producing regions in the brain are very limited.

I now feel justified in asking the following question: isn't this

simply a matter of reflex sleep originating in the brain? We know perfectly well that monotonous stimulation of the skin causes dogs and man to fall into a state of hypnosis and sleep. It is not strang that there are similar stimulations of nerve pathways which can induc sleep... Besides hypnosis brought on by tactile stimuli, which is definitely reflex inhibition caused by monotonous stimulation, hypnos can also be induced verbally. In the laboratory we can make dogs fal asleep by stimulating the skin with weak electric currents. This sle occurs so consistently that after a few experiments sleep becomes a conditioned reflex depending on the site of electrode attachment. Fo example, one needs only to cut the hair here and the dog immediately falls asleep. That shows what effect peripheral stimuli can have...

Hess used faradic current in his experiments. Consequently, thi could be only a very weak stimulation corresponding to that which we produce in the laboratory with weak direct current. We find, therefore, that the Hess experiment, which so convinced the author himself and the clinicians as well, must be questioned. The only explanation is as I have given, the existence of a sleep center being impossible. I would even go so far as to say that the crude idea that there is a group of nerve cells which produce sleep while another group is responsible for wakefulness is physiologically unsound. We are able to observe sleep in all cells; why, therefore, should we regard a special group of cells as the [sole] producer of sleep?

Chapter III

The Importance of Cortical and Cortico-autonomic Regulation in Sleep

As we have seen, Pavlov theorizes at length on the autonomy of visceral regulations and of various centers, including the so-called sleep center. He was first to recognize the important role the cortex, as the highest somatic, vegetative and psychic regulatory center, plays in directing overall body function. In his studies of epilepsy Jackson suspected that the cortex is involved in autonomic function. Mislawski, Bechterew, Barren, Spiegel, Kennart, Bussi and others held similar opinions but were not able to find experimental proof.

Pavlov and his students, mainly Bykov, showed that "the complex functions of the viscera are formed at different cerebral levels. Impulses arising in the cortex act upon adjacent subcortical centers, where the form and intensity of the stimulations reaching the working effector apparatus are determined" (K. M. Bykov).

One might say, therefore, that there are so-called coordination levels in the cerebral hemispheres. The cortex represents the highest level, the control center.

Probably, as Bykov puts it,"a struggle for the ultimate path to be taken by impulses coming from the cortex" develops in the subcortical region, where efferent impulses originate and are relayed on.

The varied, highly complex activity of the internal organs depends upon a variety of receptor fields, with each field connected by means of reflex paths to a number of working organs. These organs are located in different parts of the body and carry out specific functions. Reflex arcs that participate in many, very different reflexes originate in one and the same source. This source is the receptor neuron which connects the receptor field with the central nervous system. In our case it is the vast receptor surface of the cortex. Pavlov considered the entire cortex as the terminal portion of the peripheral receptors... With the skeletal muscles the situation is quite different. Whereas the effector paths leading to the viscera begin in the subcortical formation, the motor cortex, the terminus of receptor paths, has effector paths leading directly to the muscles. Consequently, impulses in the case of visceral activity do not arise in the cortex directly, but in the underlying subcortical ganglia or, to be more accurate, under the

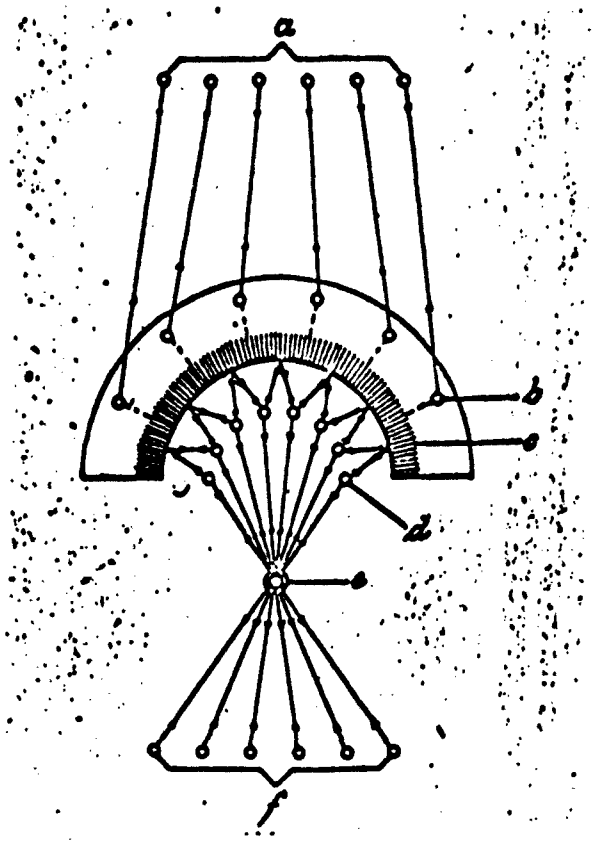


Fig. 3

a) Skeletal muscles.
b) Motor cortex with adjacent skeletal muscle centers.
c) Cortical area excitation and inhibition impulses are collected from and relayed to the internal organs.
d) Intermediate subcortical relay stations where effector paths to organs begin (subcortical ganglia)
e) Visceral relay center in mesencephalon and diencephalon.
f) Interoceptors of internal organs.

Arrows show direction in which impulses are relayed from cortex, subcortex and relay centers to organs and skeletal muscles and vice versa.

influence of subcortical structures. From this point of view, we cannot speak of the representation of a particular organ in the cortex. No cortical area can be regarded as a visceral center which is forever fixed as are the skeletal muscle centers. The connection between the cortex and the internal organs must be regarded as a process which can occur again and again in new combinations and every time create a complex pattern of impulses in the brain, depending upon the various afferent stimulations from the external and 'internal world'".

Bykov states very clearly that the visceral center is under the influence of the cortex and should be regarded merely as a relay and collection center. Thus, the mesencephalon and diencephalon, under the influence of the cortex, control low-order autonomic functions. In a schematic drawing (Fig. 3) I have tried to represent the relation of the cortex to underlying levels (relay stations). The "centers" that are connected to the cortex convey cortical impulses to the internal organs and, on the other hand, collect impulses from the internal organs in order to transmit them to the cortex. Consequently, the visceral relay centers have only relative autonomy, that is, under cortical control they provide constant innervation and are responsible for the status of internal functions. Only under pathologic conditions (loss of cortical function) do these centers become independent.

The Prague physiologist Roth[10] has the following explanation for this: "Under certain pathologic conditions the hypothalamus, through its regulatory, reflex activity is able to maintain internal conditions necessary for life even without cortical support. This is how an anencephalus as well as an animal deprived of its cortex can still live. After decortication life is reduced to purely vegetative existence although the regulation of this function is not so precise as in intact animals... By studying the behavior of dogs and monkeys whose cortex has been removed and observing the behavior of an anencephalus, we find that these animals are not able to adapt autonomic regulatory processes

[9] K. M. Bykov: Grosshirnrinde und innere Organe (The Cerebral Cortex and the Internal Organs) VEB Verlag Volk und Gesundheit, Berlin, 1952.

[10] B. Roth: Über einige allgemeine Eigenschaften der vegetativen Regulation unter besonderer Berücksichtigung des Schlafes (Some General Characteristics of Vegetative Regulation with Special Reference to Sleep) Čas. lék. čes., Vol. XCI, No. 19.

to external environmental conditions. We assume, therefore, that the role of the cortex in autonomic regulation is to modify the function of underlying "levels" of control so that the body displays a unified, integrated reaction to stimuli from the ever-changing environment. Only a very delicate, precise and rapid adaptation equips the body for struggle with the external world. Cortico-autonomic integration accomplishes this with extremely sensitive sensory and cortical association mechanisms always ready to act. Moreover, this integratic provides the capacity for full functional analysis, effective adaptation reactions and, in addition to unconditioned reflexes, the very important conditioned reflexes which enable the body to make very fine discriminatory adjustments to the external environment. This is also true of autonomic functions. A conditioned reflex in which the sight of food causes salivary and gastric secretion is a good example. Its expediency is obvious. However, integration of closely related viscer and somatic functions does not take place exclusively in the cortex bu also in the lower "levels" of the hypothalamus... Whenever the regula ting influence of a higher integrative level is removed, a lower level takes over... If in the cat, for example, all connections from the uterus to the spinal cord are interrupted, spontaneous birth is still possible. Naturally, in these cases control is not so complete as in an intact organ, where low-level regulatory impulses are appropriately modified by higher 'levels'.

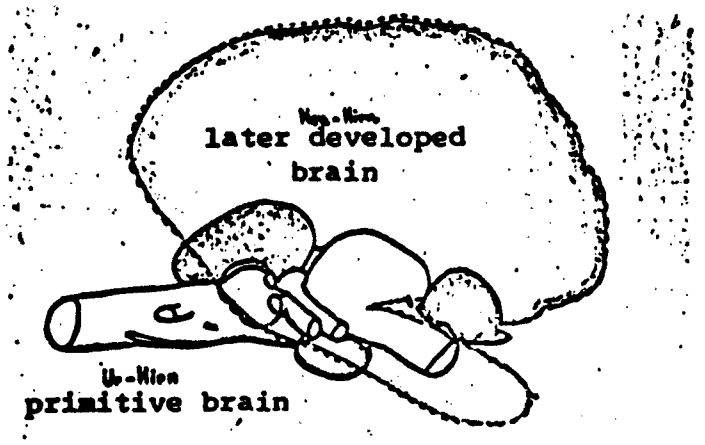


Fig. 4. Human and Animal Hypnosis, F. Völgyesi, Zürich, 1938.

In the process of phylogenetic development encephalization is evident. In other words, the integration of all vital functions has shifted to the newer* portions of the central nervous system. That

*Author's comment: i.e. phylogenetically more recent.

is above all the case with man whose cortex is most highly developed and possesses a greater integrative significance than lower animals."

Several stages of encephalization are shown here. Fig. 4: The ancient brain (paleencephalon) and the new brain (neencephalon). Figs. 5 and 6: Brain of a pigeon and of the human embryo with the system of five cerebral vesicles. Fig. 7: Surface of the dog, horse, and elephant brain showing the development of sulci. Fig. 8: Lateral view of dog brain. Fig. 9: Lateral view of chimpanzee brain.

Phylogenetically speaking, the encephalization of functions in the entire zoological series proceeds in an ascending order from the lower parts of the brain to the highest. It is in the cortex, as the highest stage of development, that the most highly differentiated union of all impulses conveyed through the interoceptors and the exteroceptors takes place.

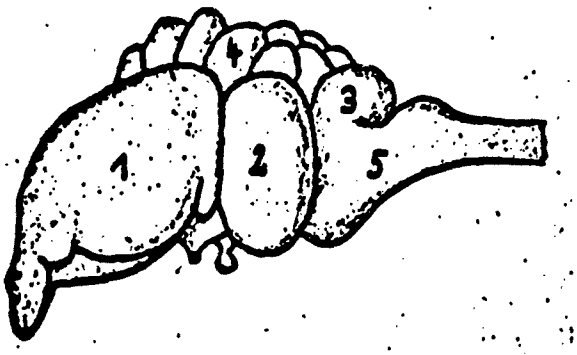


Fig. 5*

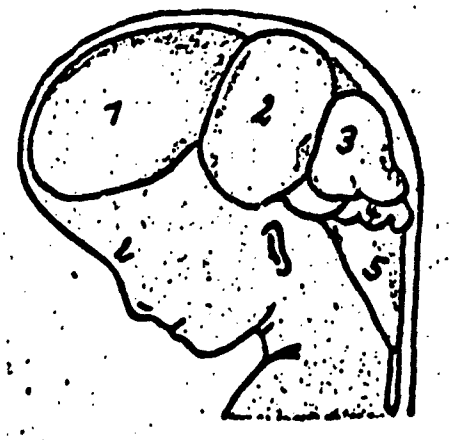


Fig. 6*

*Figs 5 & 6, F. Völgyesi, ibid.

