EEG CHANGES IN ANIMALS WITH NEUROSIS AS A CORRELATE OF DISTURBANCES OF BRAIN METABOLISM

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Electrophysiological methods are effective ways of studying the mechanisms of development of emotional reactions. The electroencephalogram (EEG) contains information on widely different aspects of processes taking place in the body — from metabolic processes at the cellular level to higher psychological functions. That is why one of the most widespread and objective methods of studying the whole brain is electroencephalography [1, 8]. Electrical activity of the brain is an objective criterion of its functional state, as it undergoes regular changes depending on motivational excitation. It is generally accepted that desynchronization of the EEG, a decrease in its amplitude, the development of asymmetry, and so on, are electrophysiological correlates of emotional reactions [10, 12]. The object of this investigation was to compare changes in the EEG of various animals (rats, cats, monkeys) in a state of neurosis and during treatment with the dynamics of neuronal metabolism.

EXPERIMENTAL METHOD

Experiments were carried out on 80 noninbred male rats classed as highly emotional in their type of behavior, on seven adult cats, and five adult monkeys (*Macaca rhesus*). Experiments on monkeys were carried out at the Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR, Sukhumi. The animals were numbered in accordance with the Institute's catalog. A state of neurosis was induced in rats by the method described previously [5], in cats by 3-weekly injections of thyroid extract, and in monkeys by keeping them in special restraining cages, which induced a typical state of neurosis in the animals with manifestation of rage, aggressiveness, etc. The EEG of the monkeys was recorded on an eight-channel electroencephalograph and analyzed on an integrator (Orion, Finland); the EEG of the cats and rats was recorded on a four-channel 4EEG-3 electroencephalograph. Electrodes were implanted into deep structures and cortical formations [4, 11], and the position of the electrodes was verified histologically. The rhythm change response was assessed as the coefficient K_S and energy (ΣA_S) of synchronization [9]. ATPase activity of brain homogenate was determined by measuring the increase in inorganic phosphorus concentration in the incubation medium [13]. Samples for incubation (15 min, 37°C) contained in a final volume of 1 ml: ATP 5 mM, Tris-HCl 50 mM, NaCl 100 mM, KCl 20 mM, $MgCl_2$ 5 mM, ouabain 1 mM; pH 7.4. The reaction was stopped with 10% TCA. Protein was estimated by the usual method. Na,K-ATPase activity was calculated as the difference between total ATPase and Mg-ATPase activities. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

A state of emotional overstrain, leading to neurosis in the animal and subsequently to stress, was manifested as a sudden disturbance of spontaneous electrical activity. These changes depended on the behavioral type of the animal. In highly emotional rats in a state of anxiety neurosis, the EEG predominantly showed low-amplitude polymorphic activity, α-rhythms of irregular frequency, and distinct γ- and β-rhythms. Low bilateral paroxysms of polymorphic character were frequently found. Changes in the EEG of the cats depended on the individual typological characterisitcs of their emotional and behavioral status and the times of development of neurosis. In the animals of group 1 (three cats), characterized by a complete spectrum of emotional activity, by evenness of temper, and by a tendency toward positive

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TABLE 1. Changes in Rhythm-Binding Response of Cats with Thyrotoxic Neurosis and during Its Treatment, to Photic Stimuli

State of animals	K_S, %		ΣA_S, μV	
	Frequency presented, Hz			
	5	20	5	20
Control	98,6±1,8	92,9±2,4	10 944,6±856,0	8361,0±624,0
Neurosis (21st day)	68,8±2,0*	41,2±3,1*	5 504,0±254,0*	2060,0±156,4*
5th day of nikogamol treatment (10 mg/kg)	92,4±3,2**	78,9±3,0**	9029,3±298,5**	5351,0±201,7**

Legend. Number of observations in all experiments was over 20. Here and in Table 2: *P < 0.05 compared with control, **P < 0.05 compared with neurosis.

