CHANGES IN THE ELECTRICAL ACTIVITY OF THE SPINAL CORD CAUSED BY COPPER IONS

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Despite the great importance of trace elements in the metabolism of the living organism [3, 4], their influence on the functional state of the central nervous system has received little study. Only isolated reports of a relationship between the concentration of trace elements in the central nervous system and its functional state can be found in the literature [1]. It has been shown that nociceptive stimulation and emotional excitement bring about an increase in the copper concentration in the blood while lowering its concentration in the liver [5]. Administration of copper in amounts close to its content in the organism depresses the level of excitability and conductivity of peripheral nerves, the reflex excitability and lability of the spinal cord centers, and the excitability of the cholinergic systems [10], facilitates and stimulates the development of Sechenov inhibition, and deepens the level of ether anesthesia in animals [11]. Chronic poisoning with copper salts leads to severe and prolonged disturbances of the cortical dynamics in animals [9]. Several authors have reported the successful use of copper salts in the treatment of states of excitation in certain mental diseases [2].

In the present communication the changes in the background (spontaneous) electrical activity of the spinal cord caused by the trace element copper are described.

METHOD

Experiments were conducted on cats anesthetized with ether and urethane. Ether anesthesia (10-15 ml) was induced for a short period (5-10 min) before the operation; the animal was then fixed and all subsequent manipulations were carried out under urethane anesthesia (1 g/kg), the depth of which was judged by the presence of the corneal reflex. The animal's body temperature was maintained throughout the experiment at the level of 36-37° by means of an ultrathermostat. The spinal cord was exposed by a longitudinal incision of the dura in the lumbosacral region at the level L_5-L_7. Its surface was covered with a layer of mineral oil warmed to 37°. To abolish the influence of respiratory movements on the detection of potentials, the spine was firmly fixed above and below the exposed region. The potentials of the spinal cord were recorded from its dorsal surface by means of platinum needle electrodes by both bipolar and unipolar methods, and the potentials from the depth of the cord by means of a focal microelectrode (Nichrome wire in glass insulation), implanted to a depth of 2.0-2.5 mm by means of a rigidly mounted micromanipulator. The position of the tip of the microelectrode was determined in sections of the cord 10-20 μ thick, stained with hematoxylin-eosin. The potentials were recorded by means of a twin-beam cathode-ray oscillograph with an ac amplifier, symmetrical input, and a transmission band from 0.2 to 3500 cps. The solution of copper chloride (0.001 M and 0.01 M) was made up immediately before the experiment in physiological saline, and injected intravenously in a dose equivalent to 0.1-1.0 mg/kg body weight of the pure metal (i.e., in "biological" doses), and was also applied locally at the point from which the potentials were recorded. Experiments were conducted on 26 cats.

RESULTS

The investigations showed that the potentials recorded from the dorsal surface of the spinal cord consisted of waves with an amplitude of 10-15 μV and a frequency of 40-50/sec. When the microelectrode was inserted to a

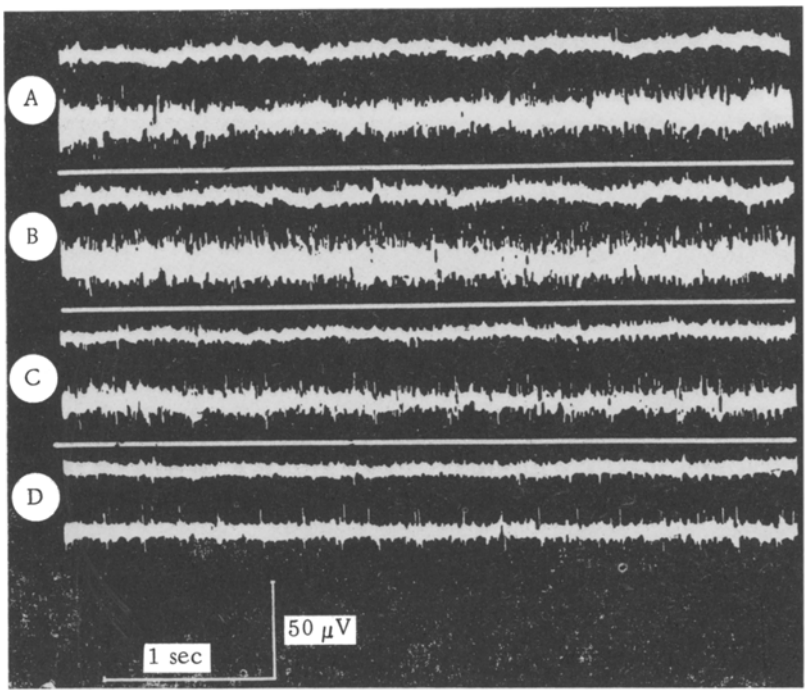

Fig. 1. Effect of copper (0.1 mg/kg) on the spontaneous electrical activity of the spinal cord of the cat. A) Initial background; B, C, D) 1, 30, and 70 min respectively after intravenous injection of copper chloride. Top curve—potentials recorded from dorsal surface of spinal cord; bottom—potentials recorded from electrode buried in spinal cord to a depth of 2.5 mm.

depth of 2.0-2.5 mm, into the region of the motor nuclei of the tibial muscle, the waves of potential recorded had an amplitude of 25-30 μV and a frequency of 50-60/sec.

