EFFECTS OF ELECTRICAL STIMULATION OF THE MESENCEPHALON AND DIENCEPHALON ON THE PARADOXICAL PHASE OF SLEEP

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Abstract. During paradoxical sleep electrical stimulation of the mesencephalic reticular formation and emotiogenic structures in the mesencephalon and diencephalon produced depression or an increase in the theta rhythm of the hippocampal and entorhinal electrical activity. However, stimulation not involving behavioral arousal did not cause a transition from paradoxical phase into slow wave sleep. The cessation of stimulation restored the normal structure of the paradoxical phase. Stimulation of the reticular formation causing the depression of the hippocampal and entorhinal theta rhythm without behavioral arousal did not affect duration of the paradoxical phase, which was shortened, however, by electrical stimulation of the emotiogenic structures evoking an increase in the hippocampal and entorhinal theta rhythms. Stimulation of ventromedial hypothalamus or septum (during wakefulness inhibiting motivational behavior and emotional stress) caused transition from the paradoxical into slow wave sleep. This is probably caused by a decrease in emotiogenic stress, which during the paradoxical phase is usually on a high level.

INTRODUCTION

Since the discovery of the so-called paradoxical sleep new aspects of study have been planned for the investigation of neurophysiological mechanisms regulating the structure and regular alternation of the different phases in the wakefulness-sleep cycle. According to EEG shifts
it has been concluded that the activating brain stem reticular formation must play a decisive role in the regulation of the paradoxical phase of sleep (20). First of all this is indicated by the presence of the neocortical desynchronization during paradoxical sleep (9, 18). Since the classical experiments of Moruzzi and Magoun (27) are considered unquestionable, the fact that a neocortical desynchronization leads to wakefulness is a result of the activating of the ascending mesencephalic reticular formation. However, such an explanation of the development of the desynchronization of the paradoxical phase of sleep is faced with certain difficulties, i.e., the absence of the behavioral arousal during this phase, which was the reason for its being named paradoxical sleep. Further experiments with transection of the brain stem on its different levels allowed a more precise localization of the structures responsible for triggering the paradoxical phase of sleep. It has been shown that these structures are located in the pontine reticular formation (8, 19, 41).

However, the paradoxical phase is a highly complex phenomenon and can scarcely be regulated by the reticular nuclei only. There is no doubt that the paradoxical phase of sleep is a result of the coordinate activity of the entire brain. According to the data available, the nervous formation responsible for the triggering of the different phases of sleep are located in the mesencephalon, but further structure of these phases is undoubtedly formed by means of the active participation of the other systems of the brain integrating the emotional and motivational processes (14, 20, 30, 31). In this respect of especial significance is the presence of hypersynchronization in the electrical activity of such archipaleocortical structures as the hippocampus (19, 24, 33) and entorhinal cortex (31), which shows that the activity of the hypothalamo-cortical system must be on a high level (12, 30, 44).

On the basis of the results obtained in studying the morphology and changes of sleep, a hypothesis has been suggested that there must be a causal dependence between the slow and paradoxical phases (21, 43). But this theory demands further examination.

In the structure of the sleep cycle the paradoxical phase appears as a temporary interruption of slow wave sleep. By the EEG evidence this phase of sleep is analogous to wakefulness. However, according to behavioral tests, the paradoxical phase of sleep was reported to be a deeper state of sleep (3, 16, 17, 26, 42). Hubel (17) by means of electrical stimulation of the reticular formation during the paradoxical phase provoked slow wave sleep. This fact indicates that the paradoxical phase is deeper than the slow wave sleep. On the other hand, the EEG, vegetative and somatic effects show the presence of high activity in the brain structures during paradoxical sleep (32).
From this review of the literature it is clear that further experiments are necessary to evaluate more exactly the evidence reported and to elucidate the new aspects in the sleep-waking cycle. In particular, in our opinion, it is necessary to study the effect of the electrical stimulation of the mesencephalon and diencephalon on the structure of the paradoxical phase of sleep.