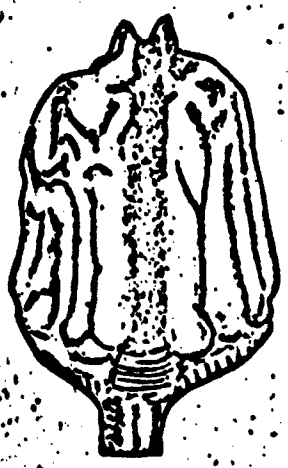


Fig. 7a*

Fig. 7b*

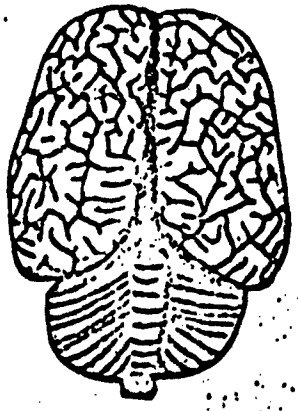


Fig. 7c*

Fig. 8*

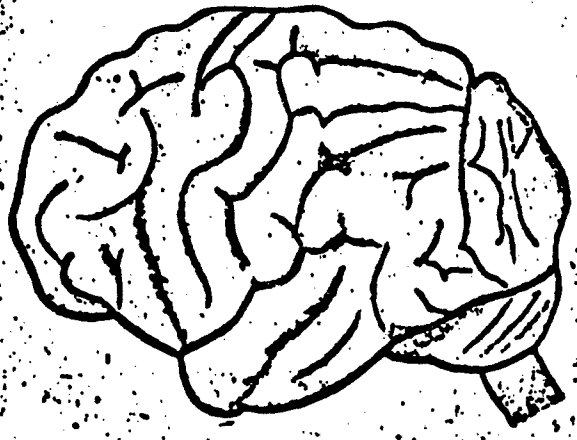


Fig. 9*

*Figs. 7a-9, F. Völgyesi, ibid.

Bykov explains, "the capacity for forming temporary connections is not the property of cortical cells alone. In the lower vertebrates (fishes and amphibia) the diencephalon possesses this capacity, in birds the cerebrum has this function and in mammals this organ is undoubtedly the cerebral cortex... The union of 'animal' as well as 'vegetative' functions takes place in the cortex. As a result, the organism is capable of reacting on an extremely broad scale."

Elsewhere Bykov states that the internal organs are regulated by a mechanism consisting of several layers: "To a limited extent the brain stem first determines the activity of vital functions. The higher portions of the brain, and the cortex in particular, as flexible parts of the mechanism, play the leading role: in determining visceral activity, they are influenced at any one time by a great variety of external influences which act incessantly on the cortex through the exteroceptors... Every complex function e.g. thermoregulation, can be influenced by the cortex on pathways that also serve for other functions, as the polypnea reaction, for example. It is therefore difficult to decide, when a particular area in the cortex is destroyed, just exactly which part of the entire functional complex is affected by the resulting disturbance of cortical activity or of underlying centers connected with the cortex".

We have been discussing the integrative ability of the cortex. Essentially, the cortex controls all lower portions of the central nervous system, adapting them to needs created by ever-changing environmental conditions.

The role the cortex plays in man's differential adaptation to the external environment is evident in the sleep and wakefulness rhythm of decerebrate animals and of the human anencephalus. Gamper has described the behavior of decerebrate animals. Although these animals also alternate between sleep and wakefulness, their sleep period is completely independent of the day-night cycle (or a light-dark cycle) as well as of any other environmental stimuli. A similar situation exists with human newborns in whom encephalization is not yet complete.

In decerebrate animals and the anencephalus, therefore, adaptation to the external environment is more primitive and less adequate as far as the necessities of life are concerned. These animals lack the ability to adapt their sleep habits to the demands of maintaining life in a constantly changing environment. Not only does the sleep and wakefulness rhythm appear to be uncoordinated and lacking in

purpose, but the sleep and wakeful states themselves contradict biologic needs, that is, there is a change in the quality of sleep. The animals cannot be easily aroused; as the Speranski and Galkin experiments showed, only strong stimuli are effective here. In the wakeful state they often exhibit a hyperexcitability which is completely unwarranted in view of their needs at the time. Decorticate animals adapt to the environment by means of the highest portions of the nervous system which are still intact, as we observed in animals whose cortex had been experimentally removed. Thus, the intact cortex is capable, by means of the conditioned reflexes, chiefly the so-called orientation and exploratory reflexes, to adapt the sleep a wakefulness pattern to the internal needs of the body through both the exteroreceptors and the interoreceptors, and to control it accordingly.

Chapter IV

Acquired Conditioned Sleep Reflexes and Foci of Arousal

Every person, I would say, acquires during his lifetime certain transitory [conditioned] sleep and waking reflexes which are peculiar to him. We are aware, for example, that a particular position in bed, familiar surroundings and known temperature conditions, all greatly contribute to the sleep rhythm of every individual.

When these environmental conditions are suddenly changed, sleep is delayed and a person finally falls asleep due to new orientation reflexes. Cortical adaptation is so great that man, for example, can sleep surrounded by loud noises yet be quickly aroused by an auditory stimulus which, based on his experience, is biologically very important. We know that a mother can be awakened by her child's faintest whimper while other common stimuli such as street noise, a thunderstorm, etc., do not interrupt her sleep. The same can be said of the organically conditioned arousal stimuli due to interoceptors. A person acquires these during his lifetime by experiencing and "learning" their importance.

The adult can control his kidney function reflexes during sleep to such an extent that if he is aroused by the physical stimulus his sleep is interrupted. Infants, however, have no control over their kidney function because of deficient encephalization. Special precautionary measures must be taken to prevent infants and small children from falling out of bed. The adult, on the other hand, has learned to lie on the bed without falling during deepest sleep even when the space is limited. This demonstrates that in spite of [sensory] unconsciousness man can react during sleep to critical expectation stimuli since in limited areas of the brain consciousness remains active even when he sleeps. Pavlov explained this phenomenon by saying that during the delicate process of adaptation by the cortex to environmental factors, isolated foci are not affected by the general inhibition present during sleep.

Consequently, these foci have a "watch-duty" function. [Trans. note: based on Pavlov's "watch-duty" theory]. When a conditioned reflex is evoked by a critical stimulus, inhibition is then immediately suppressed by the appropriate focus. Under these conditions excitation predominates and the person awakens.

Chapter V

Foci of Arousal and Dreaming

It is perhaps possible that these so-called foci of arousal are not affected by generalized inhibition hold the key to the p of dreaming. Throughout the history of mankind dreaming has ret a veil of mystery. In the history of ancient civilizations ther many references to the observation and interpretation of dreamin found in Egyptian hieroglyphics as well as in Greek mythology. Kerenyi has written a book on divine sleep and A. Mäder on templ and modern psychotherapy. Both authors mention that already aro 500 B.C. sleeping was used as a healing therapy in the sanctuary Asklepios [Lat.: Aesculapius] near [the city of] Epidaurus on th of Cos*. The healing of the patients was attributed to the drea was believed that they were inspired by Asklepios, i.e. to be hi and his message. The patient was asked to lie in a dark, underg room, removed from auditory and visual stimuli. He then fell as most probably, by means of autosuggestion. In some cases, sleep to the healing dream which was undoubtedly due to the limited fo arousal in the brain. It is obvious that the interpretation of dreams and the many resulting cures were based on mythology.

How can we now analyze dreaming on the basis of the Pavlovi school of thought? We mentioned earlier the possible presence o "foci of arousal", namely noninhibited areas of the brain, which not affected by generalized inhibition during sleep. When in a discussion [following a lecture] Pavlov was asked to explain, on basis of his theory of inhibition, sleep in which dreams occur, answered as follows: "Sleep is an inhibition which gradually an spreads to the lower levels of the brain. It is comprehensible, fore, that when sleep or fatigue begin to set in, the highest po

*Trans. Note: Temples were erected to Asklepios in many parts o Greece, near healing springs or on high mountains. The practice sleeping in these sanctuaries was very common, it being supposed the god effected cures or prescribed remedies to the sick in dre All who were healed offered sacrifice (especially 1 cock), and m tablets, recording their names, their diseases and the manner in they had been cured, have been discovered at Epidaurus the god's famous shrine.

For additional information reference Walter A. Jayne, M.D., The H Gods of Ancient Civilizations, 1962, p. 276.

of the cerebral hemispheres which controls verbal activity* becomes inhibited first, since we constantly operate with words. To this can be added that the inhibitory process is brought about by external and internal stimuli. One of the internal stimuli of inhibition is the humoral element, consequently, some by-products of cellular chemistry which evoke this inhibition. On the other hand, the external inhibitory stimuli are primarily monotonous and weak. It is obvious that, during the day, you and I perform with the highest portion of our brain - the higher cortical activity which controls our verbal function. Fatigue brings about inhibition and this portion becomes inactive. In addition to this verbal function of the hemispheres there is a function we share with animals and which I call the first signalling system** i.e. the perception of sensations produced by

*Author's comment: Speech, thought and consciousness processes, termed by Pavlov as the second signalling system, corresponding to the latest phylogenetic stage of evolution.

**Author's comment: The temporary connections or conditioned reflexes which inform the animals about environmental factors through the sensory organs, are termed by Pavlov as the first signalling system. The more highly developed the CNS became the greater the differentiation of this signalling system in phylogeny. The senses of seeing, hearing, smell, touch, etc. have enabled animals to meet the challenge of the environment. Search for food, reproduction, etc. represent a valuable reenforcement of permanent connections or unconditioned reflexes based on the experiences acquired through the temporary connections or conditioned reflexes. In addition to the first signalling system, in man evolved also a second signalling system: speech, which developed along with the most recent and highly differentiated region in the cerebral cortex. This second signalling system, linked to the ideational process through speech, has given man a highly differentiated adjustment to the environment by means of the "word reflex", i.e., the conditioned stimulus which is associated with words and their meaning as learned through experience. By means of this second signalling system and due to the degree of its evolution man is able to adapt himself in every way to the environment.

all incoming stimuli*. It is quite clear that when we are alert, function inhibits the first signalling system. Consequently, whe are alert (except for artists, an unusual group of individuals) a speak, we never imagine (visualize) the objects we designate by w I have closed my eyes and am thinking about a person sitting here front of me, but I do not see him in my thoughts. Why? Because excitation of the higher portion in the brain inhibits the lower portion. Consequently, when sleep sets in and embraces only the portion of the hemispheres, the adjacent lower portion, bearing a relation to sensations, prevails and is responsible for individua dreams. When the "pressure" from above is absent, there is a cer degree of freedom. A new fact, known to us physiologists, must b added here, namely, positive induction. When one area becomes in another, on the contrary, becomes excited. If we accept this, i. assume positive induction, dreams come into a clearer focus".

To analyze dreaming in greater detail would extend our topic beyond its framework. It should be mentioned, however, that exte and internal, unconditioned as well as conditioned stimuli can substantially influence dreaming. As is known, dreams are not rul by the logical laws of an ideational process. They are prevalentl uncoordinated and caused by different impulses which at times inv the cortex and the subcortex. A certain amount of urine in the bladder, gastrointestinal tonus, meteorism as well as certain circ tory conditions, etc., can, therefore, bring on dreams. Retograd memory, however, has no recollection of them, although they are th underlying cause of the content of the dream. We also know that external stimuli, be they auditory, thermic, tactile or other, can cause dreaming. It is interesting to know that a certain position of the body, or better, similar or equal stimuli of the internal o external environment can cause a repetition of the dream [patterns It is a known fact that when some persons run high fever they repeatedly see the same dream. The same is true in the case of some external stimuli or of a specific psychic state - recurring nightmares because of final examinations, professional difficultie etc. Here, however, the dream [patterns] can reoccur after an

*Author's comment: Sensory organs, food reflexes, orientation ref etc., are termed as the first signalling system, corresponding to earlier phylogenetic stage of evolution.

interval of several years.

