COMBINED ELECTRICAL ACTIVITY OF SOME SUBCORTICAL STRUCTURES IN THE BRAIN OF ALBINO RATS AT VARIOUS STAGES OF SODIUM FLUOROACETATE POISONING

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Changes in the combined electrical activity of the reticular nucleus of the thalamus and of the caudate nucleus during fluoroacetate poisoning take place in three stages. In the first stage the combined electrical activity decreases on account of weakening of the slow waves. In the second stage the decrease stops and fast waves are strengthened. In the third stage all forms of activity are reduced.

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During investigation of pathophysiological changes in albino rats poisoned with sodium fluoroacetate (FA) and a number of related compounds, a decrease in the total oxygen consumption (TOC) lowering of the body temperature, and a decrease in the tissue respiration of various organs, notably the skeletal muscles, and disturbances of cardiac activity were observed [1, 3]. Comparison of these changes in the course of poisoning with changes in electrical activity of the skeletal muscles [5] suggested that the main role in the change from one phase of FA poisoning to the next is played by predominance of the effect of the poison either on peripheral organs (especially the skeletal muscles) or on the central nervous system (CNS). Effects on the CNS were confirmed in special experiments in which FA was injected directly into various CNS structures [4].

In the course of poisoning, a stage of temporary delay in the lowering of body temperature and TOC was distinquished, and this was regarded as the result of compensatory reactions of the body developing under the influence of the CNS. An expression of the compensatory reaction was an increase in electrical activity of the skeletal muscles [5]. The suggestion was made that this compensatory reaction developed under the influence of afferent impulses evoked by the hypothermia, and that it was expressed as "thermoregulatory impulses" of the CNS.

When investigating the combined electrical activity (CEA) of certain brain structures it was important to determine whether stages exist in this parameter in the course of poisoning and whether they can be connected with the stages described previously [5].

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 200-220 g. Electrical activity was recorded in the reticular nucleus of the thalamus (R), highly sensitive to the action of FA, and in the caudate nucleus (Cd), with low sensitivity to FA. The CEA was recorded with bipolar electrodes (nichrome wire 50 μ in diameter, insulated with a double layer of varnish, and covered in addition with a layer of plexiglas), a distance of 2 mm apart in a vertical plane. The position of the electrodes was determined by a stereotaxic apparatus using a method described previously [4]. The animals were used in the experiments 24 h after the operation to implant the electrodes. Before injection of the FA (which was given intraperitoneally in a dose of 5 mg/kg body weight, equal to 1 MLD), the CEA of the selected brain structures was recorded.

The potentials were fed into a type UBPI-02 amplifier (transmission band 1-1000 Hz), and then summated by a special integrator, enabling data for relative changes in the CEA to be obtained. The potentials were recorded by means of a type N-102 loop oscillograph, usually every 20 min. Readings of the integrator

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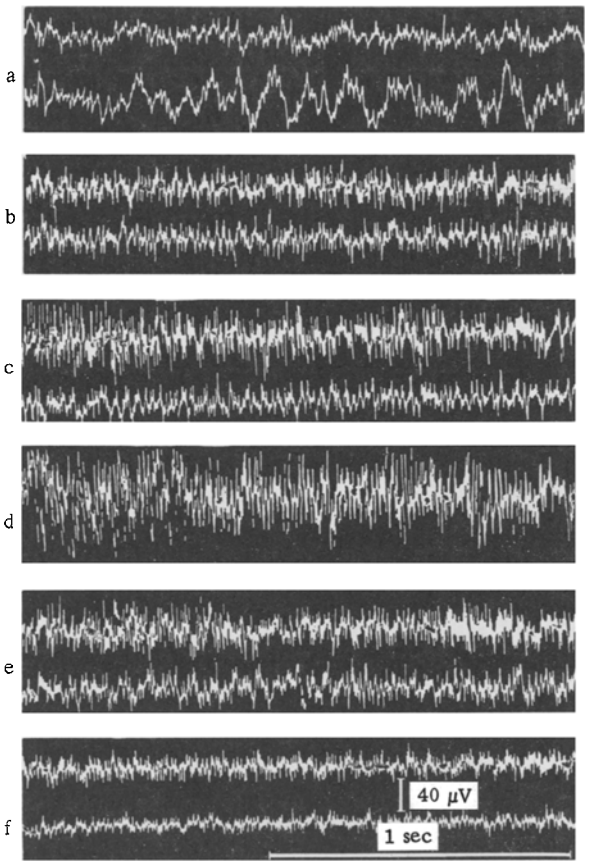

