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CHANGES IN FUNCTIONAL ACTIVITY OF THE CEREBRAL CORTEX AND CENTRAL GRAY MATTER IN RESPONSE TO ELECTROACUPUNCTURE

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KEY WORDS: electroacupuncture; central gray matter; evoked potential.

Experimental and clinical investigations suggest that the effectiveness of reflex analgesia can be determined largely by the degree of activation of the central gray matter (CGM), one of the principal antinociceptive structures of the brain, by electroacupuncture (EAP) [3, 9, 11].

Both facilitatory and inhibitory influences of the cerebral cortex are known to play an important role in determining the functional state of nonspecific brain structures [1, 2, 4]. However, there is no information as yet in the literature on the possible mechanisms of corticofugal control of excitability of antinociceptive structures and, in particular, of CGM, during the use of EAP.

The aim of the present investigation was accordingly to study integration of nociceptive and non-nociceptive afferent impulsation in CGM and the cerebral cortex during EAP stimulation.

EXPERIMENTAL METHOD

Acute experiments were carried out on 17 cats anesthetized with hexobarbital (40 mg/kg, intraperitoneally), immobilized with suxamethonium, and maintained on artificial ventilation of the lungs. After fixation of the animal in a stereotaxic apparatus and trephining of the skull all regions of operative procedures were infiltrated with local anesthetic. Recording and stimulating electrodes were arranged on the surface of the cortex at stereotaxic coordinates (A 1.0-2.0; L 0.5-2.0; H 0.5 to +1) in CGM. The interpolar distance between the cortical stimulating electrodes, to which a pulsed current was applied (0.1 msec, strength up to 1 mA), was 1-1.5 mm. A silver electrode (diameter of tip 0.8 mm) was used for recording. The subcortical recording electrode was a steel rod up to 200 μ in diameter, insulated throughout its length except at the tip, 50-70 μ in diameter. Nociceptive responses were evoked by single stimulation of the dental pulp (lower canine tooth) through a bipolar electrode, inserted into a hole drilled in the dentine and secured there with acrylic glue. The duration of the stimulating pulses was 1-3 msec and their intensity up to 20 mA. Non-nociceptive responses were evoked by stimulation of the lower lip by means of a bipolar needle electrode with a current with pulse duration 0.1 msec and strength up to 5 mA. EAP was applied through three acupuncture needles, inserted into the base of the concha auriculae of the cat, to which a current was applied (1.2 msec, strength up to 16 mA, frequency 1-3 Hz, for 15-30 min).

Electrical responses in the form of evoked potentials (EPs) were assessed after averaging of 16 presentations on a specialized computer. To monitor the animal's functional state the arterial blood pressure, ECG, and brain surface temperature were recorded. At the end of the experiment a lethal dose of hexobarbital was injected into the animal and the position of the subcortical electrodes was then verified histologically.

EXPERIMENTAL RESULTS

In the experiments of series I, with single stimulation of the frontal, motor, and first (SI) and second (SII) somatosensory areas of the cortex, cortical area SII was found to have the strongest corticofugal connections with CGM. This was proved by the fact that responses in CGM to stimulation of different parts of SII were most stable in form and had maximal amplitude if all areas of the cortical surface were stimulated by currents with equal parameters

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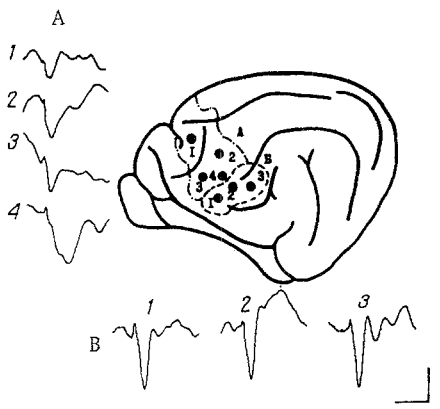