Undoubtedly dreaming is associated with temporary connections or a conditioned reflex. The content of the dream is probably influenced by the summation of the exogenous or the endogenous stimuli. Since the knowledge of the ideational process during wakefulness, i.e., during [sensory] consciousness, is still incomplete, it is difficult to give an exact explanation of the occurrence and the process of dreams. Auditory or visual phenomena often prevail in the dream. This, of course, depends on whether the dreamer is predominantly an auditory or a visual learner. Unusual color combinations and odd sounds in "musical" dreams define the psychic mood which can be euphoric or depressive. Humoral, endocrine and nervous factors, which cause definite impulses in the cortex and subcortex, are also very important. Moreover, intrapsychic conflicts or suppressed complexes can also influence some dreams. [Sensory] consciousness is to a lesser or greater degree curbed during a dream. The ability to criticize, i.e. the critical judgment and evaluation of the dream is highly inhibited, although some individuals are aware during the dream that they are dreaming. The dream occurs mainly in a state of [sensory] "unconsciousness". The ability to remember dreams differs greatly from individual to individual. Retrograde amnesia of the dream is often observed upon awakening. Some persons, however, remember their dreams relatively well and are able to reconstruct them. Dreams frequently can cause also motor reactions which are observed mainly in sleep walkers whose movements are very exact and perfectly coordinated. Somnambulists are only partially asleep, and a limited area within the uninhibited brain is responsible for their movements. Many persons have the tendency to talk in their sleep, whereby the innervation of the larynx as well as of the tongue and labial muscles is normal.

Chapter VI

Foci of Arousal and Hypnosis

In the previous chapter we discussed the foci of arousal pre natural sleep and also in dreaming. We shall now turn to the rel phenomenon of hypnosis, which also could be described as "partial Basically, the physiologic process is the same in hypnosis and i natural sleep. It differs in gradation only. Pavlov stated that sleep is partial (not total) sleep, spreading from a given point cerebral hemisphere. He cites a very interesting experiment wit which slept continuously after three of his sensory organs were i Yet this dog could be awakened by stimulation of the remaining re in the skin. He then could be led to the laboratory and placed c experimental stand, where tests revealed that his condition was a to a hypnotic one. In this dog, only one reflex could be evoked; impossible to simultaneously evoke two, three or four reflexes i would easily be possible with normal animals. Pavlov explained t observation in the following way: the tonus of the cortex, i.e., effective excitatory potential of the entire cortex is so low tha concentration takes place at one point, the remaining cortical ar depleted of excitability, thus making it impossible for additions to provoke reaction.

Pavlov's concept of hypnosis correlates with [the observatio in] this experiment. He said:"The hemispheres are not totally emb inhibition. There are some remaining areas in which excitation c When the hypnotizer gives his instructions, concentration takes p a given point and the hypnotized subject then carries out the com All other areas are absolutely immune to other stimuli; when the resumes normal waking state, the effect of the suggestion as an i stimulus is eliminated. In summation: hypnosis is not total, but sleep. This is the difference between hypnotic and natural sleep

Natural sleep is a general inhibition of the cerebral hemisp excluding only those areas which act as "alert centers" [foci of Hypnosis is partial inhibition, limited to a restricted area, wit other areas remaining in waking state. When hypnosis with its sl process of sleep induction is used to bring about general, normal sleep, the identical process takes place as the one already descr concerning transformation from localized to general inhibition.

sleep, originally localized in a small area, gradually irradiates until it embraces not only the hemispheres, but also the subcortex. The same phases are known in hypnosis (depending on its intensity) as already described in the analysis of the phases of sleep: the phase of equalization, the paradoxical phase, the ultra-paradoxical phase and the narcotic phase. In hypnosis, these phases are termed hypnotic phases. Their slower pace differentiates them from the transitory phases in sleep. Depending upon degree of intensity, hypnosis can be suspended at any of these phases.

In hypnosis, the noninhibited areas are mediated in man not only through the first signaling system (sensory organs) as in animals, but also, and predominantly so, through the second signaling system (speech, etc.). Pavlov stated: "To man, the word is as much of a true conditional stimulus as all those he also has in common with the animal, but the word is so polyvalent that it neither quantitatively nor qualitatively compares to the restricted stimuli applicable to animals. All vital activity of adult man is connected through the word with all exogenous and endogenous stimuli reaching the cerebral cortex. The word can convey all stimuli, the word can represent all stimuli; and therefore it can effect all of the organism's functions and reactions provoked by such stimuli."[12]

In addition, Pavlov offered the following explanation in regard to suggestion or autosuggestion:

"It [suggestion or autosuggestion] is concentrated stimulation at a given point or portion of the cerebral hemispheres by a particular excitation, sensation or a trace thereof, effecting (either by emotion or by subcortical stimulation) a concept which assumes predominant, irregular and overriding significance through association. It [suggestion or autosuggestion] exists and operates, i.e., it activates this or that motoric function without being based on association, i.e., on connection with past and present excitations, sensations and conceptions. That would constitute a powerful mental process such as would occur in a normal strong cortex. Instead, the working method of suggestion [and autosuggestion] is based on the simultaneous co-effect of negative induction, which separates it and isolates it from all unrelated influences. This is also the principle of post-therapeutic suggestion. In hypnosis we have, due to irradiated inhibition, a weak positive tonus in a healthy and strong cortex. When the hypnotizer's verbal instruction

[12] Platnov, K.I. Suggestion und Hypnose im Lichte der Lehre I.P. Pavlov's (Suggestion and hypnosis as advanced by I.P. Pavlov) Zeitschr. Ärztl. Fortb

falls on a given point of such a cortex, this stimulation will conce the excitation process at that given point and is immediately accomp by negative induction which, due to the minimal degree of resistance, irradiates over the entire cortex; therefore the word, the order, em completely isolated from all other influences and remains even after subject's return to waking state as an absolute, determining factor.'

Discussions of particular details pertaining to hypnosis are be the framework of this book. The hypnotizability of the different typ of nervous systems will be discussed in detail in the second part of Chapter XIII.

[13] Practical Knowledge Gained during Twenty Years of Objective Studie of Higher Nervous Activity in Animals, p. 590, 1938.

Chapter VII

Sleep Theories

We dealt in the previous chapters with the development of sleep, which is based on the fundamental law of nervous activity: the interrelationship of excitation and inhibition. It is this constant interchange which controls nervous activity. Pavlov was able to prove, that in the untraumatized central nervous system inhibition irradiates from the cerebral cortex as the highest center to the lower parts of the central nervous system. As we have seen, predominance of inhibition causes a cortical tonus decrease, as is characteristic of sleep. On the other hand, predominance of excitation causes an increase in tonus, as is characteristic of wakefulness. The fundamental law of the nervous process, which is based on the incessant interchange between excitation and inhibition, is, as Pavlov emphatically stated, inconceivable "without [presupposing] a special mediating element as part of the cellular chemical process." Regarding sleep, Pavlov explained:

"This condition of inactivity [inhibition] which arises in a given cell irradiates until it embraces not only the hemispheres, but even the lower brain sections. In other words: a working cell's exhaustion will spread to resting cells. This process still remains a mysterious phenomenon. One must admit to the presence of a special physicochemico process within the cells which, when initiated by the exhaustion of a working cell will stop all activity in this particular cell in order to prevent overtaxation. Moreover, this process will also involve surrounding cells which had not been exhausted by work... This indicates the existence of a humoral factor, i.e., some metabolic product which causes this suppression."

The nature of this chemical substance (or of this humoral factor) has not yet been determined. In Chapters I and II we presented the basic law of generalized inhibition of sleep as proven by Pavlov, and we explained that (according to Pavlov's research) there cannot be an actual sleep center. Let us now discuss the different sleep theories as well as the questions raised on the chemical aspect of drowsiness and sleep, which has been the object of so many research projects.

Kleitman and Camill[14] assumed that sleep ensues when weaker or fewer stimuli reach the cerebrum, whereas wakefulness can be sustained by increasing the afferent impulses relayed primarily by cutaneous, but also by internal sensory receptors. This theory is based to a certain extent on Pavlov's research, but it remains incomplete and superficial. Heubel[15] tried to explain sleep as being induced by interruption or cessation of sensory stimulation. Mautner[16] believed that a fatigue edema in the regions of the tegmentum and aquaeductus cerebri is responsible for sleep by blocking the stimulus path, thereby causing sleep to ensue. More widespread was the opinion that a circulatory change in the brain, i.e., a variation in oxygen supply, causes sleep. This seemed logical in view of the observations on patients with cerebrocirculatory disorders, cerebral anemia or cerebral ischemia, accompanied by symptoms of dimming or loss of consciousness or of syncope. We know that oxygen deficiency reduces cerebral function. This led Bernard and Mosso to believe that deficient cerebral circulation is the underlying cause of sleep. They reasoned that reduced cerebral circulation, which we find during normal and pathologic shifts in blood distribution throughout the body, must be the initiator of the sleep process.

The rapid progress in chemical science moved physiologic chemistry into the interest sphere of medical research and brought with it the temptation to seek clarification of the sleep process by means of a strictly chemical approach. Weichardt[17] and Piéron[18] supported the conception that the accumulation of metabolic wastes, produced in the dissimilation phase, is the initiator of the fatigue process. Piéron spoke of hypnotoxins as fatigue or sleep toxins.

[14] Studies on the Physiology of Sleep. VI. The Behavior of Decorticate Dogs. Amer. J. Physiol. 100, (1932) 474.

[15] Pflüger's Archiv 14, 1877.

[16] Wien. klin. Wochenschr. 1910, Nr. 22.

[17] Über Ermüdungsstoffe (Fatigue substances), Stuttgart 1910, Enke.

[18] Le problème physiologique du sommeil (The physiologic process in sleep), Paris 1913.

In recent times it was chiefly Kroll[19] who believed that sleep-inducing substances could be obtained from the brain extract of sleeping animals. He was convinced that the brain produces sleep-sustaining humoral substances during sleep. Kornmüller[20] believed in the existence of a specific sleep hormone; Scharrer and Gaupp Jr. were of the opinion that this sleep hormone is formed in the secretory cells of the hypothalamus[21].

Salmon advanced the theory of three elements being decisive in the physiology of sleep. In his opinion, the waking state is sustained by psycho-affective stimuli proceeding from the cerebral cortex and being transmitted to nuclei in the infundibulum. He regards the infundibulum as a waking center which together with the cerebral cortex stimulates metabolism. On the other hand, he presumes that antagonistically functioning secretion products of the hypophysis initiate sleep.

Friede[22] stated that defined, restricted sulcal fields in the walls of the third and fourth ventricle facilitate the interchange between cerebrospinal fluid and nuclei and that the fluid contains a humoral substance which produces sleep. Zondeck[23] was of the opinion that the hypophysis releases a bromine-containing substance of sleep-inducing efficacy into the blood stream. Ivy and Schneedorf[24] believed that hypnotoxins contained in the cerebrospinal fluid of tired animals are capable of producing sleep. In their experiments, they obtained cerebrospinal fluid from animals which had been worked into a state of exhaustion, and they injected this fluid into the ventricles of dogs. These dogs fell asleep after the injection. However, this experiment did not prove valid, inasmuch as the same results could be obtained by using cerebrospinal fluid from untired animals. This fact led to the assumption that increase in fluid pressure as such must be the decisive factor. The extent of the role which pressure increase in the cerebral ventricles plays in fatigue and sleep conditions has not yet been determined. We know that with acute

[19] Gibt es einen humoralen Schlafstoff im Schlafhirn? (Is there a humoral sleep substance in the brain during sleep?), Dtsch. med. Wochenschr. 1952, Nr. 27/28.

