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The Influence of Low LSD Dose Administration during Sleep in Rats

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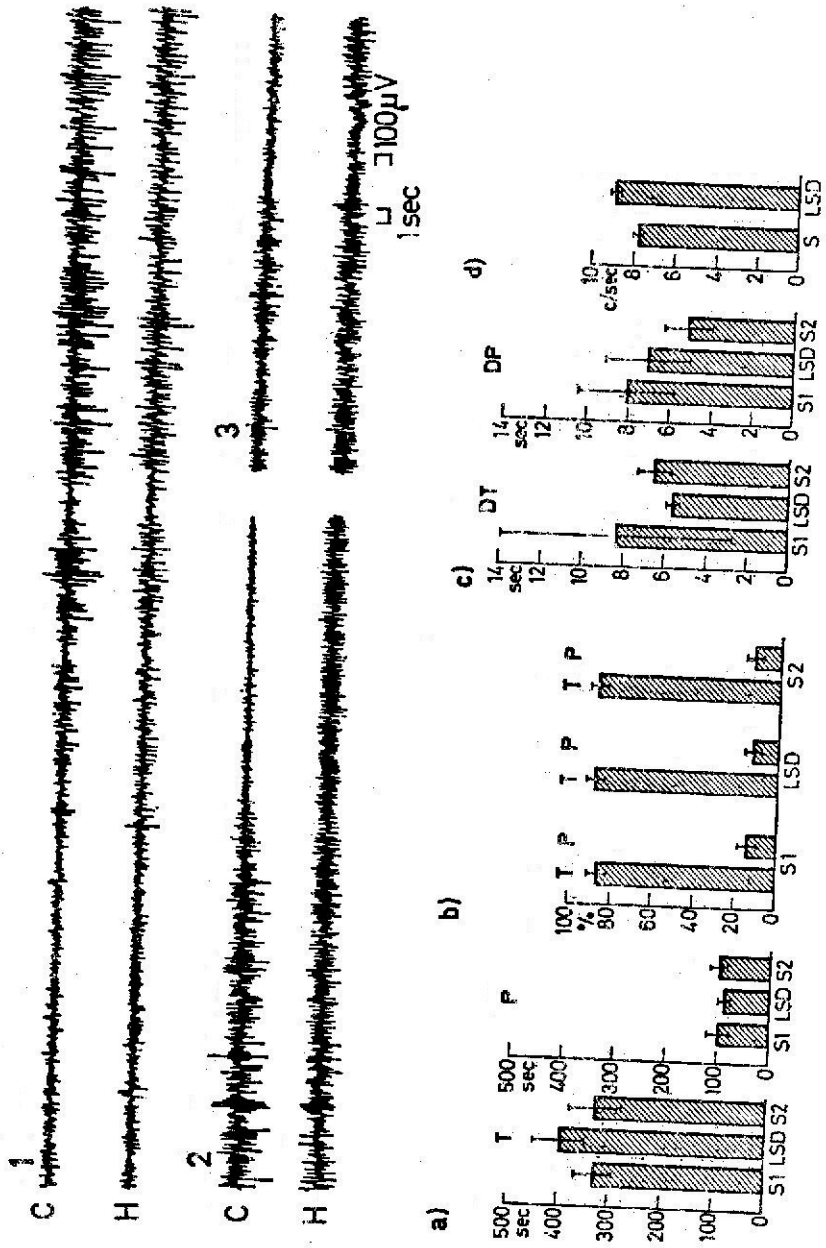
Abstract. LSD (subcutaneous infusion of 125 γ/kg of body weight in 1 ml during 60 min) administered during sleep in rats with implanted electrodes increases the frequency of hippocampal theta activity during paradoxical sleep. Neither the duration of slow wave and paradoxical sleep phases nor the total amount of slow wave and paradoxical sleep was influenced by the drug.

Key-Words: Sleep — EEG — Rats — LSD.

It is known that paradoxical (rapid eye movement, rhombencephalic) sleep (PS) is correlated with dreams (Aserinsky and Kleitman, 1955; Dement and Kleitman, 1957) and that a certain degree of psychological similarity between dreaming and the state following LSD administration (Stoll, 1947) seems to exist in humans (Cartwright, 1966). It might be of some interest therefore to analyse the influence of LSD upon sleep cycle alternation and mainly upon the duration and electroencephalographic characteristics of the PS.

Method

10 hooded female rats 2—3 months old and weighing about 200 to 250 g were used in this study. Bipolar electrodes (tip distance about 0.5 mm) were implanted in the frontal cortex and dorsal hippocampus bilaterally under ether anaesthesia. About 10 days later the EEG activity was recorded continuously from 9 a.m. to 4 p.m. in animals kept on a cotton bed in a glass container placed in a sound proof box (for details see Radil-Weiss and Stýblová, 1967). Before the experiment a syringe was fixed subcutaneously in the region of the neck. The animal was connected by a flexible cable with the EEG apparatus and by a thin polyethylene tubing with an infusion pump. The experiment started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S1
LSD
S2
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Fig. 1

after continuous slow wave (SWS) EEG activity (lasting for more than 5 min) developed with slow infusion of saline (1 cm^3 during 80 min) for approximately 2 h. Saline was then replaced by 125 γ/kg body weight of LSD in 1 ml of solution administered over 60 min, without awaking the rat. In two animals the dose of LSD was repeated immediately after the first. In the remaining 8 rats 1 ml of saline was slowly injected for the second time over a 80 min period. The EEG recordings and the behavior of the animals were observed throughout the experiments and the results of the visual scoring of the EEG recordings was analysed statistically.

