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COMPARATIVE STUDIES OF PGO-DEPRIVATION AND REM-DEPRIVATION OF PARADOXICAL SLEEP ON THE STRUCTURE OF CAT'S SLEEP-WAKEFULNESS CYCLE

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Summary

Under conditions of polygraphic recording of the parameters of the sleep-wakefulness cycle (SWC) deprivation of paradoxical sleep (PSD) was made in cats by means of nonemotional awakening, in one case after the transition of deep slow-wave sleep (DSWS) to paradoxical sleep (PS) and appearance of rapid eye movements (REMs) (REM-deprivation), while in the other - after appearance of single ponto-geniculo-occipital (PGO) spikes during DSWS (PGO-deprivation). At REM-deprivation the accumulation of specific inner need for PS appeared to occur more intensively than at PGO-deprivation. This is expressed, first, in the PS onset being more frequent at REM-deprivation than at PGO-deprivation, and secondly, there is far greater rebound of the deprived phase in the postdeprivation SWC with the first version of deprivation than with the other. The both facts are explained by that that at PGO-deprivation, in contrast from the REM-deprivation, PS deprivation is paralleled also by a partial DSWS deprivation.

Key Words: The sleep-wakefulness cycle, deep slow-wave sleep, paradoxical sleep, PGO-deprivation, REM-deprivation.

Introduction

In order to study the functional significance of paradoxical sleep (PS) in general, and in particular, to detect the specific inner need for it the various techniques (Dement 1960; Jouvet D. et al. 1964; Van Hulzen and Coenen 1980; Rechtschaffen et al. 1983) of nonpharmacological deprivation of this state of the brain has been successfully applied. The automatized methods (water tank method (Jouvet et al. 1964; Dement et al. 1967) and the method of disk (Rechtschaffen et al. 1983) as compared to the nonautomatized ones have been shown to create an additional stress situation and, thereby hindering the normal course of sleep-wakefulness cycle (SWC) complicate the possibility of analysing the results obtained (Fishbein 1970; Oniani 1984; Oniani and Lortkipanidze 1985). Nonautomatized method of paradoxical sleep deprivation (PSD) is accomplished by means of mere nonemotional awakening of the sleeping animal immediately after the PS onset in response to sensory stimulation or direct electrical stimulation of the brain activating structures. However, determination of the PS onset is complicated by the specific signs of its appearance being developed not synchronously, but asynchronously. The earliest messengers of approaching PS onset appear to be the ponto-geniculo-occipital (PGO) spikes (Jouvet and Michel 1959), which start arising during well developed slow-wave sleep (SWS) (see Dement 1972). Another basic parameter of PS as rapid eye movements (REMs) (Aserinsky and Kleitman 1953) starts to develop in the cat (Dement 1958) only after the onset of desynchronized electrical activity in the neocortex and violent development of the hippocampal theta rhythm (Jouvet 1965), i.e. considerably later after the appearance of the PGO spikes. Precisely this may perhaps explain that PSD mainly coincides with the appearance of REMs and more seldom with the appearance of PGO spikes (see Dement 1972).

The essential difference between the two versions of PSD consists in the following that during PGO-deprivation occurs a partial deprivation also of the most strongly developed SWS, while in the case of the other version, i.e. at REM-deprivation SWS is not affected. This difference between the two versions of PSD incites special interest considering the data published earlier (Oniani et al. 1984, 2000), suggesting the possibility of total and selective PSD via a partial deprivation of the preceding deep SWS (DSWS).

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Proceeding from this it may be expected that during application of PGO-deprivation the SWC structure may be influenced, during deprivation and postdeprivation period, not only by selective PSD, but more or less by partial deprivation of DSWS.

Methods

Experiments were carried out in 10 adult mature cats of either sex. For the reasons of polygraphic recording of SWC metallic electrodes were chronically implanted in the sensorimotor and visual areas of the neocortex, dorsal hippocampus, lateral geniculate body, posterior hypothalamus, the cervical and oculomotor muscles. The cardiac rhythm was also recorded. Surgery of the electrode implantation was made under nembutal anesthesia (30-35 mg/kg). Coordinates for the brain structures were derived from the atlas of Jasper and Ajmone-Marsan (1954). Experiments on the SWC registration were started 5-10 days after the surgery. To that end, the animals were placed in an experimental chamber comfortable for falling asleep, to which they had been habituated preliminarily. 24-hr recording of SWC was made. For a few days (3-5) the background recording was run, after which deprivation procedures were started. For the animal's awakening both during PGO- and REM-deprivation, we used electrical stimulation of the posterior hypothalamus with threshold parameters (100 per sec, 2-5 V, 0.1-3 msec) in order to elicit a mere nonemotional short fragment of behavioral awakening. Duration of deprivation procedure was either 24-hr or 12-hr. For the observations to be made on the recovery process a continuous recording of the SWC lasted for 24-hr after cessation of PSD with both versions.