[20] Dtsch. med. Wochenschr. 75, 1950

[21] Cited in Kroll, Dtsch. med. Wochenschr., 1952, Nr. 27/28.

[22] Akta neuroveget. II, 1-2, 1951 and II, 3-4, 1951.

[23] H. Zondeck und A. Bier, Klin. Wochenschr. 1932, 759-760.

[24] An examination of the hypnotoxine theory of sleep. Amer. J. Physiol., 1925, 1939.

pressure increase (especially in the third ventricle), for instance, du ventriculography or during hemorrhage, sle p or loss of consciousness c occur. F ture research might reveal the widely suspected existence of specific "sleep substance" in hibernating animals.

Birkhäuser, Pighini, Nachmannsohn and others attempted to substant the theory of fatigue substances with their experiments. They ascertai: that certain portions of the brain show a definite cholinesterase conte especially high in the region of the putamen and the nucleus caudatus, lower in the globus pallidus and lower yet in the thalamus opticus and : the cortex.

The white matter showed the lowest cholinesterase content. It was therefore suspected that a certain function can be attributed to the am of cholinesterase present in portions of the brain which serve as relay centers for afferent impulses.

Weber[25] determined the cholinesterase content in different brain regions in patients suffering organic CNS diseases. The most striking result of these tests was the revelation that no appreciable amount of cholinesterase could be detected in the putamen, globus pallidus and nucleus ruber of patients with postencephalitic Parkinson's disease. This led him to the conclusion that chemico-enzymatic disturbances play an essential part in clinical symptomatology. Weber suspected lack of cholinesterase in the basal ganglia to effect elimination of inhibition, thus enabling the afferent impulses to pass these relay centers unchecke thereby producing hyperkinetic symptoms.

The nature of this specific metabolic product has not yet been determined, nor is it known which humoral factor emerges in the course of the inhibition process. It is conceivable that the so-called "fatigu or sleep substances", which develop through cellular exhaustion and may spread to other cells, could be the chemical link in the inhibition proc which leads to a cortical tonus decrease. But this would, in my opinion

25
Zum Cholinesterasegehalt des Gehirns bei Gehirntumoren und bei Parkinsonismus (Cholinesterase content of the brain in the presence of brain tumors and in Parkinson's disease) Bull. Schweiz. Akad. Med. Wis April 1952.

suggest that on the other hand a tonus increase should be attributed to a specific excitatory agent of anabolism.

From the physiologic point of view, I consider it debatable and too restricting to think in terms of specific sleep or excitatory substances. The complex metabolic process with its assimilation and dissimilation phases [anabolism and catabolism] is not that simple; nor can the functions of higher nervous activity be evaluated apart from hormonal, humoral and mineral metabolism. Hormone-metabolic disorders are clinically known to produce tendencies toward hypersomnia. I call to your mind the sometimes severe comatose conditions occurring with idiopathic or symptomatic hypoglycemia, brought on by (variously caused) overproduction of insulin. We also know of the symptoms of drowsiness or sleep associated with addisonism or Addison's disease. Here, too, mineral metabolic disorders play a part which will be discussed later.

Chapter VIII

Mineral Metabolism and Electrobiologic Processes in Fatigue or Sleep

Studies of mineral metabolic changes (chiefly by Eppinger and his school) revealed that extensive transmineralization takes place under fatigue conditions.[26] K ions, PO_4 and Ca ions pass from muscle fibers, nerve and hepatic cells into blood and connective tissue, whereas Na and Cl ions pass from blood and connective tissue into muscle fibers, nerve and hepatic cells. The theory of attributing inhibited or reduce glycogen resynthesis in skeletal and cardiac muscle and in the liver to a potassium loss in fatigued muscle is not new. Eppinger observed tran mineralization in rats and dogs, chiefly.

Mineral Values in Controls and in Rats Fatigued by Running

Organs	Controls						Fatigued						
	No. of animals	K mg %	Na mg %	Ca mg %	Cl mg %	K/Na	No. of animals	K mg %	Na mg %	Ca mg %	Cl mg %	K/Na	Duration of running
Muscle...	20	439	109	11	40	2.38	31	439	117	12	35	2.09	
Heart....	29	411	125	11	—	1.94	31	394	142	10.0	—	1.64	
Liver....	29	428	99	8	69	2.55	31	350	117	9.0	60	1.76	Hc

Fig. 10

It is important to note that not only potassium but also phosphoru decreases in the muscles during work. Similar to glycogen, lactacidoge (the glucose phosphoric acid) is broken down into lactic acid and phosp salts, and a decrease in organically fixed phosphoric acid occurs. Inversely, during the phosphorylation process phosphoric acid, bound again to glycogen, is transformed during rest into lactacidogen. Durin

[26] H. Eppinger, Ermüdung, Entzündung und Tod (Exhaustion, inflammation and death) Zeitschr. klin. Med., Vol. 102.
H. Kaunitz und L. Meltzer, Veränderungen des Sauerstoffverbrauchs und des Mineralstoffwechsels der Leber bei Ermüdung (Hepatic changes in oxygen consumption and in mineral metabolism during fatigue).

fatigue or exhaustion, the assimilation phase (relative vagotonia) prevails just as in sleep, and a relative potassium increase occurs in the blood serum. The potassium-calcium ratio, normally 2:1=2, shifts, rising above 2, as compared to below 2 in the dissimilation phase (relative sympthicotonia).

Jesserer directed attention to this shift in ion balance. The migration of K ions from muscles and liver increases the blood serum's potassium content. It is known that normally [in the waking state] cerebral potassium content is relatively high; but only further research will reveal if it decreases during fatigue and sleep. These ion shifts through transmineralization can be regarded as electrobiologic processes based on the electrostatic potential difference between the parenchymal cells and the blood. According to Keller, blood plasma is negatively charged and the parenchymal cells positively with a differential of approx. 50 mV. According to Müller[27], the substantial difference between visceral cells and blood plasma (in concentration of potassium and phosphoric acid on one hand and of sodium chloride on the other) indicates the important part electrobiologic forces play in the maintenance of the vital metabolic shifts and therefore in all vital functions. By this we mean a high Na content in blood plasma and high K and PO_4 content in parenchymal cells. Death, severe illness and inflammation as well as exhaustion will cause migration of K and PO_4 from muscle and liver cells and an inflow of Na, C_ℓ and H_2O into the muscle cells through the cell membrane. This osmotic equalization of the mineral content between blood serum and parenchymal cells reduces the electric potential difference. The diffusion of H_2O into the fatigued muscles causes an increase in their volume. The selective permeability of the cell membrane is affected, resulting in transmineralization. This is comparable with Eppinger's findings in the case of serous inflammation.

During the recovery Na and C_ℓ ions flow from muscles, parenchymal and nerve cells into connective tissue, blood serum and myelin sheaths, whereas K, PO_3-O and Ca ions travel in the opposite direction.

[27] L. R. Müller: Über den Schlaf (On the subject of sleep), Urban und Schwarzenberg, Berlin-Munich 1948.

Ion Exchange

Schematic Illustration of ion shifts during sleep and wakefulne

Positive storage site				Negative storage site
Muscles Liver Pancreas Adrenal cortex Erythrocytes Nerve cells and fibers	Charge	Calcium Potassium group	Discharge	Blood serum Lymph Cerebrospina Mucous membr digestive t Nerve sheath
	Sleep	Tissue substances	Wakefulness	
	Recovery		Activity	
	Discharge	Sodium group Body-fluid salt	Charge	
	Wakefulness	Water	Sleep	
	Fatigue		Recovery	

Ion Movements in Sleep
(Charge of potential energy = recovery)

Neuromuscular substance Liver Erythrocytes	Calcium, Potassium Tissue substances Sodium group Body-fluid salt	Blood serum Lymph Mucous membrane Cartilage

Ion Movements during Wakefulness
(Discharge of potential energy = mental and physical activity)

Neuromuscular substance Liver Adrenal cortex Pancreas	Calcium, Potassium Tissue Sodium group Body-fluid salt, water	Blood plasma Lymph Cerebrospinal fluid

Fig. 11

Tests by Vallace, Oven, Eppinger, Keller and others proved that in the recovery phase of sleep the "tissue substances" of the potassium group pass back into the muscles, blood corpuscles and nerves, whereas the sodium group travels in the opposite direction. Thus, potential energy is stored during the recovery phase and is supplied to the body through oxydation of nutriments. Reduction in oxygen decreases the electric potential.[28]

Concerning the change in electro potential, Müller was of the opinion that "potassium accumulation and sodium deficiency in hepatic, muscle and nerve cells bring about a positive charge, whereas the negative charge in blood serum, lymph and nerve sheaths must be attributed to a sodium accumulation. The bioelectric tensions which trigger nervous, muscular and glandular activity are created by the difference in ion concentrations between blood serum and parenchymal cells".

This leads us to the dis ussion of Bykov's classic experiments concerning the influence of : nervation on cell permeability. This research was based on his conviction "that cell metabolism, excitability, colloidal condition and membrane permeability all partake in a process not yet fully understood, but best described as dynamics of cellular life".

After Bykov had determined nervous and neurohumoral influences on metabolism, he concerned himself with "the nature of the influences which change internal cellular life". He investigated the possibility "of cerebral influence on cellular membrane permeability".

At this point, Bykov was more concerned with the question of whether permeability changes could be effected by impulses originating in the cerebral cortex than with the mechanics of these changes. In his research on permeability of the salivary gland, one of his tests involved investigation of the excretion of iodine ions in saliva after oral administration of potassium iodide. Figs. 12 and 13[29] illustrate his experiment.

[28] Re: Footnote 25.

[29] Figs. 86 and 87 from Bykov, Cerebral Cortex and Internal Organs VEB-Verlag Volk und Gesundheit, 1952.

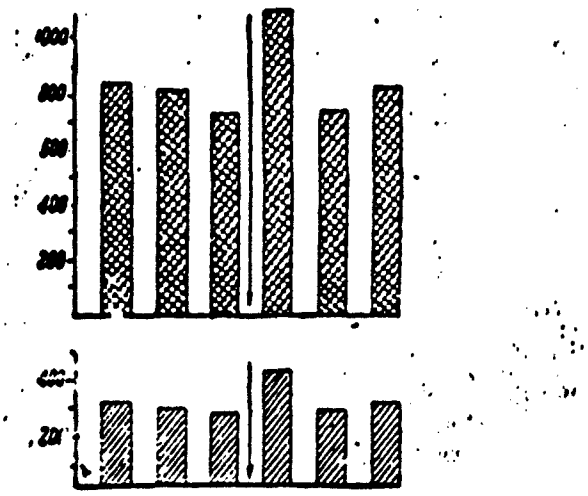


Fig. 12. Change in Iodine Permeability of Glandular Tissue Under Ini of a Conditioned Inhibitory Stimulus.

Ordinates: Iodine amount in grams.

Abscissa: Various saliva specimens.

Dark columns: Iodine content in 1 cc saliva.

Shaded columns: Iodine concentration in saliva.

Effect of a conditioned inhibition process.

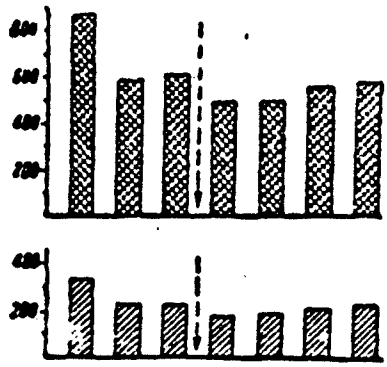


Fig. 13. Change in Iodine Permeability in Glandular Tissue Under Inf of a Positive Conditioned Stimulus. Legend same as in Fig. 12.