Fig. 1

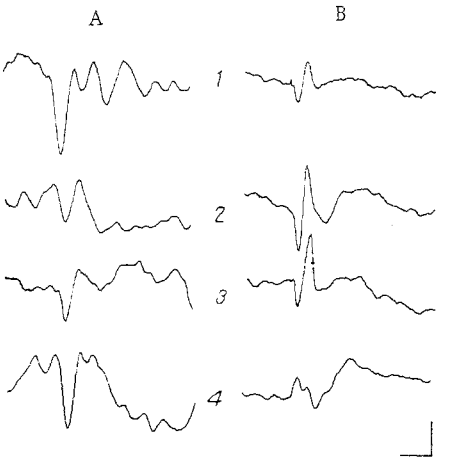

Fig. 2

Fig. 1. EPs recorded in central gray matter in response to stimulation of cortical areas SI (A) and SII (B). Serial numbers of evoked potentials (A and B) correspond to sites of stimulation on brain diagram. Here and in Figs. 2 and 3, calibration of amplitude 50 μV, of time 100 msec.

Fig. 2. Changes in shape of EPs arising in response to stimulation of dental pulp in cortical area SI (A) and in central gray matter (B) after EAP and injection of naloxone. 1) Control experiments, 2 and 3) evoked responses 3 and 12 min respectively after EAP, 4) evoked responses after EAP, and injection of naloxone.

(Fig. 1). EPs recorded in CGM in response to stimulation of areas SI and SII are shown in Fig. 1A, B. EPs arising in CGM in response to stimulation of SII consisted of positive–negative waves with a latent period of 2-5 msec. The amplitude of the positive wave was 70-100 μV and its duration up to 50 msec. The negative phase of the response was observed irregularly and its amplitude did not exceed 20 μV. EPs appeared in CGM recorded by an electrode in the same location, but in response to stimulation of area SI, appeared after a longer latency period (up to 10 msec), had a positive wave of longer duration (up to 100 msec), but the amplitude of the response was unstable and it varied, depending on what part of SI was stimulated, from 25 to 100 μV.

In the experiments of series II, with simultaneous recording of EPs in CGM and SII to nociceptive and non-nociceptive stimulation, differences were observed in the responses in these structures after EAP, in the form of marked inhibition of responses to nociceptive stimulation in SII on average by 50%, and facilitation in CGM on average by 70% (Fig. 2). Systemic administration of the opiate antagonist naloxone in a dose of up to 5 mg/kg, against the background of the phenomena described above, as a rule led to recovery of the amplitude of EPs in SII to the control level and recovery of EPs in CGM, but with a considerable increase in duration of the positive wave (Fig. 2A, B, 4). A study of the character of changes in the non-nociceptive responses in the brain structures tested after EAP showed facilitation of responses in both SII and CGM on average by 40% (Fig. 3). Changes in the functional state of SII (by cooling), reflected in absence of the response in SII to nociceptive stimulation of the lip, did not lead to facilitation of EPs in CGM after EAP (Fig. 3A, B, 3). On recovery of the functional state of area SII, facilitation of EPs in CGM likewise was not observed (Fig. 3A, B, 4).

The results of these investigations showed that EAP can have an activating effect on excitation of CGM by nociceptive and non-nociceptive afferent impulses, as shown by facilitation of the responses to stimulation of these kinds in CGM and simultaneous inhibition of nociceptive responses and facilitation of nonciceptive responses in SII.

The fact that EAP stimulation increases the amplitude of EPs in CGM to nociceptive stimulation, unlike in SII, where the amplitude of the responses is reduced, does not, in the writers' opinion, contradict the biological significance of the existence of antinociceptive

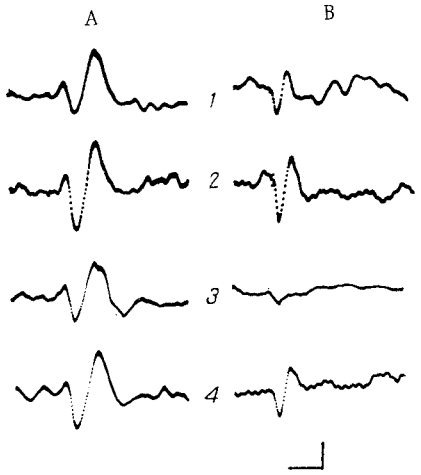

Fig. 3. Changes in shape of EPs arising in response to stimulation of lip in central gray matter (A) and cortical area SII (B) against the background of changes in the functional state of the cortex and of EAP. 1) Control responses, 2) responses after EAP, 3) responses after EAP and cooling of the cortex, 4) responses after EAP and restoration of the functional state of the cortex.

structures. Probably the arrival of nociceptive impulses activates this structure and, through negative feedback, controls the transmission of nociceptive impulsation into the CNS [10].