Results and Discussion

1. Analysis of the SWC structure in baseline records.

In baseline records, when the experimental animal has been already well habituated to the experimental chamber and electroencephalographic (EEG) manifestations of DSWS develop on the face of convenient for this position of the body (the cat is curled up, its head is lying so that the cervical muscle tone is virtually completely relieved) the appearing single PGO spikes do not always develop optimally for DSWS to pass regularly into PS. Perhaps, because of the enhancement of inhibition of the spinal cord motor reflexes (Pompeiano 1965), some hardly noticeable shifts occur in the animal's posture, leading to a weak activation of the brain, which in its turn slightly alters, in terms of EEG parameters, the depth of SWS (Fig. 1A), but is sufficient to block the generation of PGO spikes at the level of the midbrain pons. Similar situation, on the face of hardly seen fluctuation of EEG manifestation of SWS, may be repeated until proper transition of SWS to PS. It makes impression that the PGO spikes in these conditions are but one of the components of DSWS (see Dement 1972). They, in these cases too, are actually but the most cogent signs for the approachment of PS onset. This fact holds interest for the comprehension of delicate neurophisiological mechanisms of triggering and maintenance of PS. It is known that between the mesencephalic and diencephalic structures regulating the triggering and maintenance of wakefulness and SWS there is a reciprocal interrelationship (Bremer 1970; Moruzzi 1972). On the other hand, these structures of wakefulness via the inhibitory influence strictly control the triggering mechanisms of PS as well. Therefore during well developed DSWS as a result of intensive inhibition of the mesencephalic activating structures the PS triggering mechanisms are released from the inhibitory influence of the structures of wakefulness and trigger PS properly (Oniani 1977), the so-called third state of the brain (Jouvet 1962; Snyder 1963).

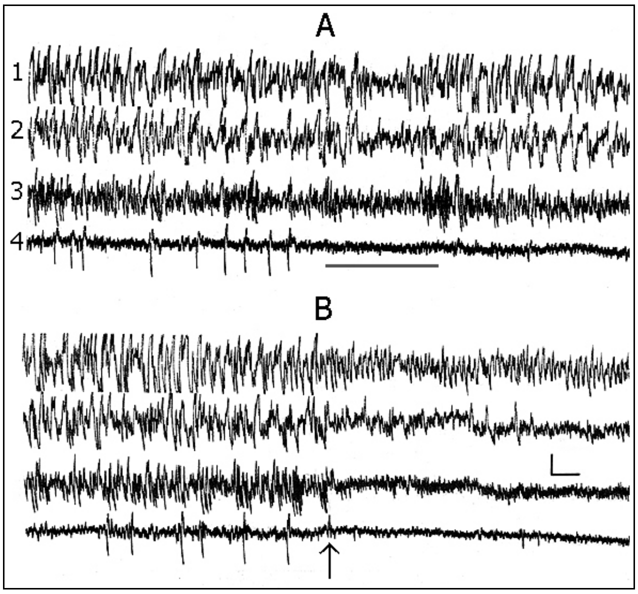

Figure 1. Dynamics of PGO spikes on the face of DSWS and at arousal.
A, spontaneous appearance and blocking of PGO spikes on the face of DSWS.
The horizontal line under recordings marks the moment of spontaneous slight EEG arousal.
B, a sample of PGO-deprivation through nonemotional awakening from DSWS; the moment of awakening in response to electrical stimulation is marked by an arrow.
Leads: 1, dorsal hippocampus; 2, visual area and 3, sensorimotor area of the neocortex; 4, lateral geniculate body. Calibration: 200 μV; 1 sec.