"Examination of iodine discharge in saliva secreted while under influence of a fading [in original paper: "no longer re-inforced by f supply"] conditioned stimulus revealed the following: the first appli tions of the conditional stimuli (still acting as a positive agent) w

always result in a decrease of iodine concentration in the saliva. But as the reflex is gradually extinguishing, i.e. as the positive stimulus comes to be an inhibitory agent, the effect will change. When the stimulus has become an inhibitory agent, its action increases the amount of iodine secreted by the salivary gland."

Bykov assumed that the increased splitting of the secretory granules caused by positive cortical stimuli develops simultaneously with a fall in the permeability of the gland, whereas the inhibitory impulses conveyed from the cortex, which increase the permeability of the glandular cells to iodine, are connected with a simultaneous decrease of granular formation and secretion. Numerous other experiments, some also involving the kidneys, prove cell permeability to be governed by cortical influences. This fact is of extraordinary importance, especially in connection with transmineralization, which plays an important part in both anabolism and catabolism.

In connection with his studies of the effect of cortical impulses on metabolism, Bykov very correctly pointed out that "only those innervating influences which change metabolism without changing the working function of a given group of cells may be regarded as having a primary effect on metabolism... The difficulty of solving the problem of 'nervous trophism' lies in proving that the change in metabolism occurs as a result of nervous impulses which do not affect the external result of tissue activity such as for instance, the degree of muscular tension, the level of secretion, etc.

....at present from a study of the chemical processes developing in organs and tissues it appears highly probable or even certain that tissue metabolism can change in response to nervous impulses without a manifest change in the specific working function of the tissue...

The fact is that it seems impossible to imagine in cell metabolism any change which would not induce a change in its state, i.e., in its excitability and its readiness for work... With the development of the so-called somatic innervation which secures an urgent and rapid reaction of the tissue to nervous impulses, taking the form of the activity specific for the given tissue, the excitability of the given cells with respect to the products of its metabolism decreases. The automatism of the tissue is depressed... The regulating influence of the nervous system on the functional properties of the cells (particularly on their metabolism) is still retained in the higher phases of development, this

regulation being effected by the sympathetic nervous system"...

Orbeli has suggested for this regulating influence of the sympath system the term 'adaptive-trophic' effect... Bykov stated: "Although admitting the existence of transitional forms between the typically trophic effects (e.g., the effect of the sympathetic nerve on glycoly in the liver) and the typically priming effects (e.g., the effect of so-called somatic fibers on the electric organ) we, nevertheless, ent reject the idea of regarding the former as phenomena belonging to 've tative' function, and the latter as belonging to 'animal' function... however, the initiation of skeletal muscular activity requires the di charge of a rapid electric potential in the motor terminus, then the capacity of the motor nerve fibers to transmit and to reproduce in th terminal apparatus the rapid oscillations of electric potentials appe to be but a quantitative development of the properties peculiar to veg tative fibers. The oscillations of electric potentials also undoubte accompany the activity of vegetative fibers..." All our work was dictated by the idea that the cerebrum—the highest organ for regulat the behavior of an animal toward its external environment—also regula the entire activity of the body in response to the influences of its internal environment... At the time of our first investigations, the cortical regulation of metabolism in an organism as a whole had not y been studied, and the whole problem of nervous influences exerted on the energy balance, a problem which had been advanced in its general form by Claude Bernard, Pflüger, Mosso and others, was for a time neglected in physiological studies.

Chapter IX

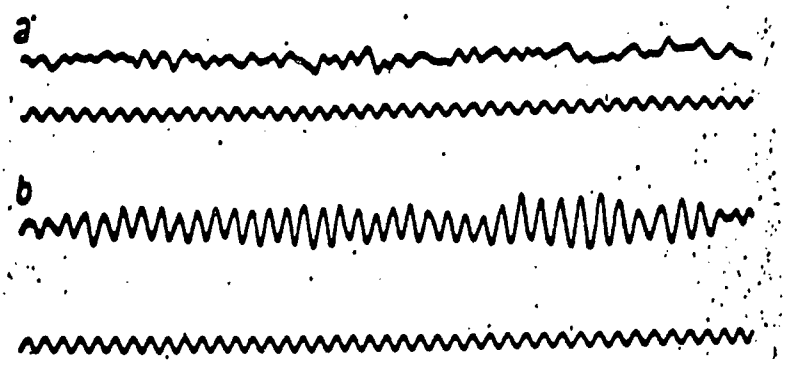
The EEG in Sleep and Wakefulness

Studies of the electric potential fluctuations during physiologic and experimentally induced excitation led to the investigation of impulses arising from the peripheral nervous system on one hand and from the central nervous system (cortex and subcortex) on the other, i.e., with respect to their possible correlation. Berger attempted to clarify the electric potential fluctuations in the brain by means of the EEG[30].

He was convinced that the bioelectric activities recorded in the EEG are concomitants of the constant excitation processes in the cerebral cortex: "the electric activity is the result of a difference in concentration of the electrically active ions at the excited and resting regions. Bioelectric occurrences are necessary concomitants of all vital processes and therefore also of the vigorous processes within man's cerebrum".

The electric potential fluctuations present larger waves in the resting or sleeping state than in the waking state and during physical or mental activity. Certain stimulus impulses from the sensory organs effect an amplitude decrease. The EEG shows alpha waves with a frequency of approx. 10/sec; their frequency and intensity decreases from the occipital to the frontal region. Besides the alpha rhythm, there is also the beta with smaller waves and a higher frequency (20/sec) and the delta with slow, relatively large waves and a frequency of 8/sec. Of interest is the marked difference between the EEG during wakefulness and that during sleep. Moreover, various phases between light and deep sleep can be differentiated (Figs. 14 and 15).

[30] Electroenzephalogramm des Menschen (Electroencephalogram of man) Nova Acta. Leopoldina, Neue Folge, Vol. IV, No. 38.



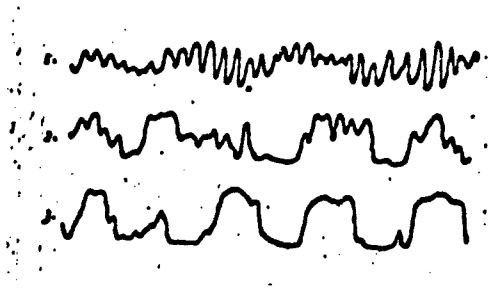
35-year old physician. EEG yield from frontal-occipital (silver f
leads. Lower line: tenths of a second.

a) In deep sleep b) After awaking from 2 hours of

Measured by moving-coil galvanometer

From: Berger, Nova Acta Leopoldina, Neue Folge, Vol. 6, No. 38, Fi
Verlag der Kaiserlich-Leopoldinischen-Carolinischen Deutschen Akad
der Naturforscher, Halle (Saale) 1938.

Fig. 14



1 Sec.

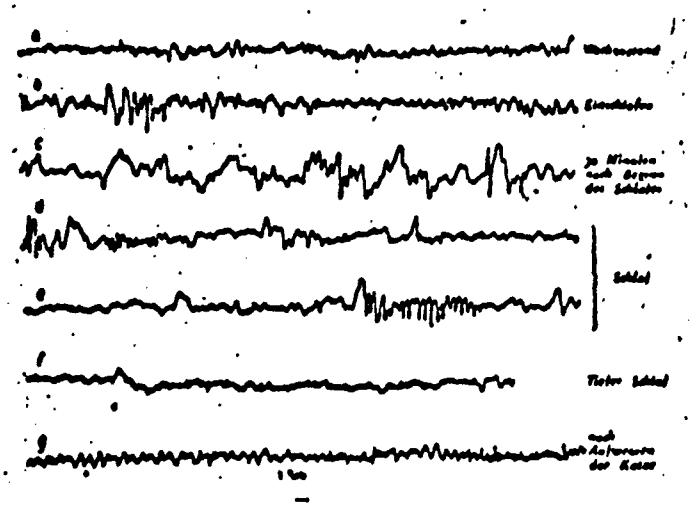
1. Brain potential fluctuations in wakefulness.
2. Brain potential fluctuations in light sleep.
3. Brain potential fluctuations in deep sleep.

From: H. Blake and R. W. Gerard: Brain potentials during sleep. A
J. Physiol., Vol. 119, No. 4, (1937), Fig. 1, p. 695.

Fig. 15

In this connection, Klaue's[31] experiments on cats were especially revealing. He observed that in the initial phase of sleep the EEG of the animals was characterized by irregular bioelectric activity which was, on the average, twice as high as in the waking state. He described this phase as the first bioelectric stage of sleep. Yet, in the progression of sleep he observed that activity decreased to below the activity in wakefulness. This occurred during the deepest sleeping phase. He concluded therefrom that the cerebral cortex is more active during the onset of sleep than in wakefulness. In deepest sleep, electrobiologic activity decreased. Millivolt output was half as high as in wakefulness.

During the first phase of sleep, waves of increased amplitude and slower rhythm were recorded (Fig. 16).



a. Waking state.

b. Onset of sleep.

c. After 30 min. of sleep.

d. [Sleep.

e. [

f. Deep sleep.

g. After awakening.

1 Sec.

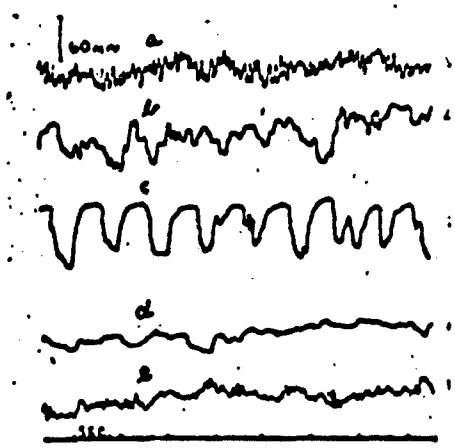
Electrobiologic potential pattern in area 21 of a cat during normal sleep. From K. Klaue (see Footnote 31).

Fig. 16

[31] Die bioelektrische Tätigkeit der Grosshirnrinde im normalen Schlaf und in der Narkose durch Schlafmittel (Bioelectric activity in the cerebral cortex during normal sleep and during drug-induced narcosis) J. Psychol. Neurol., Vol. 47, No. 5, 1937.

The study of electrobiologic potential differences in the vari phases of sleep completely confirms Pavlov's findings as presented i our first chapter (equalization phase, paradoxical phase, narcotic phase and deepest sleep phase). I am referring to the law of negat induction, etc.

Blake, Gerard and Kleitman also studied EEGs of the sleeping s They noticed that alpha rhythm predominates during wakefulness. D fatigue and the onset of sleep, higher and slower waves—the so-cal delta waves—appeared. They differentiated between the alpha, delt and "null" period in the EEG (Fig. 17).



a. Alpha rhythm during wakefulness.
b. Alpha-and-Delta period during light sleep.
c. Delta period during deep sleep.
d. Null period during light sleep.
e. Alpha rhythm during wakefulness.

From: H. Blake, R. W. Gerard and N. Kleitman: Factors influencing brain potentials during sleep. J. Neurophysiol. II (1939) pp. 48-60 Fig. 3.

Fig. 17

[32] Factors influencing brain potentials during sleep. J. Neurophysiol. II, (Jan. 1939) pp 48-60.

It is my opinion that the changes in electrobiologic potential are related to the excitation and inhibition processes as regulated by higher nervous activity. It is of interest to note that Myasnikov[33] attempted to classify nervous systems by means of the EEG. The EEG's of patients whose overall clinical picture indicated predominance of excitation processes reflected these same characteristics, as did those of patients in whom predominance of inhibition processes could be assumed. Patients of an apparent stable type presented a stable EEG pattern. In patients with predominating excitation processes, the EEG showed a fast rhythm; every now and then the alpha rhythm would pass into a smooth and often irregular beta rhythm with occasional spikes. Synchronization was disturbed. Different brain regions yielded different wave patterns; reaction to stimuli was rather pronounced (Fig. 18).

In patients with predominant inhibition, the EEG recorded just the opposite. The tracings show a torpid, feeble and slow rhythm of low amplitude, partially without any differentiation. Almost no reaction to stimuli could be observed (Fig. 19).