After injection of copper chloride solution into the general circulation of the animal in a dose of 0.1 mg/kg, the potentials recorded from the dorsal surface of the spinal cord showed no appreciable change in either amplitude or frequency throughout the experiment.

When the potentials were recorded from the depth of the spinal cord at a level 2.0-2.5 mm from its dorsal surface, the electrical activity was intensified 1 min after injection of the copper salt: the amplitude of the potentials rose to 40-70 μV. Under these circumstances the frequency of the potentials increased very slightly or remained unchanged by comparison with the original background level (Fig. 1A, B). Later, starting from the 5th-15th minute, the recordings from the spinal cord showed a gradually increasing depression of the amplitude of the potentials (Fig. 1C). After 50-70 min (Fig. 1D) their amplitude had fallen to $\frac{2}{3}$-$\frac{1}{2}$ its initial value. After 90-100 min (or less frequently, after 2 h) had elapsed following injection of the copper chloride, a gradual recovery of the electrical activity of the spinal cord began to take place in its depth, up to the original level. It should be noted that often a decrease in the amplitude of the spinal potentials alternated with an increase—i.e., the changes in the spontaneous electrical activity under the influence of the trace element copper were fluctuating in character.

Between 5 and 30 sec after injection of copper into the general circulation in a dose of 1 mg/kg, the electrical activity of the spinal cord was intensified: the amplitude of the potentials rose by 20-40% by comparison with the original background when recordings were taken both from the dorsal surface and from the depth of the spinal cord (from the region of the motor nuclei of the tibial muscle) (Fig. 2A, B). After 2-5 min a decrease in the amplitude of the spinal cord potentials by 10-20% was observed, changing after a further 4-5 min into a increase by 20-40% (Fig. 2E, F). This alternation of stimulation and depression of the electrical activity of the spinal cord was observed throughout the experiment, but the periods of depression were more marked, lasting for 5-10 min, while the periods of stimulation were brief and usually did not exceed 2 min. Individual periods of stimulation of the spinal potentials were characterized by the appearance of peaks of high amplitude (up to 100 μV), at first having a frequency of up to 20/sec, but rising to 100/sec after 30 sec or 1 min (Fig. 2C, D). It may be supposed that these high-amplitude peaks

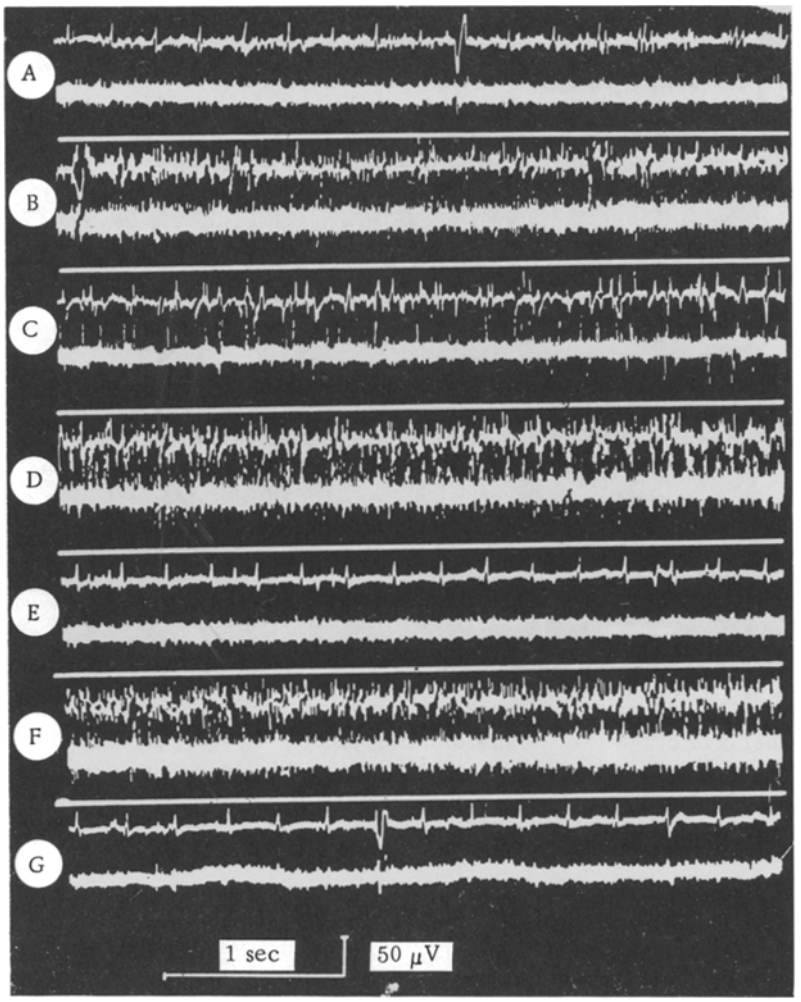

Fig. 2. Effect of copper (1 mg/kg) on spontaneous electrical activity of the spinal cord of the cat. A) Initial background; B, C, D, E, F, G) 30 sec and 1, 2, 5, 30, and 40 min respectively after intravenous injection of copper chloride. Significance of curves the same as in Fig. 1.

were synchronized discharges from motor neurons [6-8], the activity of which was stimulated by the copper ions. In some of the experiments these discharges recurred periodically at intervals of 25-30 min. After 30-40 min maximal depression of the potentials of the spinal cord was observed: their amplitude fell by 30-40% from its initial background level (Fig. 2G).