However, during DSWS and after the appearance of PGO spikes even a slight activation of mesodiencephalic structures of wakefulness (in this case as a result of change of the sleeping animal's body position) is sufficient to restore the inhibitory influence from the structures of wakefulness on those of PS. Analysis of this kind of the given fact leads to a speculative assumption that the brain structures triggering and maintaining SWS are not able to exert an inhibitory influence on the PS triggering mechanisms. Otherwise it would be hard to fancy even the fact that PS is being triggered namely on the face of DSWS, when the brain structures regulating the development of this phase work most intensively (Jouvet 1972). Here one should admit the existence of effective inhibitory influence on SWS regulating brain structures on the part of PS mechanisms. This would determine, as it were, unexpected transition of SWS to PS. It is likely that the assumption of Moruzzi (1972) concerning an unexpected appearance of PS was based namely on this, as though paradoxal fact. However, in our opinion, at more comprehensive analysis of the presently available facts there is nothing unexpected in that that the brain mechanisms regulating SWS namely during their maximal work stipulate triggering of PS, through inhibition of mesodiencephalic mechanisms of wakefulness, as well as further maintenance of this phase through the formation during its course of inner specific need for PS; this is clearly indicated by the below described results on PSD with different versions of nonpharmacological method.

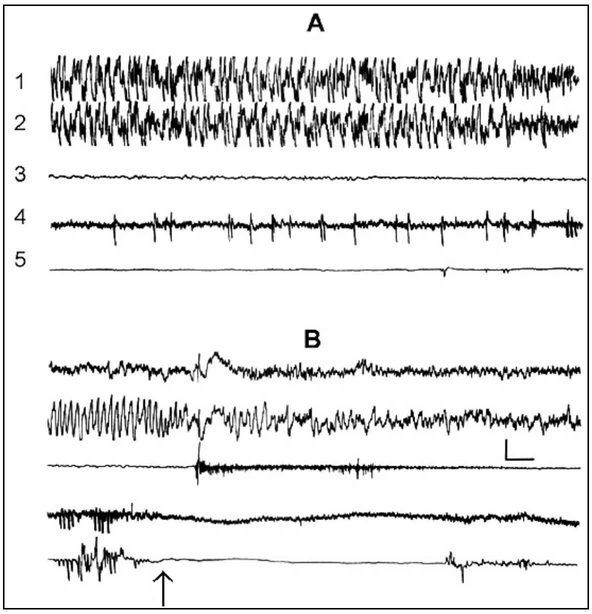

Figure 2. The electrical activity of the neo- and archipaleocortex, skeletal muscle tone and eye movements at REM-deprivation.
A, transition of DSWS to PS.
B, the onset of PS with REMs and fragment of wakefulness arised following evoked awakening; the moment of the electrical stimulus application is marked by an arrow.
Leads: 1, sensorimotor area of the neocortex; 2, dorsal hippocampus; 3, cervical muscle; 4, lateral geniculate body; 5, oculomotor muscles. Calibration: 200 µV; 1 sec.

Following a full adaptation of the animal to the experimental chamber, single PGO spikes appearing during DSWS, at the beginning, as a rule, get more frequent, then they are grouped, after which other parameters of PS are also triggered. It is namely at this stable course of SWC that the two versions of the classic nonpharmacological PSD method could be successfully compared.

2. Effect of REM-deprivation of PS on the SWC structure during deprivation and postdeprivation period.

The transient stage from SWS to PS is known to be characterized by desynchronized electrical activity in the neocortex and by partial EEG desynchronization in the hippocampus (Oniani et al. 1978). At this stage no conspicuous REMs are observable. However, soon against the background of prolonged EEG desynchronization in the neocortex a regular theta rhythm starts to develop in the hippocampus. Characteristically, development of the hippocampal theta rhythm is correlated with the appearance of REMs and there occurs a full-fledged formation of the so-called REM phase of sleep (see Kleitman 1963). If after the appearance of REMs nonemotional awakening of the animal in response to electrical stimulation of posterior hypothalamus is effected, then against the background of continuous EEG desynchronization in the neocortex, both the PGO spikes and REMs vanish (Fig. 2B). On the face of nonemotional awakening the hippocampal theta rhythm is also considerably suppressed. After the animal's awakening from PS, short fragments of wakefulness are followed by SWS restoration and after a certain time PS appears in the layout as described above. Systematic awakening of the animal with the onset of each subsequent PS phase causes an increase in the frequency of applied arousing stimuli (Fig. 3, column 2). More frequent PS onset in similar experiments is considered to be a result of accumulation of the intracerebral specific need for the deprived phase of SWC in view of lack of development of full value PS in duration (Dement 1960). In the course of REM-deprivation, in parallel with fall out from the cycle of proper duration PS, marked changes occur in the other two, as it were, spared phases - wakefulness and SWS (Fig. 4, column 2). Apparently, total amount of both phases (and especially of SWS) is increased as compared to baseline (Fig. 4, column 1) because of PS elimination from the cycle.