METHODS

The experiments were carried out on 15 adult cats. Metallic electrodes with a bare tip of 100–200 μm were chronically implanted in different structures of the brain and in the oculomotor muscle. To record the neck muscle electrical activity special “San’ei” bipolar electrodes were used. The brain structures were stimulated by means of bipolar electrodes. Rectangular pulses from a generator with high-frequency output were used. Identification of the different phases of sleep has been made by recording the electroneocorticogram, electrohippocampogram, electrooculogram, electromyogram and electrocardiogram. The registration of the above mentioned parameters was carried out on a 13-channel ink-writing “San’ei” electroencephalograph. Spectral analysis and integration of delta, theta, alpha, beta₁ and beta₂ rhythms of the EEG were made on a 2-channel “San’ei” analyser-integrator. Record of the integrated values was made in consecutive order, the first 5 rhythms for one lead, and the next 5 rhythms for the other in a 5 sec epoch.

The experiments lasted from 10 a.m. till 6 p.m. The rest of the time animals were placed in a special chamber on a small support surrounded by water. The selective deprivation of paradoxical sleep was made according to Jouvet (19, 22).

On the morning before the beginning of the experiment the cats were fed, after which they soon went to sleep.

When the experiments were completed, under Nembutal anesthesia, the brain tissues were coagulated around the electrode tips by means of a direct current through the implanted electrodes. After this, the cats were killed; the brain was fixed in a 10% formalin solution; and localization of the implanted electrodes was checked in serial sections of the brain.

RESULTS

In order to make clear the neurophysiological mechanisms of the paradoxical phase it would be interesting to study the effects of electrical stimulation on brain structures during this phase of sleep. An
investigation in this direction and analysis of the data obtained would be useful in discussing the dynamics of excitability in brain structures during different phases of sleep.

*Effect of electrical stimulation of the posterior hypothalamus.* In our recent paper (32) we reported that the excitability of the mesencephalic and diencephalic as well as archipaleocortical structures during the paradoxical phase was increased as compared with deep, slow-wave sleep. This phenomenon was observed in the present experiment too. The threshold stimulation of the mesencephalic and diencephalic structures evoking EEG arousal without the hippocampal theta rhythm, during deep slow wave sleep, becomes supra-threshold for the EEG shift during the paradoxical phase.

As to the behavioral arousal thresholds of the mesencephalic and diencephalic electrical stimulation, they become higher during paradoxical sleep. The threshold electrical stimulation of the posterior hypothalamus, evoking EEG arousal with an increase in the hippocampal theta rhythm and weak behavioral arousal, during deep slow wave sleep (Fig. 1A), becomes sub-threshold for behavioral arousal during the paradoxical phase (Fig. 1B). However, as can be seen from this Figure, EEG shifts in the case of increasing of hippocampal theta rhythm are more prominent in the paradoxical phase than during deep slow wave sleep. This fact indicates that the excitability of the hypothalamo-archipaleocortical system during the paradoxical phase is higher as compared with deep slow wave sleep. The fact that the thresholds are higher for behavioral arousal during the paradoxical phase seems to be due to the active inhibition of the spinal reflexes affected by descending impulses from the brain stem reticular formation (37). That, on the one hand, makes movement difficult in the paradoxical phase, but on the other hand, these are good conditions for studying the effects of electrical stimulation of the different parts of the brain on the structure of the paradoxical phase, since behavioral arousal itself produces its cessation.

*Effect of electrical stimulation of the mesencephalic reticular formation.* Electrical stimulation of the reticular formation, evoking during deep slow wave sleep EEG arousal without an increase in the hippocampal theta rhythm, produces in the paradoxical phase a temporary disturbance of its structure. In such a case depression of the hippocampal theta rhythm and deceleration of rapid eye movement can be observed (Fig. 2A). The cessation of the electrical stimulation restores the normal structure of the paradoxical phase. Experiments with repeated electrical stimulation have shown no transition of the paradoxical phase into deep wave sleep. On the contrary, repeated stimulation, decreasing the effectiveness of the stimulation, may produce the recovery
of paradoxical sleep, before the cessation of electrical stimulation. The complete disappearance of the effect of repeated stimulation can be observed when such stimulation is delivered 8–12 times during one paradoxical phase. This experiment shows that the decrease in the effectiveness of the stimulation must be determined by the development of habituation.