This phenomenon also agrees with data showing that afferent projections into CGM consist mainly of high-threshold thin fibers of the A-delta group [5, 6] and that, accordingly, for effective activation of this structure, strong peripheral stimuli must be used.

The results suggest that the cerebral cortex and, in particular, area SII may play an essential role in the activation of CGM during EAP. This hypothesis agrees with the views of Liebeskind and Mayer [8], who postulated that signals activating the neuron populations of CGM may also arrive via higher structures.

Direct stimulation of CGM, giving rise to analgesic effect, is known to be accompanied by an increase in the concentration of endogenous opiates in the cerebrospinal fluid [7]. In the present experiments injection of naloxone abolished facilitation of evoked responses in CGM after EAP; it can accordingly be postulated that the mechanisms of activation of CGM during EAP may be based on liberation of endogenous opiates.

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ACTION OF MENINGOCOCCAL LIPOPOLYSACCHARIDE ON PLATELET FUNCTION

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In the generalized form of meningococcal infection toxemia is one of the factors which disturbs hemostasis and promotes thrombohemorrhagic complications. Definite views on the origin of these complications have now been formed. Disturbance of the integrity of the vessel wall [4, 5, 14] and injury to the blood cells [6, 13] under the influence of menigococcal endotoxin lead to the release of thromboplastic substances activating the blood clotting system into the blood stream. Developing intravascular blood clotting involves the consumption of procoagulants (especially fibrinogen), thrombocytopenia, and protective activation of the anticlotting component of the blood clotting system, which in conjunction with injury to the vessel wall, leads to hemorrhages [5].

In our opinion, in patients with generalized meningococcal infection (meningitis with meningococcemia) the aggregating properties of the platelets (in the first 2 days after admission to hospital) are depressed, especially in seriously ill patients. By the time of recovery (the 17th-20th day of treatment) this function of the platelets is back to normal. The ability of platelets to carry out reversible endocytosis likewise is modified. Uptake of the fluorescent label is increased, the liberation reaction is depressed during the first days of the disease, but starting with the 2nd day of treatment it is distinctly intensified and is not yet back to normal when the patient leaves hospital. We thus found that in patients with a generalized form of meningococcal infection not only is thrombocytopenia observed, but the functional properties of the membranes and subcellular apparatus of the platelets also are disturbed. The mechanism of action of meningococcal endotoxin on platelet function has virtually not been studied.

The object of the present investigation was to study the direct action of meningococcal endotoxin on the state of the plasma membranes and the subcellular apparatus of the platelets.

EXPERIMENTAL METHOD

Experiments were carried out *in vitro* on plasma from blood donors enriched with platelets. Platelet-enriched plasma was obtained by centrifugation (at 2000 rpm for 10 min) of blood stabilized with citrate (9:1). Samples of plasma were incubated with meningococcal endotoxin (in a concentration of between 0.5 and 75 μg ml plasma for 5 to 60 min). According to data in the literature [15], the toxic principle of the meningococcus is a lipopolysaccharide which, besides its toxic activity, also has pyrogenic and antigenic properties.

The complex antigen, consisting of cell wall lysate from group A *Neisseria meningitidis*, was obtained by treatment of this strain with a 0.5% solution of Triton X-100 in an alkaline medium.

The lipopolysaccharide was isolated by extraction with aqueous phenol and subsequently purified with Cetavlon.

The antigen complex in the culture fluid was obtained by chromatography of a supernatant of a liquid culture on a column with Acrylex P-6. The action of all three preparations on the state of platelet function was tested in the experiments.

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