Accumulation of the specific inner need for PS during REM-deprivation has its impact on the rate of transition of SWS to PS. It is expressed in a gradual shortening of duration of that part of DSWS in which PGO spikes develop before turning into the full-fledged PS phase (Fig. 5). It is interesting to mention that if in the process of REM-deprivation of PS there arises a prolonged fragment of wakefulness that is naturally followed by SWS regularly passing into PS, then partially recovers duration of that part of DSWS during which develop PGO spikes (Fig. 5, the last circle). This fact indicates that a more or less prolonged fragment of wakefulness somehow delays the accumulation of the need for PS, or attenuates the level of its need already accumulated during deprivation. A conclusion can be drawn that accumulation of the PS need during REM-deprivation may affect also DSWS expressed in the shortening of its quota duration for PS triggering.

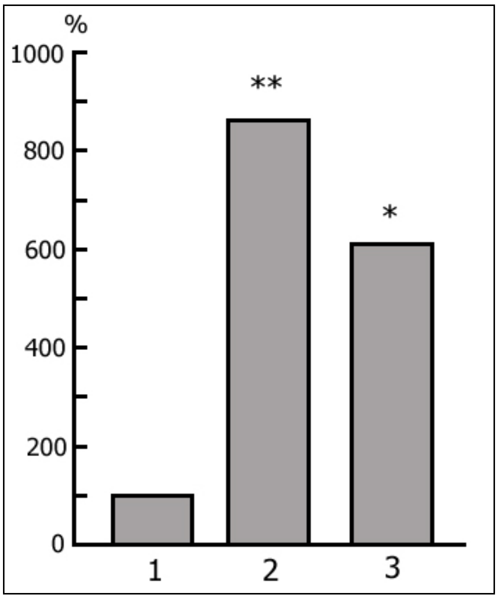

Figure 3. The quantity of evoked awekenings at REM-deprivation (column 2, ** P<0.001) and PG)-deprivation (column3, * P<0.01) compared to the number of PS phases onset in the baseline SWC (column 1, is taken as 100%).

A more or less prolonged elimination of PS from the SWC through REM-deprivation exerts a significant influence also on the structure of cycle in the postdeprivation period that manifests itself in a marked increase of PS amount and respectively, a decrease of the share of wakefulness (Fig. 6, column 2), compared to the baseline SWC (Fig. 6, column 1). At this time the phase of SWS undergoes less pronounced alteration. Here particularly interesting seems the reciprocal interrelationship between the phases of wakefulness and PS in the SWC. Similar concurrence is apparently realized in the satisfaction of the inner need accumulated during REM-deprivation. It has been demonstrated earlier (Oniani et al. 1988a, 1988b, 2001) that replacement of PS phases in the SWC by the fragments of active wakefulness equivalent in duration causes the cessation of PS accumulation, as a result of which during this version of deprivation there is neither rise in frequency of PS onset during deprivation, nor its rebound in the postdeprivation period. This fact, too, indicates on the concurrent interrelationship between wakefulness and PS in the SWC in consuming the inner need formed in the brain during SWS.

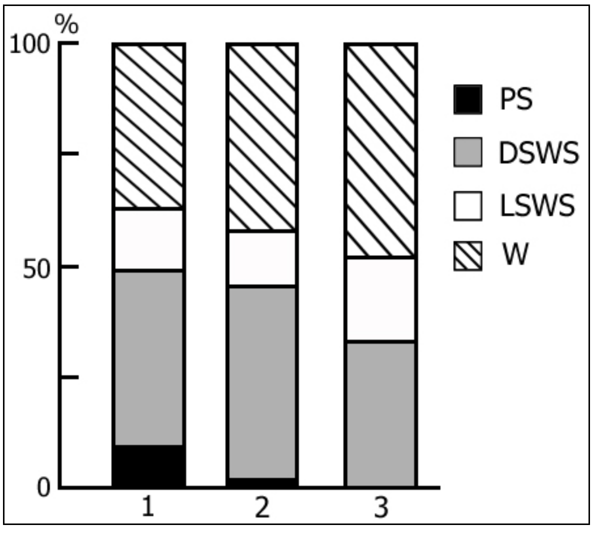

Figure 4. Percentage ratio of various SWC phases in the baseline (column 1), during REM-deprivation (column 2) and PGO-deprivation (column 3).
Notations: W- wakefulness; LSWS - light SWS; DSWS - deep SWS; PS - paradoxical sleep (are the same on the Figure 6).

