It is known that PFTBA emulsion is not eliminated from the body but accumulates in the organs and tissues. Intensive research is accordingly now in progress with the aim of finding emulsions free from this disadvantage (perfluorodecalin, adamantan, perfluorotributylpropylene). Meanwhile the character of gas transport in all emulsions is the same, and their physiological study has enabled us to discover some of the particular features of gas transport characteristic of all known emulsions of perfluoro-compounds.

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EFFECT OF STIMULATION OF ANTINOCICEPTIVE BRAIN ZONES ON THE ANALGESIC EFFECT OF ELECTROACUPUNCTURE IN RATS

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The mechanisms of production of acupuncture analgesia have not been finally explained, but there is experimental evidence that acupuncture induces activation of inhibitory processes and disturbs the conduction of nociceptive information at different levels of the CNS [5, 7, 11, 13]. It has recently been suggested that so-called antinociceptive brain systems, electrical activation of which is accompanied by the development of analgesia in animals and man, may participate in the analgesic effect of acupuncture [6, 9].

The object of the investigation described below was accordingly to study the effect of activation of antinociceptive brain zones on the intensity of the analgesic effect of acupuncture in rats.

EXPERIMENTAL METHOD

Altogether 26 experiments were carried out on male rats weighing 250-300 g with monopolar nichrome electrodes implanted into the posterior zones of the lateral hypothalamus and the central gray matter of the mesencephalon in accordance with coordinates in the atlas [8]. Nociceptive stimulation of the base of the tail was applied as volleys of square pulses (1 msec, 100 Hz, 1 sec, 30-100 V) through bipolar electrodes in the tunica elastica. The complex nociceptive response arising to stimulation of gradually increasing intensity was assessed on a scale which took into account five groups of features: 1) twitching and contraction of the tail, 2) rotation of the head and trunk, stepping movements with the paws, 3) squeaking, single rotations around an axis, 4) intensive and repeated crying, 5) crying with running away, repeated rotations, and aggressiveness. The features of group 1 were assessed as the animal's response to perception of aversive stimulation and it appeared to stimulation with an intensity of 30.5 ± 2.6 V, which was taken as the threshold. The two next groups of features reflect the animal's response to intensive yet tolerable nociceptive stimulation. Features of groups 4 and 5 were interpreted as manifestations of the emotional and behavioral response to intensive nociceptive stimulation; they appeared to stimulation with a strength of 1.9-2.2 thresholds.

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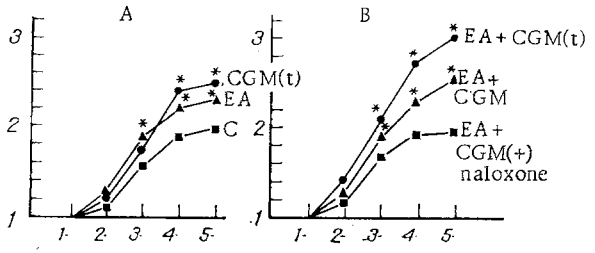

Fig. 1. A) Changes in structure of nociceptive response during EA and stimulation of antinociceptive brain zones at threshold intensities [CGM (t)]; B) effect of naloxone, 5 mg/kg, and of antinociceptive stimulation of below threshold (CGM) and of threshold [CGM(t)] intensity on manifestation of the analgesic effect of EA. C) Control (initial structure of nociceptive response). *) Difference significant compared with control at $P < 0.05$ level. Abscissa, groups of features of nociceptive responses (explanation in text); ordinate, intensity of stimulation in thresholds necessary for appearance of corresponding components of nociceptive response during stimulation of base of tail of rats.

Electroacupuncture (EA) was applied with acupuncture needles to the analog of the acupuncture point (AP) Yao-yang-kuan (3 TM). The AP was activated by square pulses for 20 min, with a frequency of 1 Hz; the pulse duration was 1 msec. In each case the amplitude was chosen individually up to the appearance of small fibrillations of the muscles in the region of the needle. Stimulation of the central gray matter (CGM) and posterior zones of the lateral hypothalamus (LH) continued for 30 sec with pulses of increasing intensity (50-250 μA) with a frequency of 100 Hz. The localization of the electrodes was identified in histological brain sections.