Fig. 1. Changes in the electrical activity of the neo- and archipaleocortex during deep slow wave sleep (A) and the paradoxical phase (B) in response to electrical stimulation (3.5 v, 200 cycle/sec, 0.1 msec) of the posterior hypothalamus. Leads: 1, electromyogram (EMG); 2, auditory cortex; 3, entorhinal cortex; 4, dorsal hippocampus; 5, signal line (signal line downward indicates the onset of the electrical stimulation); 6, integrated values of delta (2–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta_1 (13–20 Hz) and beta_2 (20–30 Hz) rhythms of the auditory cortex (the first five deflections) and dorsal hippocampus (the other five deflections) during a 5 sec epoch. Calibration in this and in the subsequent Figures is 200 μV, 1 sec.

The transition of the paradoxical phase into deep slow wave sleep by means of electrical stimulation of the reticular formation occurs only when it produces behavioral arousal. Sometimes behavioral arousal is so short and weak that it is scarcely noticeable. Occasionally it is expressed as a momentary restoration of the neck muscle tonus (Fig. 2B), but this is sufficient for the cessation of the paradoxical phase, after which as a rule the cycle begins with slow wave sleep (Fig. 2B, the end of the recording).

No changes in the duration of the paradoxical phase or in the ratio
of the durations of the different phases of sleep are observed during electrical stimulation of the mesencephalic reticular formation which evokes a temporary disturbance of the paradoxical phase without behavioral arousal.

Fig. 2. Changes in the electrical activity of the dorsal hippocampus and neocortex during paradoxical sleep in response to electrical stimulation of the mesencephalic reticular formation. Leads: 1, EMG; 2, dorsal hippocampus; 3, sensorimotor cortex; 4, electrooculogram, 5, signal line; 6, integrated values of delta, theta, alpha, beta1, and beta2 rhythms of the dorsal hippocampus (the first five deflections) and sensorimotor cortex (the other five deflections) during a 5 sec epoch.

As mentioned above, electrical stimulation of the mesencephalic and diencephalic structures during deep slow wave sleep may produce EEG arousal with or without an increase of the hippocampal theta rhythm. The second type of EEG arousal may occur during the paradoxical phase too. Figure 1B illustrates a similar occurrence evoked by high-frequency electrical stimulation of the posterior hypothalamus. The same effect can be produced by electrical stimulation of the mesencephalic reticular formation (Fig. 3), the central grey matter, the lateral hypothalamus or other structures, which contribute to the activation of the motivational and emotional reactions. In the end, apparently, these electrical stimulations must determine the increase in the hypothalamic activity, since hippocampal and entorhinal theta rhythms are regulated by the impulses from the hypothalamus, spreading in the archipaleocortical structures through the septum (36, 38).

It is worth noting that electrical stimulation of the mesencephalic
and diencephalic structures, evoking an increase in the hippocampal theta rhythm without behavioral arousal, does not disturb the structure of the paradoxical phase. On the contrary, an increase in the signs characterizing the paradoxical phase is observed on such occasions. An increase in the hippocampal theta rhythm is one of these signs. Apart from the increase in the hippocampal theta rhythm, rapid eye movement and ponto-geniculo-occipital spikes become more frequent (Fig. 3A). With the cessation of electrical stimulation the normal paradoxical phase is restored.