Hence, the changes in the electrical activity of the spinal cord depend on the concentration of the solutions used: the effect of administration of the trace element increases with an increase in its dose. In control experiments (in which physiological saline was injected) no appreciable changes were found in the electrical activity of the spinal cord.

Somewhat different changes in the electrical activity of the spinal cord were observed in experiments on spinal animals, in which the spinal cord was preliminarily divided (under ether anesthesia) at the level of T_1-T_2, preserving diaphragmatic respiration. In these experiments, after intravenous injection of copper, only a depression of the electrical activity of the spinal cord was recorded, starting after 5-10 sec: the amplitude of the potentials fell by 20%. After 70 min the depression of the potentials of the spinal cord was maximal, amounting to 50% (Fig. 3B, C, D).

During the local action of copper, by application of a pad of cotton wool soaked in 0.01 M copper chloride solution to the dorsal surface of the spinal cord in the region from which the potentials were recorded, the amplitude of the potentials rose after 15-20 sec by 30-50% over the initial background level. By the 10th-20th minute it had

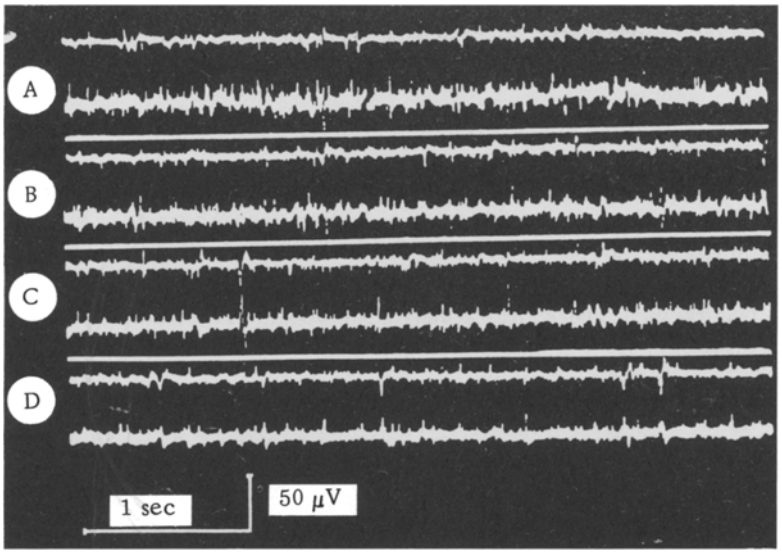

Fig. 3. Effect of copper (1 mg/kg) on spontaneous electrical activity of the spinal cord of the spinal cat. A) Initial background; B, C, C) 1, 30, and 70 min respectively after intravenous injection of copper chloride. Significance of curves the same as in Fig. 1.

returned to its original value: throughout the remaining period of the experiment these potentials showed no appreciable change in either amplitude or frequency. The potentials recorded from the interior of the spinal cord by burying the microelectrode in the region of the motor nuclei of the tibial muscle were at first indistinguishable from the initial background, and not until 15-20 min had elapsed did their amplitude fall by 15-20%, evidently as a result of the gradual penetration of copper ions into the deeper portions of the spinal cord. After washing with physiological saline, the electrical activity recorded from the interior of the spinal cord returned to its initial level in 15-20 min.

Hence, copper salts in small doses, when injected into the general circulation of animals with an intact nervous system and when applied locally, have a biphasic effect on the spontaneous electrical activity of the spinal cord, causing an initial transient stimulation, followed by a prolonged depression of this activity. Further, the prolonged periods of depression of the electrical activity of the spinal cord that were observed alternated with transient periods of its intensification. When potentials were recorded from the interior of the spinal cord (from the region of the motor nuclei of the tibial muscle), more obvious changes were observed than when the recordings were made from its dorsal surface.

After injection of copper into the general circulation of the spinal animal, the phase of increased electrical activity of the spinal cord was absent, and only depression was observed. These findings suggest that the phase of stimulation of the electrical activity of the spinal cord, which arises during the first minutes after injection of copper into an animal with an intact nervous system, is evidently due to the influence of copper ions on the suprasegmental structures.

It may also be concluded that the depression of the spontaneous electrical activity of the spinal cord observed following administration of copper ions does not depend on descending inhibitory influences reaching the spinal cord from the higher segments of the central nervous system, but develops as a result of the action of copper ions on the functional state of the spinal cord itself.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.