EFFECT OF STIMULATION OF THE CENTRAL GRAY MATTER OF THE MIDBRAIN ON HEMODYNAMIC NOCICEPTIVE RESPONSES

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Many recent investigations have shown that electrical stimulation of various brain formations — the central gray matter (CGM), limbic structures, hypothalamus, etc. — induces marked analgesia, manifested as elevation of the pain threshold and an inhibition of emotional behavioral manifestations of pain [2, 7, 11]. However, there is virtually no information on the effect of stimulation of the brain structures associated with analgesia on the hemodynamic correlates of nociceptive responses.

Accordingly, in the investigation described below changes in responses of the arterial pressure (BP) and intersystolic intervals (ISI) evoked by nociceptive stimulation were studied during stimulation of "analgesic" structures of CGM of the midbrain.

EXPERIMENTAL METHOD

Fourteen experiments were carried out on six unrestrained cats. As a preliminary step under pentobarbital anesthesia a catheter was introduced into the animal's aorta, an electrode into the pulp of the upper canine tooth [10], and nichrome monopolar electrodes with an active surface 150 μ in diameter stereotaxically [15] into structures of CGM at level AP0-A4. The position of the electrode tip was verified by electrolytic tagging in serial brain sections. CGM was stimulated by square pulses with parameters of 150-350 μA, 1 msec, 100 stimuli/sec; the intensity of stimulation of the dental pulp was measured in threshold values [4].

In the course of the experiment BP, ISI [3], the pneumogram (with a carbon transducer), and total motor activity (on a strain gauge platform) were recorded and the behavioral response of the cat was assessed by means of a special scale [4].

EXPERIMENTAL RESULTS

In animals in a state of rest in the experimental chamber BP was 75-95 mm Hg, ISI 380-520 msec, and the respiration rate 20-35 cycles/min.

The character of the emotional-behavioral [4] and autonomic [3] responses to stimulation of the dental pulp in cats has been described by the writers previously. Electrical stimulation of CGM led to inhibition of the emotional-behavioral response of the animals to nociceptive stimulation. As was shown previously [4], the degree of inhibition of the nociceptive response depended directly on the intensity of central stimulation. The present investigation showed that stimulation of midbrain structures by itself, with an intensity inducing the maximal analgesic effect, did not change the spontaneous behavior of the cats or the initial autonomic parameters (Fig. 1, 1-3). A further increase in the strength of CGM stimulation (Fig. 1, 4-6) led to the development of marked motor responses, a considerable rise in BP, a decrease in the depth and increase in the frequency of respiration, and all these effects disappeared after cessation of central stimulation. Accordingly, in the present investigation only those parameters of brain stimulation were used which did not change the background parameters of the state of the animals.

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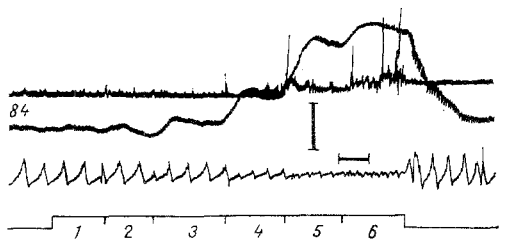

Fig. 1

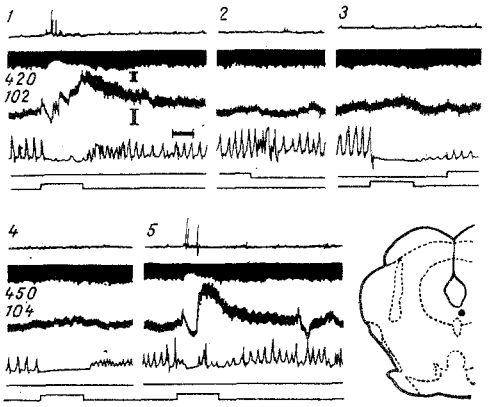

Fig. 2

Fig. 1. Effect of stimulation of CGM of midbrain on BP, respiration, and motor activity in waking cats. 1-6) Stimulation of CGM with intensity of 250 to 500 μA. Top to bottom: motor activity, BP (calibration 20 mm Hg), pneumogram, marker of stimulation. Time calibration 5 sec.