Fig. 3. Changes in the electrical activity of the neocortex and hippocampus in response to electrical stimulation (2 v, 200 cycle/sec, 0.1 msec) of the mesencephalic reticular formation during paradoxical sleep. A, the first trial; B, the second trial of electrical stimulation. Leads: 1, visual cortex; 2, dorsal hippocampus; 3, electrooculogram; 4, signal line; 5, integrated values of delta, theta, alpha, beta1 and beta2 rhythms of the visual cortex (the first five deflections) and dorsal hippocampus (the other five deflections) during a 5 sec epoch.

During repeated electrical stimulation of the mesencephalic and diencephalic structures evoking an increase in the hippocampal theta rhythm during the paradoxical phase there is no gradual weakening of the effectiveness of the stimulation as a result of habituation. On the contrary, in such experiments there is often a significant increase in the effectiveness of the stimulation. For instance, the effect of the first trial of the mesencephalic reticular formation evoking an increase in
the hippocampal theta rhythm is illustrated in Fig. 3A. This effect disappears with the cessation of the electrical stimulation and the normal paradoxical phase appears (Fig. 3B, beginning of the recording). The second trial of the electrical stimulation evokes more prominent shifts in the electrohippocampogram. The frequency of the hippocampal theta rhythm during the second trial increases (6 sec), while the delta rhythm undergoes a significant decrease (Fig. 3B).

No transition of the paradoxical phase into slow wave sleep has been observed during the electrical stimulation of the mesencephalic and diencephalic structures evoking an increase in the hippocampal theta rhythm without behavioral arousal. Occasionally, electrical stimulation may result in a weak and momentary behavioral arousal expressed in barely noticeable movements, which is succeeded by slow wave sleep.

The repeated electrical stimulation of the mesencephalic and diencephalic structures evoking an increase in the hippocampal and entorhinal theta activity during the paradoxical phase may produce shortening of its duration. Statistical analysis of the data by Student's $t$-test shows that regular 15 sec electrical stimulation with 30 sec intervals results in a marked shortening (15–20%) of the duration of the paradoxical phase. However, similar stimulation does not affect the ratio of the different phases of sleep during the post-stimulation period.

Thus, electrical stimulation of the mesencephalic and diencephalic emotiogenic structures and mesencephalic reticular formation during paradoxical sleep may produce considerable EEG shifts (increasing or decreasing the hippocampal and entorhinal theta rhythm), but if this stimulation fails to produce even a momentary weak behavioral arousal, no transition of the paradoxical phase into slow wave sleep is observed.

Effect of electrical stimulation of the ventromedial hypothalamic nucleus. Electrical stimulation of some limbic structures may produce the transition of the paradoxical phase into slow wave sleep. It was shown that electrical stimulation of these structures inhibits emotional stress and motivational behavior in the wakeful animal.

Of the structures which inhibit emotional stress and motivational behavior, a particular study was made of the ventromedial hypothalamic nucleus, known as the "satiation center" in opposition to the "hunger center", which is located in the lateral hypothalamus (1, 2, 34, 35). In our experiments, electrical stimulation of the ventromedial hypothalamic nucleus inhibited feeding behavior without any somatic or emotional reactions (29). Such electrical stimulation causes an interruption in the feeding behavior, but with the cessation of the stimulation the cats continue to eat. If electrical stimulation of the ventromedial hypothalamic nucleus is applied to semisatiated or satiated cats, its cessation
produces activation of the feeding behavior on the rebound. All of these facts indicate that electrical stimulation of the ventromedial nucleus evokes genuine inhibition of the feeding center. Naturally, such electrical stimulation has a calming effect on the hungry animal and, as a result, there is a reduction in emotional stress.

At higher intensities of electrical stimulation of the ventromedial hypothalamic nucleus the behavioral reaction is qualitatively different. Instead of inhibition of feeding behavior, now there is a reaction of aggression, which, as the strength of stimulation increases, causes the cat to attack. On this occasion, the feeding behavior is again inhibited, but because of the aggression the inhibition is not genuine.