Fig. 1. Changes in character of CEA in reticular nucleus of thalamus (top curve in each frame) and in caudate nucleus (bottom curve) during development of poisoning of a rat with FA in a dose of 5 mg/mg given intraperitoneally. a) CEA before poisoning of animal: top curve shows waves at 4-6/sec; b) early stage of poisoning (1 h after injection of poison; disappearance of slow waves at 4-6/sec and appearance of waves at 12-15/sec; c-e) next stage of poisoning: 1 h 20 min after poisoning fast and frequent waves appear; d) period of paroxysm in R; e) after 3 h, depression of fast waves; f) late stage of weakening of all types of waves.

were taken for 5 min every 15 min. The integrator readings for each channel were used to plot diagrams of relative changes in CEA in a given brain structure.

The experiments were carried out without anesthesia. The position of the electrode tip was established by subsequent morphological examinnation. The observations were made from September to March at room temperature (18-20°).

EXPERIMENTAL RESULTS AND DISCUSSION

To determine the effect of the experimental conditions themselves and the state of an animal not poisoned with FA but fixed to a frame, the CEA of such an animal was investigated for 6 h. During this time no significant changes in CEA took place. A characteristic feature of the nonpoisoned animal was slow waves (4-6/sec) observed mainly in R and appearing throughout the course of the control experiment.

In the initial period of poisoning the character of the CEA showed little change: slow waves at 4-6/sec were recorded, with waves at 12-15/sec superposed upon them (Fig. 1a). The reading of the integrator remained as before (Fig. 2a). Toward the end of the first hour and during the period immediately after, changes were observed in the character of the CEA: waves of the slowest frequency disappeared and those with a frequency of 12-15/sec became more obvious (Fig. 1b). The integrator readings fell at this time (Fig. 2a).

Later, fast waves appeared and their frequency continued to increase, as also did their amplitude (Fig. 1c), reading 60-80 μV. According to some data, waves of this type, although admittedly without any marked increase in amplitude, are characteristic of the activation reaction of subcortical structures arising under the influence of adrenalin, amphetamine, pipradrol, and other agents [2] when given in doses not producing convulsions. At this stage the integrator readings again fell, especially rapidly in Cd, i.e., in the structure in which the fast waves were less pronounced. At the same time, a marked decrease in the body temperature took place (Fig. 2a).

Later, with the onset of the phase of poisoning, characterized by a temporary delay in the lowering of body temperature and TOC (Fig. 2a), a further increase was observed in the frequency and amplitude of the fast waves, particularly pronounced in the period of paroxysms (Fig. 1d), but also before and after them. Similar phenomena in various cortical structures of the cat poisoned with FA (although these animals were given relaxants and maintained on artificial respiration) were observed by Ward [9]. The period of poisoning now being described differed in that the decrease in CEA recorded by the integrator, which had begun previously, also was delayed until the 3rd and 4th hour after poisoning, and was sometimes actually replaced by a small increase. It is important to note that the electrical activity of skeletal muscles is increased in this period [5].

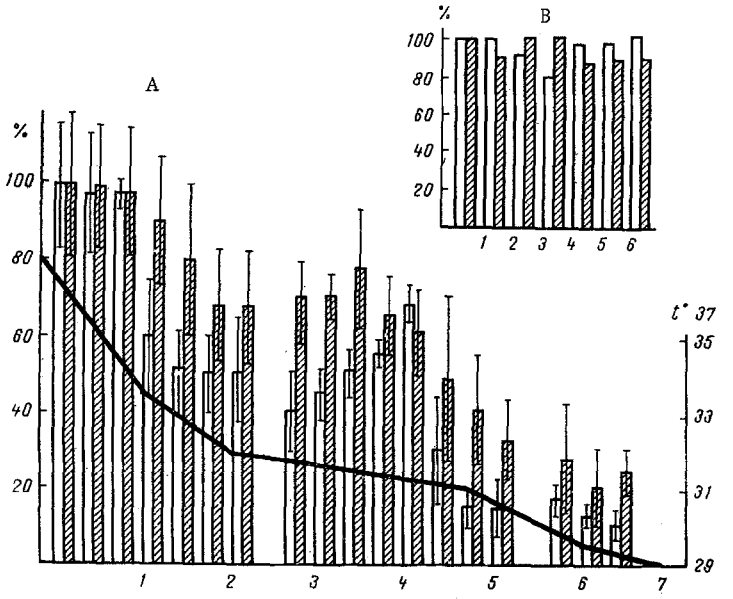

Fig. 2. Changes of CEA measured by integrator and including slow and fast waves in R (unshaded column) and in Cd (shaded column). a: mean results of 8 experiments; abscissa, time (in h); ordinate, on the left—CEA in relative values (initial activity taken as 100%); continuous curve—mean change in body temperature during poisoning in the same animals (temperature scale along ordinate on the right). Arrow on abscissa indicates time of injection of FA; b) fluctuations of CEA in the same structures in control experiment.