TABLE 2. Changes in ATPase Activity (in μmoles P_i/mg protein/h) of Various Brain Structures of Rats with Neurosis and Its Prevention by Drugs (M ± m)

Brain structure	State of animals	Mg-ATPase	Na,K-ATPase
Cortex	Control	4,54±0,06	1,86±0,12
Limbic system	Neurosis (21st day)	2,65±0,04*	1,04±0,11*
	Neurosis + nikogamol	4,09±0,11**	1,54±0,09**
	Control	3,66±0,05	1,46±0,05
Brain stem	Neurosis (21st day)	2,90±0,66*	1,09±0,11*
	Neurosis + nikogamol	3,45±0,06**	1,32±0,07**
	Control	3,68±0,05	1,57±0,06
	Neurosis (21st day)	2,99±0,06*	1,34±0,09
	Neurosis + nikogamol	3,52±0,13**	1,47±0,20

Legend. In all experiments number of observations was 9-10, dose of nikogamol 10 mg/kg.

emotions and avoidance of conflicting situations [2], the EEG was dominated by low-voltage high-frequency waves. In the experimental chamber they often became drowsy, with the appearance of slow waves, "bursts of spindles," and an increase in amplitude. In group 2 (four cats) the animals were characterized by an increased level of anxiety, a tendency toward fear, passive forms of behavior, and narrowing of the emotional spectrum. The EEG was distinguished by average amplitude of α-like waves and by the appearance of frequent "bursts of spindles" of high amplitude, synchronized in all derivations. Meanwhile, high-frequency low-amplitude waves were superposed on the slow waves. Injection of thyroid extract into the animals appreciably altered their behavior. They became restless and aggressive, their pupils dilated, a characteristic brightness of the cornea appeared, and they developed tachycardia. At the same time the character of their EEG changed. These phenomena intensified with time. Toward the end of the first week of administration of thyroid extract the amplitude and number of α-waves increased considerably in the animals of group 1, whereas in the animals of group 2, on the contrary, the voltage fell appreciably, the number of "bursts of spindles" was reduced and fast-wave activity appeared. Toward the end of the third week (completion of neurosis formation) EEG changes in animals of both groups were similar in type and were characterized by marked desynchronization. By this time the ability of the cortical neurons to modify their rhythm to bind the frequency of applied photic stimuli had worsened considerably (Table 1). The value of K_S was significantly reduced for low frequencies (5 Hz) from 98.6 ± 1.8 to

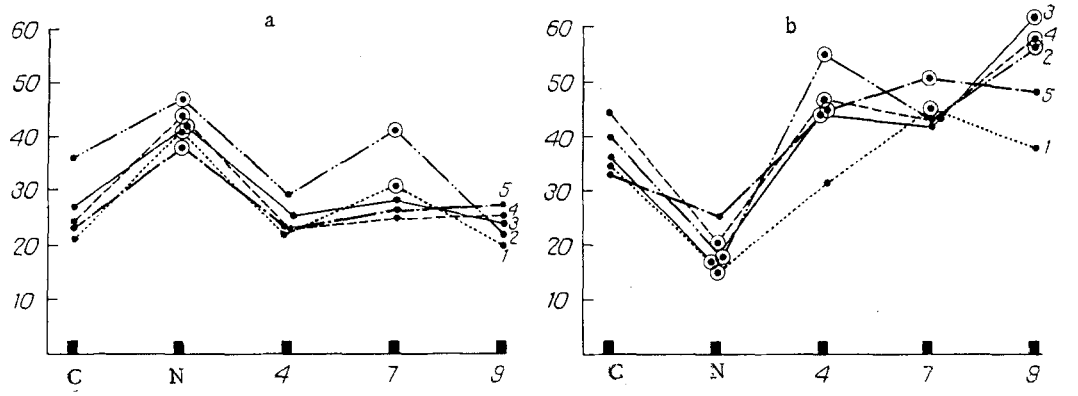

Fig. 1. Changes in total energy (in μV/sec) of EEG of monkey No. 14306 during neurosis and a course of nikogamol. Abscissa, days of administration of drug, a) fast-wave components of EEG (γ, β_1, β_2), b) slow-wave components of EEG (α, θ, δ). 1) Visual cortex, 2) sensomotor cortex, 3) hippocampus, 4) frontal cortex, 5) septum. Circled dots indicate significant differences from original data. C) Control, N) neurosis.