Depending on the strength of stimulation of the ventromedial hypothalamus, during paradoxical sleep there may be different kinds of EEG shifts. At those parameters of stimulation evoking inhibition of the feeding behavior without somatic reactions in a wakeful animal, depression of the initial hippocampal theta rhythm is observed during paradoxical sleep. These EEG shifts alternate with the subsequent synchronization of both the neocortical and hippocampal electrical activities. After cessation of stimulation, during its first application to the ventromedial hypothalamus, slow electrical activity develops in certain fragments, following which the normal structure of the paradoxical phase is restored (Fig. 4B). But with repeated stimulation during one paradoxical phase there may be a gradual increase in the synchronization and development of slow wave sleep.

The recovery of slow wave sleep depends on the parameters of electrical stimulation delivered to the ventromedial hypothalamus. The effect of threshold electrical stimulation of the ventromedial hypothalamus during the paradoxical phase is illustrated in Fig. 4. In response to electrical stimulation a significant decrease in the hippocampal theta rhythm occurs (Fig. 4A). After cessation of electrical stimulation the hippocampal theta rhythm becomes more sparse (delta rhythm increases) and then fragments of slow wave sleep appear (Fig. 4B). The duration of slow wave sleep evoked by the first application of ventromedial hypothalamic electrical stimulation may vary from several seconds to several tens of seconds. In this Figure the duration of slow wave sleep is 8–10 sec and is succeeded by recovery of paradoxical sleep (the end of Fig. 4B).

Increasing the strength of stimulation of the ventromedial hypothalamus within those limits which cause the inhibition in feeding of a wakeful animal elicits an increase in the duration of the fragments of evoked slow wave sleep, and very often after cessation of such stimulation, the paradoxical phase moves into slow wave sleep. Electrical sti-
imulation of the ventromedial hypothalamic nucleus during the paradoxical phase evokes depression of the hippocampal theta rhythm (Fig. 5A), while after its cessation it gradually leads to the development of slow wave sleep (Fig. 5B).

Fig. 4. Changes in the electrical activity of the neocortex and hippocampus in response to electrical stimulation of the ventromedial hypothalamic nucleus (2.5 v, 200 cycle/sec, 0.1 msec) during paradoxical sleep. A, beginning of the stimulation; B, the end of the stimulation. Leads: 1, auditory cortex; 2, dorsal hippocampus; 3, EKG; 4, signal line; 5, integrated values of the delta, theta, alpha, beta₁ and beta₂ rhythms of the auditory cortex (the first five deflections) and dorsal hippocampus (the other five deflections) during a 5 sec epoch.

It is significant to note that the above-mentioned EEG shifts occur without behavioral arousal. In order to evoke behavioral arousal the thresholds of electrical stimulation of the ventromedial hypothalamus and the mesencephalic and diencephalic structures during the paradoxical phase are higher than during slow wave sleep. Even those parameters of electrical stimulation of the ventromedial hypothalamus, which increase rather than suppress the hippocampal theta rhythm, are unable to produce behavioral arousal. However, electrical stimulation of the ventromedial hypothalamus, evoking an increase in the hippocampal theta rhythm without behavioral arousal, does not cause the paradoxical phase to move into slow wave sleep. After cessation of electrical stimulation there is a return to the normal paradoxical phase. However,
statistical analysis of the data shows that stimulation of the ventromedial hypothalamic nucleus, which causes rage and attack reactions in a wakeful animal, during the paradoxical phase produces its considerable shortening (the same happens with electrical stimulation of the posterior hypothalamus, lateral hypothalamus, central grey matter, etc.).

![Fig. 5. Changes in the electrical activity of the neocortex and hippocampus in response to electrical stimulation of the ventromedial hypothalamus nucleus 3.5 V, 200 cycle/sec, 0.1 msec) during paradoxical sleep. A, the beginning; B, the end of the electrical stimulation. Leads and designations are the same as in Fig. 4.](image)

As for the electrical stimulation of the ventromedial hypothalamic nucleus, causing inhibition of feeding behavior in a wakeful animal and during paradoxical sleep, suppression of the hippocampal theta rhythm with the restoration of slow wave sleep, this stimulation acts to deprive the paradoxical phase. Therefore, the succeeding paradoxical phase appears earlier than in the control experiments.