The third group of patients of the stable type showed an irregular synchronous alpha rhythm. The bioelectric potential did not differ from one brain portion to another; a decided reaction to stimuli was observed (Fig. 20).

Myasnikov raised the question if the deviations observed in the EEG's could not possible permit another interpretation. He said it is conceivable "that there could be a predominance of cortical impulses in one case, whereas subcortical impulses could be predominant in another".

[33] A. L. Myasnikov: Aetiologie und Pathogenese der Hochdruckkrankheit (Etiology and pathogenesis of hypertension) Duet. Gesundh. Wesen, Vol. 7, No. 36.

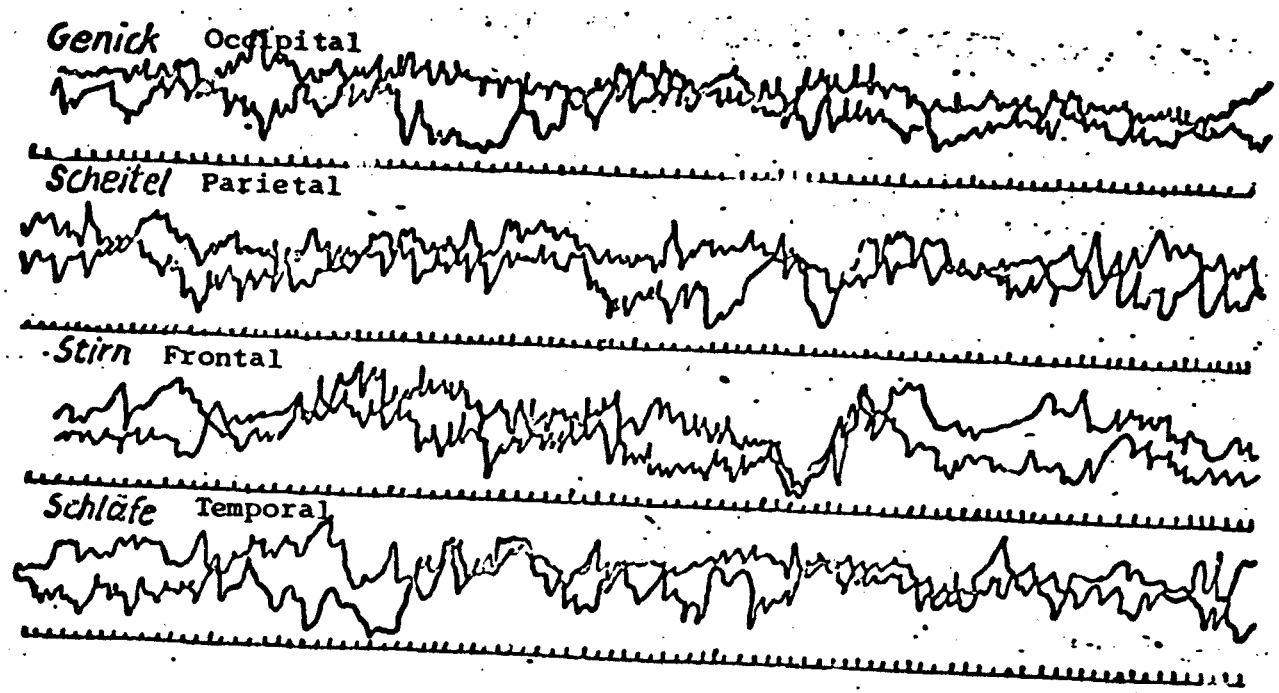


Fig. 18 Mjasnikov: Aetiologie und Pathogenese der Hochdruckkrankheit (Etiology and Pathogenesis of Hypertension) Deut. Gesundh. Wesen, Vol. 7, No. 36.

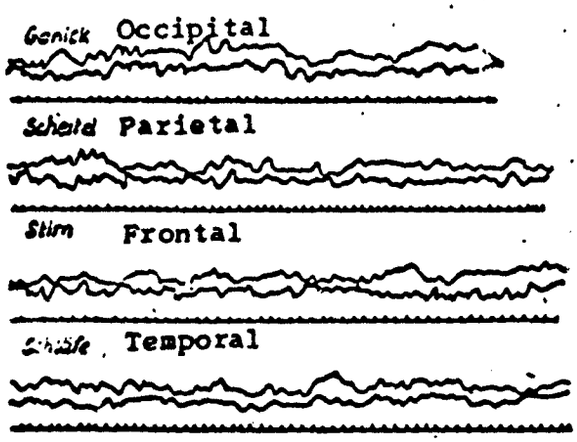


Fig. 19

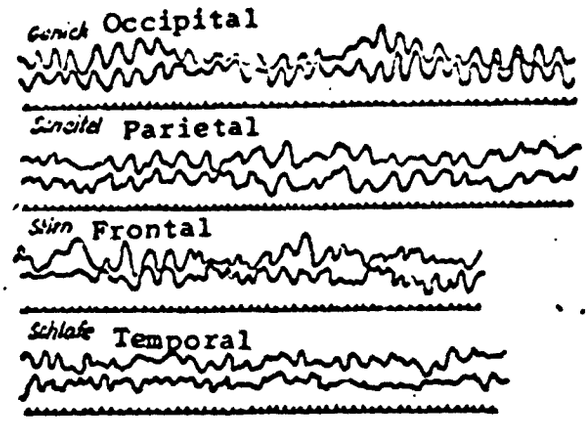


Fig. 20

From: A. L. Myasnikov (see Footnote 33).

A more detailed discussion of the EEG seems unnecessary inasmuch as the information presented in this chapter indicates that bioelectric activity in the cerebral cortex can be recorded by means of this method. It is, however, important that the EEG enables us to differentiate between sleeping and waking rhythms. Moreover, the EEG shows that even during sleep there is no absolute inactivity. This corresponds with Pavlov's findings, i.e., that localized and general inhibition as well as excitation constitute an active, dynamic process brought about by certain stimuli.

Chapter X

Cortico-autonomic Regulation in Sleep and Wakefulness

In Chapter VII we discussed sleep substances and some aspects of mineral metabolic changes during sleep. As we know, the assimilation (vagotonic) phase prevails in sleep. The sleep-wakefulness rhythm, established by various external and internal stimuli, is represented by the assimilation (vagotonic) and dissimilation (sympatheticotonic) phases. Sympathetic or parasympathetic predominance in autonomic regulation (I am not speaking of antagonism or autonomy) is evidenced by the following body reactions. In the assimilation phase: constricted pupils, reduced heart rate, blood pressure, body temperature, respiratory rate, blood sugar level and oxygenation (hypoxemia); also an altered acid-base balance with a tendency toward alkalemia, and reduced acid excretion (evidence of raised alkali excretion in morning urine). As to protein fractions in the blood, albumin content rises; cells as well as tissue fluids show an increase in nitrogenous substances. Cholesterol content in the blood serum rises, gastrointestinal activity increases, and basal metabolic rate slows down. Relative lymphocytosis and eosinophilia ensue due to hematopoietic reaction. In the dissimilation phase of the waking state, in which sympathetic regulations predominate, the opposite process takes place. The functions of the autonomic nervous system are linked in reciprocal dependence to those of the somatic nervous system. The interrelationship of physiologic functions and the reciprocal connection between assimilation and dissimilation is evidenced by the cortically controlled 24-hour periodicity. Although this sleep-wakefulness rhythm as described above has been studied by many researchers, its mechanism is still not fully understood, and there is much divergence of opinion as to the cause of this periodicity. One of the many hypotheses attributes the periodic metabolic shifts to the difference in motor activity during day and night. In so simple a form, this explanation is clearly insufficient, if only for the reason that the usual, i.e., non-perverted, picture of diurnal periodicity remains the same when an individual remains in bed throughout the 24 hours (Johannsen), in patients affected with fever, who are generally more active at night than by day (Hesser), and in persons who had been experimentally subjected to insomnia for several days (Kleitman). Bykov[34] studied the cortical influence on such physiological functions which are characterized by periodicity. He stated that there are insufficient grounds to believe that the entire diurnal periodicity of physiological functions merely

[34] Bykov: Grosshirnrinde und innere Organe (The Cerebral Cortex and the Internal Organs), Chapter XI.

follows the successive changes in the state of sleep inhibition and wakefulness of the cerebral cortex and the corresponding changes in the state of the mesencephalic and diencephalic centers...

He proved in numerous tests that the 24-hour periodicity is chiefly regulated by the cerebral cortex and is directly dependent not on the succession of sleep and wakefulness, but on the whole complex of stimuli which, in acting on exteroceptors, determine the degree of excitability of both subcortical and cortical centers. Closely resembling Isenschmidt's hypothesis, this assumption is confirmed in cases in which sleep by day and being awake at night were followed by a suitable change in the environmental conditions, i.e., when nocturnal conditions existed by day and day conditions at night—a perversion of the diurnal periodicity of physiological functions was brought on fairly easily, though not at once.

Bykov's tests proved that the rhythm of the physiological processes (in monkeys, for instance) could be wholly determined by external conditions*. Having turned day into night, i.e., having kept the cage regularly lighted at night and darkened by day, and having fed the animals at night, Shtcherbakova succeeded in shifting the maximum of temperature, motor activity, and pH of urine from day to night (Figs. 97, 98, 99 and 100). Having shortened the day (the cage was kept lighted and the animals were fed only between 8 a.m. and 6 p.m.), Shtcherbakova succeeded in demonstrating the change in the activity record. When the 24-hour period was divided into 2 days and 2 nights (i.e., the cage was kept lighted and the monkeys were fed from 9 a.m. to 1 p.m. and from 7 p.m. to 1 a.m.), Shtcherbakova obtained two periods of motor activity (Fig. 101) and two maxima of temperature and respiratory frequencies.

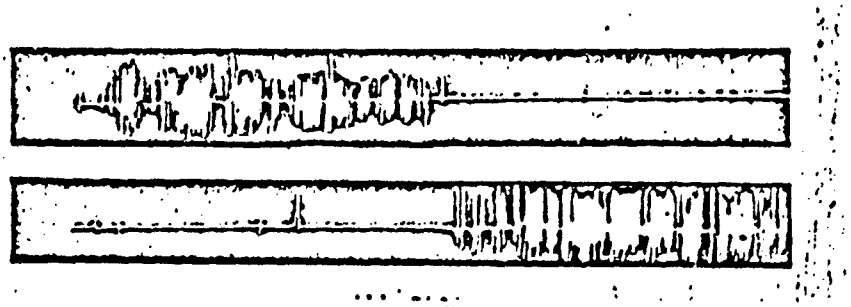


Fig. 21*

Change in Motor Activity of Monkeys during Normal and during "Inverted" Living Conditions

Fig. 21 Bykov: The Cerebral Cortex and the Internal Organs, Berlin, 1952. [in Bykov's book, Fig. 97].

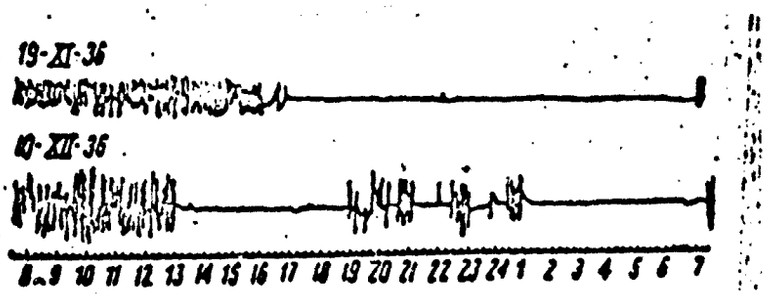


Fig. 22*

Change in Motor Activity of Monkeys during Normal and "Inverted" Living Conditions (double-phase day). Ordinate=temperature; abscissa=time of day.