Naloxone was injected intramuscularly in a dose of 5 mg/kg. Statistical analysis of the results was carried out by nonparametric methods.

EXPERIMENTAL RESULTS

Electrical stimulation of AP for 20 min led to the development of analgesia, which was manifested as an increase in the intensity of stimulation required to cause the appearance of the main components of the nociceptive response (Fig. 1A). The greatest increase was observed in thresholds of appearance of features of the animals' emotional and behavioral response to intensive nociceptive stimulation. Analgesia induced by EA persisted for a further 1-3 min after the end of electrical stimulation of AP.

Similar changes in the structure of the nociceptive response also were observed during stimulation of CGM and LH with increasing intensity. During central stimulation with an intensity of 50-100 μA the initial manifestations of an antinociceptive effect were observed, namely disappearance of vocalization and running away from the complex structure of the nociceptive response. An increase in the intensity of central stimulation was accompanied by marked analgesia, i.e., by inhibition of all components of the nociceptive response except features of group 1, evidence that the animals perceived stimuli with aversive properties. However, in isolated experiments, as a rule during stimulation of LH, the animals gave behavioral responses (most frequently an orienting or investigative reaction). After-analgesia to stimulation of CGM and LH did not exceed 3 min.

Electroacupuncture applied against the background of stimulation of CGM and LH by pulses of below threshold intensity, i.e., not evoking changes in the animal's behavior or in its response to nociceptive stimulation, led to a greater increase in the thresholds of appearance of the main components of the nociceptive response than that observed after EA alone. Combined stimulation of AP

and antinociceptive brain zones under conditions inducing initial changes in the structure of the nociceptive response was accompanied by considerable potentiation of analgesia, and in its intensity it significantly exceeded the analgesic effect of EA.

Activation of "neutral" brain points, independent stimulation of which was not accompanied by the development of an antinociceptive effect, did not induce potentiation of analgesia arising during EA.

Potentiation of the antinociceptive effect by morphine took place in the same way. In subanalgesic does (5 mg/kg), morphine led to the appearance of an antinociceptive effect during subthreshold stimulation of CGM and it potentiated analgesia arising after threshold stimulation of antinociceptive brain zones.

Naloxone in a dose of 5 mg/kg abolished the antinociceptive effect of stimulation of CGM and LH (Fig. 1B). Characteristically even an increase in the intensity of central stimulation against the background of naloxone did not induce analgesia in the animals. Naloxone completely suppressed the analgesic effect of EA in the same way. In this dose naloxone virtually completely abolished the analgesic effect produced by combined stimulation of antinociceptive brain zones and AP.

The results of these experiments thus show that analgesia arising during EA and during stimulation of CGM and LH is in many respects similar and is manifested as predominant inhibition of emotional-behavioral components of the nociceptive response. This suggests that electroacupuncture analgesia, like the antinociceptive effect, is associated not only with disturbance of the conduction of nociceptive information at the level of relay neurons [11, 12], but it may also arise as a result of inhibition of highly integrated mechanisms responsible for the emotional reaction to pain [1-3]. On the other hand, the results may point to the possibility of realization of the acupuncture effect through activation of those same mechanisms which determine development of the antinociceptive effect. This conclusion is supported by data showing the mutually potentiating influence of EA and stimulation of antinociceptive brain zones of the intensity of analgesia. Since naloxone abolishes analgesia induced by central stimulation [4] and by EA [10], it can be tentatively suggested that the main structures determining the onset of analgesia during EA and during the antinociceptive effect are regions of the brain which contain opiate receptors with which naloxone interacts. Since opiate receptors are located mainly in the region of the periaqueductal structures [14, 15], electrical activation of which is most frequently accompanied by the onset of analgesia, it can be postulated that it is these structures which are activated by electroacupuncture stimulation. However, the mechanism whereby these systems are triggered during EA is unknown and requires special investigation.

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