*Effect of electrical stimulation of the septum.* Electrical stimulation of the septum can produce a powerful transformational effect on the paradoxical phase. In our experiments, the drowsy state may be developed by electrical stimulation of the septum. The effectiveness of this stimulation depends on the level of wakefulness. However, a tendency to the drowsy state and EEG synchronization has been observed even in a wakeful hungry animal. In addition, this phenomenon develops not only in response to low-frequency, but also to high-frequency stimul-
tions. Figure 6 shows the changes in the electrical activity of the visual cortex and hippocampus in response to high-frequency septal stimulation. As can be seen from this Figure, before electrical stimulation in a hungry wakeful cat, the hippocampal electrical activity shows hypersynchronization in the theta and delta range; while the visual cortex is desynchronized and sporadic ponto-geniculo-occipital spikes may occur (Fig. 6A). After cessation of electrical stimulation while the cat is calm, both the neocortex and hippocampus show slow wave activity (Fig. 6B). This state may continue several tens of seconds, and then active wakefulness is restored.

![Fig. 6. Changes in the electrical activity of the neocortex and hippocampus in response to electrical stimulation of the septum (3.5 v, 200 cycle/sec, 0.1 msec) during active wakefulness. A, the beginning; B, the end of the electrical stimulation. Leads: 1, visual cortex; 2, dorsal hippocampus; 3, electrooculogram; 4, EKG; 5, signal line; 6, integrated values of the delta, theta, alpha, beta1 and beta2 rhythms of the visual cortex (the first five deflections) and dorsal hippocampus (the other five deflections) during a 5 sec epoch.](image)

Those parameters of electrical stimulation of the septum, which in a wakeful animal lead to EEG synchronization with a tendency to drowsiness, may provoke slow wave sleep during the paradoxical phase (Fig. 7). Before the stimulation there is a well expressed EEG characteristic of paradoxical sleep with hippocampal theta rhythm, rapid eye movements and ponto-geniculo-occipital spikes (Fig. 7A). In response to
the septal stimulation, the visual cortex shows EEG synchronization; while in the hippocampus depression of the theta activity and disturbances of the regular synchronization have been observed. In addition, the rapid eye movements become less frequent. After the cessation of stimulation, the sleep state continues as slow wave sleep (Fig. 7B).

Fig. 7. Changes in the electrical activity of the neocortex and hippocampus in response to electrical stimulation of septum (3.5 V, 200 cycle/sec, 0.1 msec) during paradoxical sleep. A, during; B, after electrical stimulation. Leads: 1, EMG; 2, visual cortex; 3, dorsal hippocampus; 4, electrooculogram; 5, signal line; 6, integrated values of delta, theta, alpha, beta₁ and beta₂ rhythms of the visual cortex (the first five deflections) and dorsal hippocampus (the other five deflections) during a 5 sec epoch.

The full restoration of slow wave sleep by electrical stimulation of the septum during the paradoxical phase does not always occur. More frequently, certain fragments of slow wave sleep develop and then there is a return to the paradoxical phase. In those instances when electrical stimulation of the septum is delivered during the first half of the paradoxical phase, the succeeding paradoxical phase appears sooner than without electrical stimulation, i.e., such stimulation of the septum may serve as a depriving factor of the paradoxical phase.

DISCUSSION

Systematic investigations of the sleep-waking cycle have shown that there are few differences in the electrical activity of the brain during wakefulness and the paradoxical phase. Depending on the degree of
the brain activity, different levels of wakefulness may be distinguished. One of the characteristic signs of different levels of wakefulness may be emotional stress of the organisms, which may vary to a great extent from passive wakefulness to affective emotional stress. It seems reasonable to assume that transition from wakefulness into sleep is characterized by a gradual decrease in emotional stress. With respect to different levels of wakefulness, it will be necessary to build up a scheme according to which emotional stress and the brain activity during the paradoxical phase is restored to active wakefulness, but does not exceed it. The more so because at present there is no doubt that the emotional stress and the degree of the brain electrical activity during the paradoxical phase may also vary to a very great extent, as during the different levels of wakefulness (30, 31).

