POSSIBLE CORRELATIONS BETWEEN ALCOHOL MOTIVATION LEVEL AND ELECTROPHYSIOLOGICAL STRUCTURE OF SLEEP IN RATS

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Deprivation of the REM stage of sleep in rats of the Long Evans line has been shown to increase the voluntary ethanol consumption [4]. This suggests that phasic processes taking place during sleep are one of the factors responsible for a craving for alcohol.

In the present investigation the electrophysiological structure of sleep and its changes under the influence of ethanol were studied in rats predisposed and not predisposed ab initio to voluntary alcohol consumption, in order to discover any possible correlations between the level of alcohol motivation and the character of the sleep structure in these animals.

EXPERIMENTAL METHOD

Experiments were carried out on 12 noninbred male rats weighing (under chronic experimental conditions) 250-380 g, divided beforehand into two groups. Animals initially predisposed to alcohol consumption and not so predisposed were selected by a method based on differences in behavioral activity under stress (enforced swimming), described in [5] and modified in [1]. The rats were compelled to swim in a tank of water (20°C) for 10 min. The total time spent by the rats in a posture of immobilization, when the animal passively floated in a vertical position, tilted forward a little, with the head just above the water surface, i.e., refrained from energetic activity, was recorded. As a result, rats with a relatively short and long duration in the immobilization posture were selected and, on the basis of this criterion, they were divided into active and inactive, respectively. The animals were anesthetized by inhalation of halothane and chronic nichrome wire electrodes were implanted into their hippocampus (coordinates A 1.0; H + 2.5; L 3.5 [3]) and into the dorsal group of cervical muscles, and fixed to the skull with the quick-hardening plastic "Protakril." One week after the operation, and after 3 days of adaptation to the experimental conditions, the animals were placed in individual Plexiglas cages (20 × 10 × 10 cm), and the electrophysiological structure of their sleep was recorded continuously for 4 h on an 8-channel electropolygraph (Nihon Kohden, Japan) from 11 p.m. to 3 p.m. When the data were analyzed the absolute duration of the waking phase, and the phases of slow and REM sleep, the number of separate episodes of REM sleep, their average duration, and also the latent period of this phase (the time until the appearance of the first episode of REM sleep) were analyzed. In the next series of experiments the effect of a single dose (1 g/kg) of ethanol (in the form of a 10% solution) on the structure of sleep of the active and inactive animals was studied. Ethanol was injected intraperitoneally 30 min before the beginning of electrophysiological recording. Five days after injection of alcohol the rats were placed for 20 days in individual cages, equipped with two graduated feeding bowls, and were allowed free choice between a 10% solution of ethanol and water, and the volume of liquid drunk was recorded daily. The results were subjected to statistical analysis by Student's test and by the nonparametric test of differences [5].

EXPERIMENTAL RESULTS

The inactive animals consumed 3.4 times more of the 10% ethanol solution than active animals ($p < 0.01$). This is in agreement with earlier data on predisposition of inactive individuals ab initio to the development of experimental alcoholism [1]. Meanwhile, in rats avoiding energetic activity (inactive) in a stress situation (obligatory swimming), a relative

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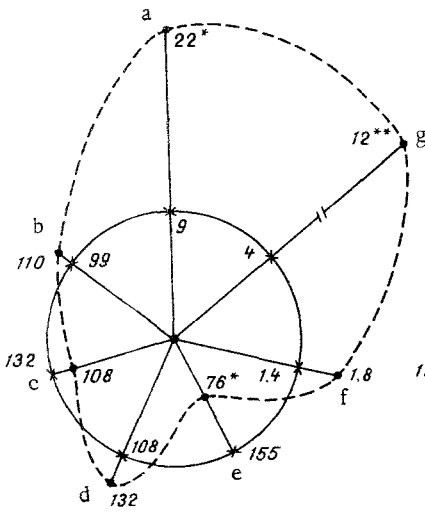

Fig. 1

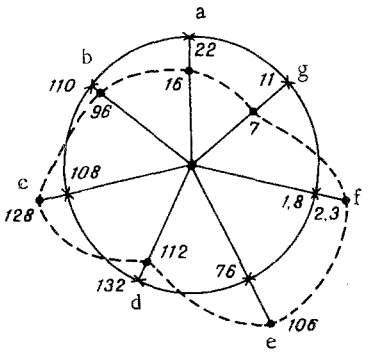

Fig. 2

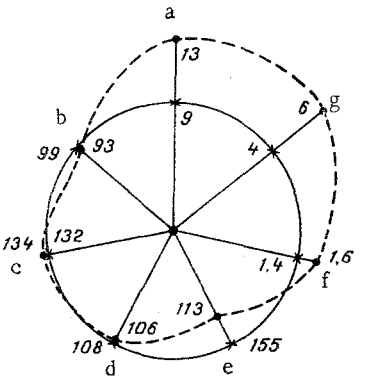

Fig. 3

Fig. 1. Differences in sleep structure of active and inactive rats. Circumference of circle represents main parameters of sleep structure in active rats, not predisposed to alcohol consumption; broken line indicates principal parameters of sleep structure of inactive rats, predisposed to alcohol consumption. *$p < 0.05$, **$p < 0.01$. Here and in Figs. 2 and 3: a) REM sleep, b) slow sleep, c) time of wakefulness, d) total duration of sleep, e) latent period, f) mean duration of episodes of REM sleep, g) number of episodes of REM sleep. Numbers: a-f) min; g) absolute number.