68.8 ± 2.0% and, in particular, for high frequencies (20 Hz) from 92.9 ± 2.4 to 41.2 ± 3.1% ($P < 0.001$). There was a parallel decrease also in the energy of synchronization from 10,944 ± 856.0 to 5504.0 ± 254.0 μV and from 8361.0 ± 624.0 to 2060.0 ± 156.4 μV ($P < 0.001$) respectively. A similar pattern was observed in monkeys (Fig. 1). In monkey No. 14306, in a state of neurosis, a significant increase was observed in the total energy of fast-wave components of the EEG (γ, β_1, β_2) and a decrease in total energy of the slow-wave components (α, θ, δ) in practically all the cortical and deep brain structures studied.

Consequently, the same rule was observed in neurosis in the background EEG of both lower and higher animals: an increase in total energy of fast-wave components and a decrease in total energy of slow-wave components, i.e., marked desynchronization with flattening of the EEG. Previously the writers showed [5-7] that in a similar situation of neurosis brain metabolism and, in particular, its energy metabolism is disturbed. Oxidative phosphorylation is inhibited, the concentration of high-energy compounds is reduced, the nucleotide pool is redistributed with a fall in the triphosphate level, and the adenylate charge is reduced. As the EEG correlate in this investigation we chose activity of one of the most important enzymes of energy metabolism, namely ATPase, which gives some idea of the utilization of energy of ATP.

The experimental results showed that in neurosis, besides characteristic EEG changes described above, changes also take place in ATPase activity of rat brain homogenate (Table 2). Mg-ATPase activity is significantly inhibited in all brain structures studied. This fact may be evidence of a switch to the level of more economic utilization of high-energy compounds by the brain, having regard to the parallel inhibition of oxidative phosphorylation. Together with inhibition of Mg-ATPase activity, activity of Na,K-ATPase was similarly inhibited (by 40%), but only in the cortex and limbic system. Activity of this enzyme in brain-stem formations was unchanged. This is in agreement with data in the literature indicating definite "inertia" of brain-stem formations in a change of metabolism [3]. Na,K-ATPase activity has a direct bearing on transmembrane processes and, correspondingly, on the formation of electrical excitability of neuron membranes, reflected in the bioelectrical activity of the brain as a whole. EEG changes in neurosis are thus evidence not only of functional disturbances, but also of metabolic disturbances in neurons.

Proof of this is given by the fact that the use of psychotropic drugs, restoring normal brain metabolism, also restores the normal EEG. A course of nikogamol prevented changes in ATPase activity developing during neurosis (Table 2). Its action was particularly effective on Mg-ATPase activity. Meanwhile the electrical activity of the brain was equalized. The rhythm-binding response was restored in cats (Table 1), and the total energy of the fast-wave components of the EEG in rats and monkeys decreased whereas the total energy of the slow components increased. The increase in slow-wave activity not only in cortical formations, but also in structures of the limbic system (hippocampus and septum) can be interpreted as predominance of inhibitory processes.

It can thus be concluded that changes in the EEG of animals developing in neurosis are a correlate of disturbances of brain metabolism and, in particular, of the processes of utilization of the energy of high-energy compounds.

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ADAPTIVE CHANGES IN RAT MYOCARDIUM DURING PERIODIC COOLING

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Investigations [2, 3] have shown that the immigrant population of the Far North develops hypertrophy of the right ventricle during adaptation to extremal environmental conditions. According to one study [5], when rats were cooled to a temperature of 5°C a significant increase in weight of the heart took place in the 4th week of the experiment on account of hypertrophy of both ventricles. However, no other data on organometric changes in the heart during cooling of animals to lower temperatures could be found in the literature.

The object of this investigation was to study the heart of rats during periodic measured cooling by morphometric and correlation analysis.

EXPERIMENTAL METHOD

Experiments were carried out on 55 noninbred male albino rats weighing initially 190 ± 10 g. The control group consisted of 15 rats. For 6 h daily for 1 week, 40 rats isolated from each other were kept in a Foutron (East Germany) climatic chamber at temperatures of +4°, 0°, −5°, −12°, and −20°C. The animals were killed 5-10 at a time by decapitation each week. Autopsy and separate weighing of the heart were carried out by Avtandilov's method [1] in the present writers' modification: Before the ventricles were opened, both atria were separated. The area of the inner surface of the ventricles was calculated by weighing replicas of them on paper. The material was then fixed in Lillie's solution. Pieces of tissue were embedded in paraffin wax. Histological sections were stained with hematoxylin–eosin, picrofuchsin and fuchselin, and by the PAS reaction. By means of an ocular hexagonal grid, the

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