The similarity of the electrical activity during wakefulness and the paradoxical phase is a decisive fact in the study of the neurophysiological mechanisms of paradoxical sleep. Since the classical experiments of Moruzzi and Magoun (25, 27), it has been considered that the main nervous substratum regulating wakefulness is the brain stem reticular formation. However, Feldman and Waller (10) have shown that the hypothalamic structures play a decisive role in behavioral arousal, whereas the mesencephalic reticular formation is responsible for EEG arousal in the neocortex. This fact points to the correctness of the early investigations of Hess et al. (15) and Gellhorn and Loofbourrow (11) about the significance of the hypothalamic structures in the regulating of behavior and the wakefulness-sleep cycle. From this position of Feldman and Waller (10), according to which behavioral arousal is regulated by the hypothalamic structures (in particular, posterior hypothalamus) and EEG arousal is caused through the mesencephalic reticular formation, the paradoxical phase is an exception, since it is a typical EEG arousal in which the active role is played by the hypothalamic structures. The sharp increase of the hippocampal theta rhythms during the paradoxical phase indicates that the so-called center of wakefulness in the posterior hypothalamus is at a high level of excitability. Since then, the classical experiments of Green and Arduini (12) provide decisive evidence that the hippocampal theta rhythm is regulated by impulses from the hypothalamus (in particular, the posterior hypothalamus) and that such an increase in the hippocampal theta rhythm as is observed in the paradoxical phase demands high activity from the hypothalamus (28).

On the other hand, new data (7, 19, 41) have shown that the trigger mechanisms for the paradoxical phase must be located in the caudal part of the pontine reticular formation. Unspecific activation from the reticular formation is the necessary and optimal background for the
subsequent development of the processes which characterize the paradoxical phase. The transition of slow wave sleep into the paradoxical phase through an initial general desynchronization, both in the neocortical and hippocampal electrical activity, indicates the significance of the unspecific reticular formation (30, 32, 33). Such changes in EEG show that it is the function of the reticular formation. The subsequent structure of the paradoxical phase is undoubtedly made by the active contribution of the specific mesencephalic and diencephalic structures regulating motivational behavior and emotional reactions. Apart from this the neocortex must play a role in the regulation of the complex neurophysiological and neuropsychological phenomena, taking place in paradoxical sleep. Although Jouvet (19) describes the presence of paradoxical sleep in the neodecorticated cats, no evidence exists as to how fully the structure of the paradoxical phase after ablation of the neocortex is maintained. In addition, the archipaleocortical structures, included in the limbic system and regulating the subjective experience during emotional reactions (4, 5), must have a particular importance in the regulation of paradoxical sleep. There has been no research into the effect of ablation of the archipaleocortical structures on the dynamics of the sleep-waking cycle.