Fig. 2. Effect of a single injection of ethanol (1 g/kg, 10% solution, intraperitoneally) on sleep structure of inactive animals. Circumference of circle indicates sleep structure of inactive rats under ordinary conditions; broken line the same after a single injection of alcohol.

Fig. 3. Effect of a single injection of ethanol (1 g/kg, 10% solution, intraperitoneally) on sleep structure of active animals. Circumference of circle denotes sleep structure of active rats under ordinary conditions; broken line — the same after a single injection of alcohol.

excess of REM sleep was found. The relative proportion of REM sleep in these rats was 2.7 times greater than that in the active rats ($p < 0.05$). These differences in the animals of these two groups were caused by the fact that the number of individual episodes of REM sleep was 2.8 times less ($p < 0.01$) and the latent period of this phase was longer (twice as long; $p < 0.05$) in the active animals than in the inactive rats (Fig. 1). The duration of wakefulness and of the phase of slow sleep, and the mean duration of the individual episodes of REM sleep in the animals of these groups did not differ statistically significantly.

A single injection of ethanol (1 g/kg, 10% solution, intraperitoneally) caused a decrease in the REM phase of sleep in inactive animals, so that the value of this parameter came close to that in active rats in which, on the contrary, there was a tendency for some increase in the REM phase of sleep under these conditions (Figs. 2 and 3). Injection of exogenous ethanol thus abolished those basic differences in sleep structure which were present under ordinary conditions, i.e., the pattern of sleep in animals of the two groups became virtually identical. These results are in agreement with earlier data showing that in rats predisposed to the development of experimental alcoholism (selected on the basis of differences in behavioral activity in a stress situation), alcohol has a specific normalizing action on behavior, whereas conversely, in rats refusing alcohol (active) it considerably shortens the duration of activity in a situation of unavoidable swimming [1], and it thus brings them more into line with the inactive rats, inclined to develop experimental alcoholism.

Meanwhile deprivation of REM sleep is known to lead, on the one hand, to hyperexcitability of the animals [2], and on the other hand to an increase in the voluntary consumption of ethanol and a change in activity of individual neurochemical systems of the brain [4]. It can be concluded from these results that the neurophysiological and neurochemical processes taking place during REM sleep play a definite role in the formation of predisposition to ethanol con-

sumption: a relative excess of REM sleep in inactive animals, reflecting their emotional status, is evidently one factor determining the high level of alcohol motivation.

LITERATURE CITED

1. A. B. Kampov-Polevoi, The Pharmacology of Experimental Alcoholism [in Russian], Moscow (1982), pp. 130-135.
2. V. S. Rotenberg and V. V. Arshavskii, Investigative Activity and Adaptation [in Russian], Moscow (1982), p. 83.
3. J. De Groot, The Rat Forebrain in Stereotaxic Coordinates, Amsterdam (1959).
4. R. Meddis, Br. J. Psychol., 66, 225 (1975).
5. R. D. Porsolt, G. Anton, N. Blavet, and M. Jalfre, Eur. J. Pharmacol., 47, 379 (1978).

ANTICONVULSANT ACTION OF SUPEROXIDE DISMUTASE

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Research in our own [1, 2, 4] and other [6] laboratories has shown that disturbances in the regulation of lipid peroxidation (LPO) are an important stage in the pathogenesis of certain forms of epilepsy. As one possible cause of disturbances in LPO regulation in epilepsy the writers have suggested the development of insufficiency of the antioxidant system and, in particular, insufficiency of the "antioxidant protection" enzymes [10]. It has been shown that the development of generalized epileptic activity (EPA) in rats is accompanied by a fall in the blood level of superoxide dismutase (SOD) activity [8]. A significant fall in SOD activity and also in the activity of another enzyme of "antioxidant protection" — namely glutathione peroxidase — has been found by the writers also in the blood of patients with generalized forms of epilepsy [8]. Simonyan et al. [9] showed that preliminary administration of SOD to rats considerably weakens the development of metrazol convulsions. These facts confirm the validity of the hypothesis mentioned previously.

When continuing our research in this direction, we studied the effect of SOD on penicillin-induced focal EPA in rats and also on activity of LPO in the brain.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 180-230 g, kept on a standard diet under ordinary animal house conditions. The development of EPA in the rats' cerebral cortex was induced, just as previously [3], by application of the sodium salt of penicillin to the sensomotor cortex. Under hexobarbital anesthesia two burr-holes 2-4 mm in diameter were drilled in the animal's skull above the sensomotor cortex of both hemispheres and the dura mater was removed from these areas. To record the electrocorticogram (ECoG) silver electrodes were applied to the dura at a distance of 0.2-0.3 mm in front of the burr-hole. The reference electrode was inserted into deep brain structures at the junction between frontal, temporal, and parietal bones of the right hemisphere. The exposed brain surface was moistened with physiological saline and covered with adhesive tape. The experiments began the day after the operation, on unanesthetized animals. A preparation of SOD obtained from bovine erythrocytes (Sigma, USA) was injected intraperitoneally, in physiological saline (1 mg/ml), in a dose of 1 mg/kg body weight 30 min before application of penicillin. Control animals received an injection of the corresponding volume of physiological saline. The ECoG

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