The alternation of diurnal periodicity was achieved in Shtcherbakova's experiments more easily when night was turned into day and less readily when the 24-hour period was split into 2 days and nights. In the first case a complete reconstruction of periodocity was achieved on the seventh or eighth day; in the second, on the fourteenth to sixteenth day. After the animal had returned from the reversed mode of life to the normal routine, the diurnal periodicity failed to return to its norm at once and did so only after 2 to 5 days, i.e., somewhat sooner than the original change in the mode of life occurred. Bykov stated in regard to these tests:

"It is highly probable that the impulses conveyed to the bulbar and mesencephalic centers from exteroceptors (those conveyed from the retina are of paramount importance in the given case) increase the excitability of the centers of the midbrain and interbrain, which is of greater importance under the conditions discussed. Thus, the excitability of the vegetative centers in the region of the hypothalami (the thermoregulating center, in particular) is increased. Because of this, diurnal periodicity may be formed independently of the activity of the cerebral cortex. Yet simultaneously with the action of the afferent impulses on the diencephalic and mesencephalic centers, they also affect the projection of all the cortical receptors. As a result, the environment in which the impulses determining periodicity have exerted their action is combined with a definite state of the lower vegetative centers and with a number of physiological functions connected with this level. Therefore, when the afferent stimulations which directly determine diurnal periodicity have been changed, but some component of the environment in

*Fig. 22 [Ibid., Fig. 101].

ent they previously acted is still present, the cerebral cortex, owing to the temporary connection formed, determines the previous periodicity in spite of a change in the mode of life.". These tests show clearly that the 24-hour periodicity is not primarily dependent on the day-night rhythm, but also on the temporary cortical connections to vegetative centers and sense organs. These temporary connections are established by the cerebral cortex according to biological importance and environmental requirements. This explains why adaptation to inverted living conditions takes time (in monkeys 7-8 days), until the metabolism adjusts to the changed diurnal regimen. They also show that the 24-hour periodicity is not arbitrary, but is based on biological adaptation. These findings are of extraordinary value to ecology and industrial medicine; they make it obvious that the working schedule should not be changed abruptly or without good reason. Moreover, the most advantageous working conditions should be determined in order to facilitate highest efficiency in work performance. In view of Bykov's findings, I deem it advisable to avoid frequently changing an employee from day to night shifts [or vice versa], inasmuch as the human body requires at least two weeks to fully adapt itself to the changed diurnal regimen.

Chapter XI

Sleep and its Connection with Corticovisceral Regulation

As discussed before, metabolic dissimilation takes place during t activity phase, whereas assimilation occurs during the restoration pha Sleep serves to maintain and restore vital functions through metabolic assimilation. We explained already that all physiologic processes are based on the alternation of the two essential processes of excitation and inhibition. When excitation reaches maximal cortical capacity, negative induction occurs as a defense mechanism and inhibition sets in automatically. In our discussion, we mentioned a humoral factor (a Pavlov called it) involved in inhibition. This product of cellular activity is the mediator for the irradiation of inhibition. General inhibition, as occurring in sleep, has a restorative function inasmuch as it prevents cellular exhaustion. This phenomenon, described by Pavlov as a protective process, embraces the entire cortex and all subordinate regions. We explained with the example of encephalitis, that when blockage in the hypothalamus prevents the afferent impulses from reaching the cortex, cortical tonus decreases.

This tonus decrease is essential for sleep whereas high tonus is essential for the waking state. Low cortical tonus facilitates inhibition, thereby effecting restoration of exhausted cortical regions. It thus serves to adapt the functional processes to physiologic needs.

When cortical function is impaired, i.e., when excitation exceeds sound physiologic limits, the regulating activity of the subcortex is affected.

Pavlov stated: "Normal, productive cerebral function [excitation] produces negative subcortical induction, whereas inhibition produces positive subcortical induction, i.e., intensifies subcortical activity.

Cortical disturbances, such as those brought about by strong emotions or excessive psychic or physical exertion, lead to cortical hyperexcitability and the cortex enters a state of fatigue which limits its normal functioning. Disturbances affecting the normal excitation-inhibition processes in the cerebral hemispheres can lead to somatic or psychic illness, visceral disorders and disturbance of the neuroendocri balance. Pathologic decreases or increases in tonus secondarily cause subcortical malfunction, resulting in functional and structural disorde

Bykov stated, "It is impossible to believe that the interaction of the two essential processes of excitation and inhibition is limited to the cells of the cerebral cortex. There is reason to think that the most complex play of these two antagonistic processes develops when the conditional reflex is in progress in the subcortical centers... In other words, any reflex act in an intact normal animal always consists of a conditional and an unconditional element... The subordination of the centers is only the tonic effect of the higher parts of the Central Nervous System, beginning with the cerebral cortex. It is possible that this phenomenon is not a congenital trait, but one that is formed by the experience of the individual. While reflexes of the lower order are segmental in nature, the cortical reflex has a far greater area of spread involving practically the entire nervous system and not the nervous system alone if we take into account the humoral elements of a temporary connection, i.e., the spread of the hormone through the blood."

In regard to the dependence of visceral processes on changes in the activity of the higher parts of the CNS, Bykov said:

"These changes consist not only in the perversion of normal activity, but also in the altered isochronism of the processes successively developing in an organ. I have already mentioned that changes in the activity of the cortex cause disturbances in the processes of renal filtration and reabsorption. Another example is dyskinesia in the motor apparatus of the stomach and the intestine under the influence of cortical impulses in dogs in which the premotor zone has been extirpated. Further, I shall discuss the disturbances of complex acts in the function of the digestive glands and of the motor apparatus. Functional lesions are not only produced in the course of an experiment, but they may develop in normal life, since they are dependent on environmental agents or agents of the animal's 'milieu interieur'. In Pavlov's laboratories, neuroses were developed in animals by means of collisions in time between the processes of excitation and inhibition or by using stimuli which were too powerful for the given animal. We have material showing that neurotic states may also occur in other situations, as will be discussed later. I should like to emphasize that the origin of a tonic state of the cortex and its changes depend on the effect on the animal not only of exteroceptive stimuli, but also of interoceptive stimuli...

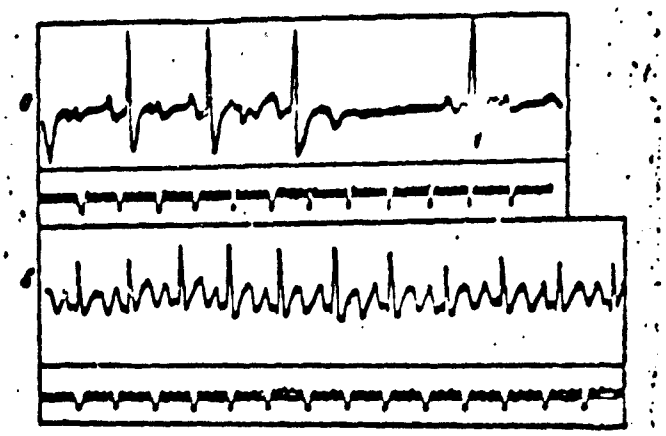
"The impulses from interoceptors reach not only the subcortex but also the cortex. The permanent stimulation of the cortex by the varying state of the viscera and their receptor apparatus produces, along with exteroceptive stimulation, a tonus level in the cortex, which affects

the peripheral effectors. As already shown by Charles Bell, a kind of 'nerve cycle' is thus formed [when a nerve carries a command from the brain to the muscle, while another nerve conducts the sensation of the state of the muscle to the brain]".

The total organ system, including humoral processes and motoricity of the skeletal musculature, is under the regulating control of the cerebral cortex. The previous explanations show clearly that cortical stimuli (temporary connections as represented by conditioned reflexes) can alter congenital unconditioned reflexes.

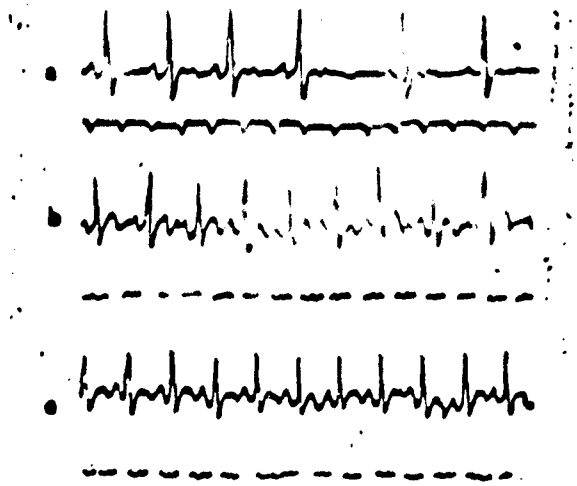
The conditioned reflex, formed on the basis of experience, can change or influence organic function for a considerable length of time—in proportion to its biologic importance. Bykov's important observation that each organ "has its own tempo" in reacting to conditional reflexes* has been confirmed by experiments. It was observed that somatic reactions are faster than the cortical regulations of vegetative functions. Bykov and his collaborators proved in numerous experiments the influence of conditional reflexes on visceral function. Let us discuss two of these, which illustrate the cortical mechanism of forming conditional cardiac reflexes. The drugs used (adrenalin, acetylcholine, nitroglycerin and morphine) produce known changes in the ECG. The experimental dog was given an intravenous injection of nitroglycerin, and the ECG's before and after the injection were compared. The latter showed accelerated heart rate, lower amplitude in the QRS complex, prominent P and T waves and a change in the form of the S-T segment, which was shifted above the isoelectric line. Also noted were an increase in atrial activity and in minute volume. When, in establishing a conditioned reflex, the nitroglycerin injection was combined with the action of an auditory stimulus, but the unwanted stimulus represented by the prick of the injection was eliminated (by repeated intravenous injections of normal saline solution not accompanied by the sound), it was later possible to obtain the same ECG changes by applying the auditory stimulus alone without the nitroglycerin.

*Trans. Note: A conditional reflex has varied temporal relations. Bykov: The Cerebral Cortex and the Internal Organs, p. 387.



a=ECG of normal dog
b=ECG 30 seconds after nitroglycerin injection; time registration in 1/5 sec.

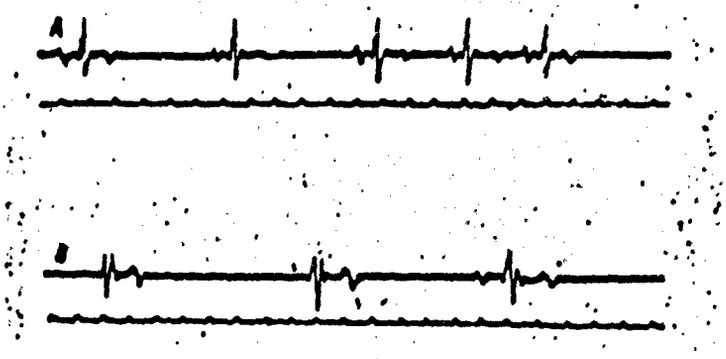
Fig. 23*



a=ECG of normal dog
b=ECG 30 seconds after applying conditional stimulus
c=ECG 30 seconds after nitroglycerin injection; time registration in 1/5 sec.

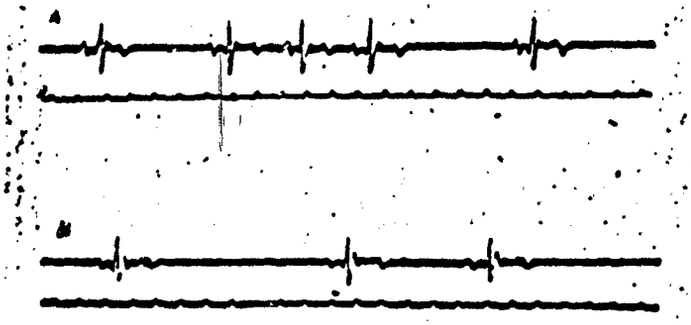
Fig. 24**

Similar results were obtained in tests with morphine injections. The upward P deflection either disappears or is greatly reduced; the R deflection and sometimes the T deflections are bifurcated. The heart develops a nodal rhythm, and a typical decrease in cardiac rate and minute volume takes place. If one now proceeds to form a conditional auditory reflex, the same results can be obtained as described in the test with nitroglycerin, i.e., the auditory stimulus alone will produce the same changes in the ECG as if morphine had been administered.



a=ECG of normal dog
b=ECG 15 min. after subcutaneous injection of 0.2 g. morphine; time registration in 1/5 2ec.