Thus, the nonspecific reticular formation and specific mesencephalic and diencephalic structures regulating the motivational behavior and emotional reactions, as well as the archipaleocortical structures must actively contribute to the organization of the paradoxical phase. From this position, of great importance is the analysis of the data obtained by studying the effect of electrical stimulation of different mesencephalic and diencephalic structures during the paradoxical phase. In such experiments two types of electrical activity in the hippocampus and entorhinal cortex may be produced, provided the strength of the electrical stimulation is sub-threshold for behavioral arousal. The first type is a decrease in the hypersynchronized theta activity, while the second type is an increase. Electrical stimulation of the reticular formation may produce both types of EEG effects, but without even a momentary behavioral arousal the structure of the paradoxical phase is disturbed only temporarily and with the cessation of the stimulation is quickly restored. Sometimes behavioral arousal is so weak that it is scarcely noticeable. On such occasions the weak behavioral arousal is followed by slow wave sleep, but there is no transition from the paradoxical phase into slow wave sleep. It is very likely that this occurred in the experiments described by Hubel (17), who reported that electrical stimulation of the reticular formation during the paradoxical phase evokes its transition into slow wave sleep and by mistake
concluded that the paradoxical phase is deeper even than deep slow wave sleep. In our experiments (32) the decrease of the thresholds of the electrical stimulation of the mesencephalic and diencephalic structures for isolated EEG arousal was observed during paradoxical sleep, as compared with slow wave sleep. Thus, the excitability in the mesencephalic and diencephalic structures (in particular in the emotiogenic structures) during the paradoxical phase has increased as compared with slow wave sleep. The reason for the difficulties for behavioral arousal during the paradoxical phase seems to be an active inhibition of the spinal reflexes affected by descending influences from the pontine structures of the brain (37). Thus, during the paradoxical phase, the ascending reticular formation must be on a high functional level. Besides, the whole limbic system is on a high level of activity and coordinates and regulates emotional stress and motivational reactions of the organism, which are characteristic of the paradoxical phase of sleep.

However, during electrical stimulation of some brain structures, the transition of the paradoxical phase into slow wave sleep without behavioral arousal may be observed. As mentioned above, this effect was observed during electrical stimulation of the ventromedial hypothalamic nucleus, basal amygdaloid nucleus and septum. Characteristically, electrical stimulation of these structures inhibits any active behavior in wakeful animals; the EEG correlate of this inhibition is a depression of the hippocampal theta rhythm. Electrical stimulation of the ventromedial hypothalamic nucleus and basal amygdaloid complex inhibits feeding behavior, whereas during electrical stimulation of the septum there develops a decrease in the active behavior and slow wave activity in the neo- and archipaleocortical structures in a wakeful animal. In the paradoxical phase these parameters of stimulation produce slow wave sleep.

It is worth noting that during such electrical stimulation, along with the inhibition of active behavior, there occurs a lowering in the emotional stress of the organism. Emotional stress, which is proved by an increase in the hippocampal theta rhythm, must be on a high level during the paradoxical phase thanks to powerful activity in the emotiogenic structures. Electrical stimulation of those structures, which inhibits emotional behavior, evokes a lowering of the emotional stress during the paradoxical phase and results in its transition into slow wave sleep. Interestingly in the paradoxical phase the effectiveness of the electrical stimulation of the ventromedial hypothalamus and basal amygdala, in the sense of producing slow wave sleep, is more significant in a hungry animal. Thus, the presence of the eating demand
in a hungry animal may play an important role in the development of emotional stress during paradoxical sleep. The inhibition of this demand, evoked by electrical stimulation of the "satiation center" located in the ventromedial hypothalamus, may produce a depression of emotional stress and transition of the paradoxical phase into slow wave sleep (fragments or full slow wave sleep).

The electrical stimulation of the septum during the paradoxical phase may produce a lowering in the emotional stress associated with inhibition of the diencephalic emotogenic structures. In this respect it is interesting the observation of King and Meyer (23), that septal lesion evokes an increase in the emotionality of animals. This fact points to the inhibitory influence of the intact septum on the emotogenic structures of the brain. Possibly that the inhibitory effect of the rostral limbic structures on the coordinated centers of motivational-emotional reactions situated in the diencephalon, in particular in the hypothalamus, is mediated via the septum. There is both morphological (6, 39, 40) and physiological (13, 38, 45) evidence for the presence of such pathways.

Thus, during the paradoxical phase, slow wave sleep without momentary behavioral arousal may be provoked by electrical stimulation of those structures only which inhibit behavioral reactions and emotional stress in a wakeful animal. The reason for the production of slow wave sleep by electrical stimulation during the paradoxical phase of sleep must be the lowering of the emotional stress.

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