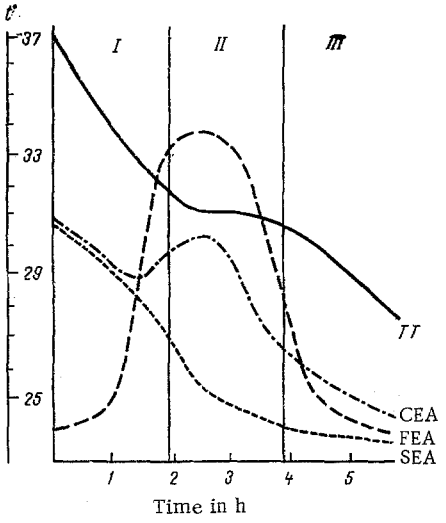

Fig. 3. Scheme showing CEA, slow waves (SEA), and fast waves (FEA) in brain structures of rats poisoned with FA. Scheme reflects hypothesis that CEA is connected with pathophysiological phenomena, one of the ultimate expressions of which is a lowering of body temperature. I-III) stages of poisoning.

In the 3rd stage of poisoning the CEA fell again, this time irreversibly. The beginning of this process, consisting primarily of a decrease in amplitude of the fast waves, can be seen in Fig. 1, e. Later the process continued in the same direction, the amplitudes of all types of waves decreasing. The integrator readings in this period fell, and were not more than 10-25% of the initial values.

The relationship between the electrical activity of the structures investigated (R and Cd) at different stages of poisoning were represented by a composite diagram based on the mean results of 8 experiments (Fig. 3). It was plotted on the assumption that the slow electrical waves and the fast waves underwent different changes during the development of poisoning. To distinquish the stages more clearly, a typical graph of changes in body temperature was also drawn on the diagram. The initial decrease in CEA was apparently due to weakening of the slow waves. By the end of the first and, in particular, during the second stage the increase in frequency and amplitude of the fast waves, together with continuing weakening of the slow waves, led to delay in the lowering of the CEA. Selective separate counts of the slow and fast waves confirmed this interpretation of the course of the decrease in CEA in the first two stages. The third stage led to a progressive decrease in amplitude of the fast waves.

The explanation put forward previously of the pathophysiological processes taking place in different stages of FA poison-

ing can now be supplemented and represented as follows. In the first stage a disturbance of the oxidative metabolism of various organs, including skeletal muscles, takes place [7, 8]. The ultimate expression of this process, which persists even longer, is a lowering of the body temperature and TOC. The following can now be added: work in our laboratory has shown that 30 min after poisoning a considerable accumulation of citrate takes place in the blood stream, indicating disturbance of the Krebs cycle in several organs, and also a disturbance of metabolism of the blood itself, as a result of which anoxia may develop.

Meanwhile, the hypothermia clearly marked by the end of the first stage, and the progressively deepening anoxia cause an increase in activity of the brain structures and involvement of neuro-hormonal regulatory mechanisms [6] on which the increase in oxidative processes in the various organs depends. In this way a group of compensatory reactions is formed, leading directly or indirectly to an increase in activity of the skeletal muscles and to delay in the decrease in oxidative processes in them. These are the main events taking place in the second or "compensatory" stage of poisoning. The deepening action of the poison on the brain structures and the strengthening of the afferent flow of impulses periodically give rise to paroxysmal activity.

The weakening of the CEA of the brain structures studied in the third stage of poisoning is evidence of profound disturbances in the CNS itself, which can no longer maintain the compensatory processes. Peripheral organs, now without protection by the CNS, lower oxidative metabolism still more rapidly.

Hence, corresponding to the three principal stages of poisoning established in previous investigations on the basis of changes in body temperature, TOC, and electrical activity of the skeletal muscles, the following changes have been found in the CEA of both brain structures: in the first stage, a decrease in CEA; in the second stage, stabilization; and in the third stage, a continued decrease in CEA.

It is postulated that the changes in CEA are connected with disappearance of slow waves at 4-6/sec and weakening of waves at 12-15/sec toward the end of the first stage. The second stage is marked by a considerable increase in fast waves, whose amplitude is reduced in the third stage of poisoning. Arguments are presented to show that the increase in CEA in the second stage reflects participation of the CNS in compensatory processes evoked by the deepening hypothermia and anoxia, leading to temporary delay in the lowering of the body temperature and TOC.

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