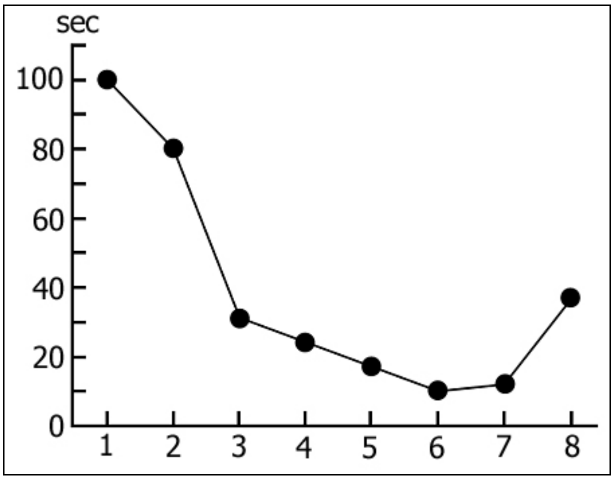

Figure 5. Effect of REM-deprivation on the rate of DSWS transition to PS.
On the ordinate: time in sec. On the abscissa: 1, 2, 3, 4, 5, 6, 7, 8 - sequence of deprivation samples.
Circles - duration of the DSWS part in which PGO spikes develop before PS onset in the REM-deprivation process.

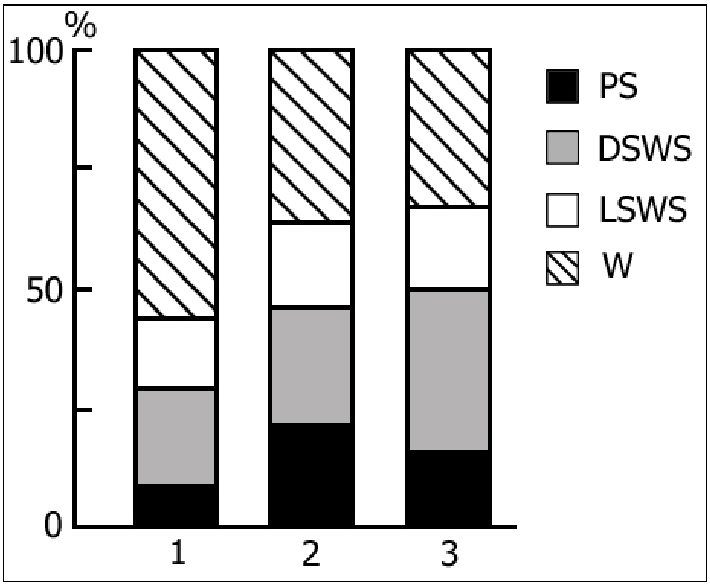

Figure 6. Percentage ratio of various SWC phases in the baseline (column 1) and in the postdeprivation period after cessation of REM-deprivation (column 2) and PGO-deprivation (column 3).

3. Effect of PGO-deprivation of PS on the SWC structure.

As been indicated above, this version of nonpharmacological PSD, the instantaneous nonemotional awakening of the animal was produced immediately after the appearance of first single PGO spikes during DSWS (Fig. 1B) so that the SWS stage also suffered partial deprivation. It appeared that with the use of this version, the number of awakenings for a standard fraction of time necessary to prevent SWS transition into PS is tangibly lower (Fig. 3, column 3) than in the case of application of REM-deprivation (Fig. 3, column 2). Naturally, partial deprivation of DSWS during PGO-deprivation has a noticeable effect on the ratio of wakefulness and SWS during the procedure that is expressed in a substantial decrease of DSWS amount and an increase both of the phase of wakefulness and light SWS (Fig. 3, column 3), compared to the respective data obtained at REM-deprivation (Fig. 3, column 2). As regards the postdeprivation ratio of various SWC phases, in this aspect, too, the results obtained at PGO-deprivation of PS, tangibly differ from those obtained at REM-deprivation. First, although in this case too significant PS rebound is available in the postdeprivation SWC, but quantitatively it is markedly less (Fig. 3, column 3) than the PS rebound after cessation of REM-deprivation (Fig. 3, column 2). Besides, following PGO-deprivation in contrast to the data obtained in the version of REM-deprivation, there is a significant rebound also of DSWS in the postdeprivation SWC.

This fact can be readily explained by that that at PGO-deprivation there occurs also a partial deprivation of DSWS and thereby a more or less intensive accumulation of inner need for this phase too. On the other hand, the partial DSWS deprivation must retard the formation of the specific PS need, what, naturally, may affect the extent of rebound of this phase in the postdeprivation period.

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