Fig. 25***



a=ECG of the same dog as in Fig. 25 before stimulation
b=ECG 15 min. after subcutaneous injection of normal saline solution in the same milieu as with the morphine injections; time registration in 1/5 sec.

Fig. 26****

The successive application of a conditional stimulus formerly combined with the effect of nitroglycerin will temporarily lift the blockage and will produce a normal RR interval. After these conditioned reflexes were established, they proved very difficult to extinguish. Bykov's tests showed that cortical impulses can, as temporary connections, affect cardiac activity either positively or negatively. These tests also proved that "stereotyped repetition of a reaction can, through a conditioned reflex, lead to structural organic changes". It was demonstrated that functional changes were transformed to organic

***Ibid., p. 69, Fig. 14.
****Ibid., p. 70, Fig. 15.

changes. The above may suffice in illustrating this point.[35]

The results of Bykov's experiments provide us with an explanation for an observation made by most physicians. When, for instance, a patient is admitted to a hospital with a severe, recurring biliary colic, his acute pain is, in most cases, alleviated by a morphine injection. When these colics become increasingly frequent, experimental substitution of a saline solution for the morphine derivative reveals the startling fact that the neutral substitute produces the same pain alleviation as morphine. This was often taken as an indication that hysteria or "functional overlapping" was involved. Bykov's findings now offer a physiological explanation: we are dealing here with a conditioned reflex. The patient's association of the injection with pain alleviation had produced the temporary conditioned reflex. However, if the application of the conditional stimulus (the saline injection) is repeated over a prolonged period of time, without being reinforced by the unconditional stimulus (morphine), the conditioned reflex will gradually become extinguished and the saline injection will cease to alleviate pain.

[35] For more information see Bykov: The Cerebral Cortex and the Internal Organs, Chapter III.

Chapter XII

"Psychosomatic" Medicine

As we have seen, conditioned reflexes are the keys to the understanding of psychosomatic phenomena in man. All organs are linked in their activity to the complex regulating system of the entire organism, including the cerebral hemispheres. Therefore, one cannot consider a disease of any one organ in isolation from the organism as a whole. This holds true for exogenous as well as endogenous diseases.

We have explained earlier how Pavlov and his school succeeded in discovering the physiological laws on which psychic phenomena are based. The clear, dialectic and materialistic meaning thereby established for "psychosomatic medicine" differs substantially from the idealistic, teleologic and mystic speculations advanced by advocates of psychosomatic medicine concepts prevalent especially in the United States. In recent years, a rising cult of psychosomatics, i.e., psychosomatic medicine, has become evident in the medical literature of Western European countries, mainly. In numerous papers, attempts are made to "analyze" the interrelationship of "body" and "soul" and to develop a special school as well as new diagnostic, etiologic and therapeutic "methods". It is especially in German literature that the subject of psychosomatics keeps cropping up. Numerous authors speak in a perfunctory manner of the reciprocal influenceability of "psyche" and "organism", but fail to explain that psychic phenomena are based on physiological laws. And the more vaguely and capriciously the topic "soul" is treated, the greater the acceptance of this unscientific information. The dissertations by the German philosopher and physician Karl Jaspers[36] show clearly how far these idealistic theorists of psychosomatic medicine are removed from a true, scientific concept. Jaspers stated:

"Although a certain categorization on an empiric basis is possible, no matter how hard it has been tried to differentiate between psyche and soma, their mutual identity cannot be conceived, and much less demonstrated. If one, so to speak, attempted to map soul structures and insisted upon the mutual identity of body and soul, one would arrive at absurdities as, for instance, memory images actually located in ganglion cells or neutral associations embedded in fibers... There is no actual location of the soul, neither in a

[36]Allgemeine Psychopathologie (General Psychopathology), Springer Verlag, Berlin und Heidelberg, 1948.

hormonal, nor atomic, nor ultra[redacted] sense ... Could it be possible that the soul does actively influence all somatic processes even to the inclusion of severe organic diseases? Anyone able to present convincing evidence of this would certainly not only open up new vistas, but would establish a radically new concept of physiological processes in their entirety. I am doubtful, and suspect that the boundaries are rather confining in this respect."

Kisskalt had the following to say about the psychosomatic problem:[37]

"There is undoubtedly a connection between entelechy and the body-soul problem—the incomparability of psychic processes with their physiologic concomitants—unsolved for thousands of years... The only solution to this problem might well lie in acceptance without analysis!"

I deem it necessary to point out the paradoxic dualism implied by the concept and the term psychosomatics. This term associates two contrasting ideas of different thought content. According to nomenclature, psyche means soul and soma means body. We are accustomed to think of psychosomatics in terms of body and soul, i.e., matter and spirit. In other words, according to terminology usually employed in medical literature, the term "psychosomatics" implies a "parallelism" between psychic, i.e. nonmaterial, and somatic, i.e., material processes. This obviously leads to very speculative and ambiguous conceptions.

In view of the outstanding discoveries by Pavlov and his school, who proved that physiological laws govern psychic phenomena through temporary connections, i.e. conditioned reflexes, the traditional concept of psychosomatics should in my opinion be abandoned. In fact, psychophysiology is based on the experimentally proven correlation of cerebral cortex, organs and tissues.

It is a known fact that drastic changes in psychic makeup, personality, thought processes, emotions, etc., can be brought about by even the slightest organic changes as shifts in the "pH-ion balance" or circulatory disturbances, just as by degenerative or inflammatory processes within the CNS (as present with lues cerebrospinalis, encephalitis, meningitis and cortical or subcortical tumors). Pavlov and his eminent disciple Bykov clearly proved psychic phenomena to be linked to physiological processes. In view of these findings,

[37] Karl Kisskalt, Theorie und Praxis der medizinischen Forschung (Theory and Praxis of Medical Research), J. F. Lehmann Verlag, München-Berlin, 1942.

it becomes quite evident that the concept of psychosomatics in its traditional meaning is self-contradictory.

If anyone should claim that this is a dispute over terminology and that the same questions could be raised concerning psychology, I would like to explain that this would be an erroneous train of thought. Psychology, the science of the psyche and psychic processes is not based on an idealistic point of view, as can be said of the antagonistic confrontation [psyche and soma] involved in the concept of psychosomatics. For as long as our scientific research fails to routinely apply materialistic and dialectic reasoning, nomenclature based on idealistic tradition will tend to be confusing. I consider it a necessity that the vague, indistinct, and scientifically ill-chosen term of "psychosomatics" be abolished from medical literature and be restricted to the vocabulary of pseudo-scientific theoreticians. I suggest "cortico-visceral" or another appropriate term which does not imply a conceptual conflict. This would eliminate misconceptions concerning two entities which are really not antagonistic.

Chapter XIII

Therapeutic Use of Protracted Sleep

The previous explanations—though seemingly digressing from our :opic—were in my opinion necessary, inasmuch as the use of sleep :herapy is based on the cognition of the corticovisceral, i.e., :orticovegetative interrelations and of their relationship to physologic and pathophysiologic processes. Before Pavlov, especially nder Virchov's influence, internal diseases were considered strictly s somatic processes confined to the affected organ. Pavlov was first n the history of physiology and medicine to abandon the dualistic oncept. He not only regarded the organism as a whole but also proved t experimentally. In fact, in the later years of his productive life, avlov applied the knowledge gained through his animal experiments to linical medicine.

Pavlov's research, of course, was aimed primarily at applying to eneral biology and medicine the physiologic and psychophysiologic aws he had discovered. His belief in the interconnection of experiental physiology, pathophysiology and general medicine was so strong s to compel him to choose a neurologic and psychiatric clinic in ich he could apply his knowledge to medicine. In this new field of ideavor, he applied his doctrine of the functions of higher nervous :tivity and his discovery of protective inhibition. As already plained, protective inhibition is a natural defense reaction by ans of which the cortex responds to excessive stimulation or to :citation beyond physiologic capacity. This defense reaction consists the spreading of inhibition, thereby preventing excessive stress to e cortex and its subregions which, in turn, could lead to a serious pairment of regulatory functions. For this reason Pavlov defined e inhibitory process as a protective inhibition which, serving as a aling measure, ensures normal functioning of the nervous system, e., mainly of its higher region, the cortex.

At first, Pavlov used sleep therapy on patients with obvious mptoms of cortical inhibition. He was of the opinion that such hibition, as present with catatonic, stuporous or similar conditions, presents a physiologic, protective reaction which should be re-enforced the healing therapy of protracted sleep. This was a completely new y of reasoning, inasmuch as heretofore the therapeutic induction of a ilight state or of narcotic sleep had been used in cases of antipodal ture, i.e., where strong excitatory reactions were involved, as in :tain forms of psychosis. Pavlov demonstrated that disorders of

higher nervous functions result when a process of excitation or inhibition becomes supermaximal (usually because of an already existing weakness of the nervous system), or when the excitation and inhibition processes lack coordination, or when the nervous processes are repressed [Trans. Note. Literally: insufficient mobility of the nervous processes.]. Pavlov pointed out that under pathologic conditions hypnotic manifestations of inhibition represent a normal physiologic defense against the pathogenic agent.[38]

Ivanov and Smolenski used sleep therapy for a variety of mental diseases characterized by inhibition. Later, other Soviet clinicians, among them Petrov, Andreyev, Vishnevski, Bussalov et al expanded the field of sleep therapy; Asratyan and Grashtshenkov also treated nervous disorders due to trauma (brain contusions or concussions) with this therapy. In addition to psychoses, neuroses, skull and brain injuries, protracted sleep therapy was also used for causalgia, phantom pain, brain tumors and as a pre- and post-operative treatment.

As already explained, Pavlov's school proved that the cortex not only plays an important role in disorders of higher nervous functions, but is also deeply involved in the development of all pathologic processes within the organism. The cerebral hemispheres "process" all external and internal influences. The resulting organic reactions (including any pathologic changes) depend upon the functional ability of the cortex as well as upon the intensity and nature of the impulses received. The Soviet clinicians thus drew logical conclusions from these findings and expanded the use of sleep therapy, utilizing the healing influence of cortical regulation on various pathologic processes.

Bykov's experiments illustrated how internal organic structures can be pathologically altered by the cortex and the subcortical regions through conditioned reflexes. Cortical weakness or exhaustion leads to chaotic subcortical reactions. The subcortical control of the internal organs becomes uncoordinated, resulting in functional as well as structural pathologic changes. It must, therefore, be the aim of all therapy to restore normal cerebral functions and to support the healing process, regardless of whether endogenous or exogenous factors are impairing cortical or subcortical functions.

Needless to say, sleep therapy is no panacea. Its effectiveness depends upon the circumstances, i.e., type of patient's nervous system and stage of the disease.

[38]Cited from F. Andreyev, Die Schlaftherapie (Sleep Inerapy), Zeitschr. Psychol., Neurol. med., Psychol., Vol. 4, p. 33ff.

We realize that, as emphasized by Andeyev, at the onset of a somatic disease, increased cortical tonus and activity is often present as a physiologic reaction. Under such conditions, it would be wrong to decrease this cortical tonus through sleep therapy and thereby inhibit the physiologic activity of the brain. The choice of medication and proper dosage are very important. By all means, sleep therapy is not suited for all diseases, as will be discussed in detail in the second part of this volume: Clinical Aspects of Sleep Therapy.