Results

The results are summarized in Fig. 1. Neither the basic EEG and behavioural pattern of alternation of the SWS-phase and the PS-phase, nor their average duration (Fig. 1 a) and the ratio of the total amount of SWS and PS (Fig. 1 b) was altered by LSD, the total sleep time being also similar. The duration of spontaneous desynchronization reactions occurring during the SWS phase and often at the end of PS-phase (Fig. 1 c) remained similar under both conditions. The only significant finding was an increase in the frequency of hippocampal theta activity during PS after LSD administration (Fig. 1 d).

Discussion

The influence of LSD on sleep patterns has been investigated by different authors with contradictory results. Hobson (1964) found a decrease in the amount of PS in cats after LSD, while an increase was reported in rats by Hartmann (1967, 1969) and in humans by Muzio

Fig. 1. Upper part: EEG recording from the frontal cortex (*C*) and dorsal hippocampus (*H*) after LSD administration. First row (*1*) — development of slow wave sleep, second row—beginning (*2*) and end (*3*) of the paradoxical sleep phase. Lower part A: Average duration of slow wave (*T*) and paradoxical (*P*) sleep phase during the first subcutaneous saline (*S1*), LSD and the second saline (*S2*) infusion, B: Proportion of slow wave and rhombencephalic sleep in the same conditions (computed from total sleep time = 100%). C: Duration of spontaneous desynchronization reactions occurring during slow wave sleep phases (*DT*) and of those following immediately after the paradoxical sleep phases (*DP*). D: Average frequency of hippocampal theta activity (counted always in two randomly chosen 10 sec intervals before and in two after LSD administration in the 10 animals). The duration of SWS-phase (A) represents the length of the record preceding the paradoxical sleep phase covered by generalized slow wave EEG not interrupted by desynchronizations longer than 60 sec. In case B the total duration of slow wave sleep periods longer than 10 sec have been considered. The beginning and end of paradoxical sleep (A and B) has been determined on the basis of the onset and disappearance of hippocampal theta activity. Only recordings clear both with respect to the EEG manifestations and gross behavior observed have been included in the statistics. Average values $\pm$ S.E. of the mean

et al. (1966) and Green (1969). The results of Khazan and Sawyer (1964) in rabbits seem to be in agreement with those of Hobson (1964). The lack of PS in their experiments is understandable, however since SWS was also absent during the observation period. We found no changes of the PS parameters described in the rat. We realize, however, that the observation period was not very long, the LSD doses were not very high (as we wanted to prevent the arousing effect of LSD), and the experiment was performed in the animals only once. Since the results of the above papers are contradictory, and the experiments were performed in different species and the amount of data on which they are based is not very extensive, it may be concluded that the facilitatory or potentionating effect of LSD on PS in mammals is not yet proved generally. It is not possible, therefore, to derive any conclusion regarding the interrelationship of dreaming and LSD induced states on the basis of neuropharmacological arguments of the described type.

A serious methodical difficulty in the evaluation of the influence of LSD (and some other drugs) upon sleep follows from the fact that it acts against the onset of sleep and/or may have an arousing effect in sleeping animals (Rinaldi and Himwich, 1955; Bradley, 1958; Schweigerdt, 1966). The neurophysiological mechanisms involved may be quite different in both cases, however. The latter possibility seems to have less experimental support than the former. Injection of LSD (and other "arousing" drugs) in the waking condition might have more influence on the onset of sleep, which is a phenomenon sui generis, than on the sleep itself. In the present experiment the influence of LSD upon sleep was studied by administering the drug during sleep, in such a way that the procedure itself could not arouse the animal.

The only significant finding, that LSD increases the frequency of hippocampal theta activity during PS, proves that the dose used was not generally subthreshold, and is in agreement with the mentioned data on the activating effect of this drug upon the ascending reticular activating system. We have found in other experiments that the theta frequency during PS is a parameter typical for rats which are interindividually different with respect to their behavioural manifestations. The PS theta frequency was well correlated in this case with the mean theta frequency appearing in the same animals as a response to novel stimuli. The average duration of the PS-phase did not differ in these animals (Irmiš *et al.*, 1971). It seems to be very probable, therefore, that the mechanisms responsible for alternation (and duration) on the sleep phases are not linked with those determining the frequency of theta activity during PS. The increase in frequency of hippocampal theta activity after LSD raises the question (which may be solved in human experiments only) whether the psychological dream content might be

influenced by LSD without a necessary change of the duration, frequency etc. of the PS.

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