Fig. 2. Effect of stimulation of CGM on vasomotor responses to stimulation of dental pulp in cats. 1) Changes in vasomotor parameters in response to stimulation of dental pulp (eight thresholds), 2) the same to stimulation of midbrain (150 μA), 3) the same to stimulation of dental pulp against the background of midbrain stimulation (30 sec after its beginning), 4, 5) the same, in response to stimulation of dental pulp, 50 and 170 sec respectively after end of midbrain stimulation. Markers of stimulation from top to bottom: of midbrain, of dental pulp. Location of electrode shown by dot on diagram of frontal section through midbrain (A −0.5, P −0.5, H +0.5). Trace of ISI (calibration 150 msec) shown below trace of motor activity. Remainder of legend as to Fig. 1.

Stimulation of midbrain structures at threshold intensity, inducing initial weakening of the manifestations of the nociceptive response — a decrease in the intensity of defensive movements, running, vocalization — led to a small but significant fall in amplitude of the BP pressor responses (by 20-30%) and the tachycardia (by 15-20%). Meanwhile the time taken for BP to return to its initial level after the end of stimulation of the dental pulp was reduced by 20-40%, and the humoral phase of BP responses diminished.

Subsequent strengthening of midbrain stimulation caused deepening of analgesia and a parallel increase in the degree of inhibition of the hemodynamic changes. Maximal analgesia, manifested as complete abolition of signs of the generalized nociceptive response and a considerable (two- to fourfold) elevation of the threshold of the mouth opening and licking reflex (the initial signs of an aversion response) was accompanied by inhibition of responses of BP and ISI (Fig. 2). Meanwhile changes in the respiration in response to stimulation of the dental pulp remained practically at the same level as before.

Stimulation analgesia developed after 20-40 sec and persisted throughout the period of central stimulation, and also for the 30-60 sec after its end. The responses of the animals (both behavioral and autonomic) then recovered gradually and reached the control level after 1.5-2 min (Fig. 2).

The experiments showed that analgesia arising during electrical stimulation of CGM of the midbrain is accompanied by simultaneous inhibition of the hemodynamic manifestation of the nociceptive response. This distinguishes stimulation analgesia essentially from that produced by analgesics and narcotics and which is characterized by preservation of the hemodynamic changes triggered by nociceptive afferentation from an operation wound [1, 5, 8]. A definite parallel was found between the time course of inhibition of the behavioral [4] and cardiovascular nociceptive responses, it was found to be directly dependent on the intensity of central stimulation, and specificity of the modulating influences of the "analgesic" systems of CGM was demonstrated against manifestations of pain belonging to different modalities.

It can be postulated that the initial fall in the hypertension and tachycardia during threshold activation of the "analgesic" systems of the midbrain is associated with inhibition

primarily of the hypothalamo-limbic mechanisms of formation of the hemodynamic basis of nociceptive responses. The morphological and functional basis of this regulation may be provided by anatomically identified connections of CGM in the midbrain with different parts of the hypothalamus and limbic brain [6], which have the character of reciprocal interrelationships [14]. At the same time data in the literature indicate that elevation of the threshold of defensive reflexes (the mouth opening reflex, licking) in response to activation of the "analgesic" system of the brain is the result of strengthening of descending inhibitory influences oriented against segmental mechanisms of the nociceptive afferent input [2, 12]. Similar results also have been obtained in respect of central control of the afferent input at the level of the trigeminal nerve nuclei [9], whose morphological and functional organization is similar to that of the segmental apparatus [13]. In all probability, restriction of the overall nociceptive flow through the trigeminal nuclear complex during activation of the "analgesic" system of the brain leads to a reduction, on the one hand, of the ascending nociceptive flow into higher levels of the CNS and, on the other hand, to activity of structures of the medulla and spinal cord participating in regulation of the circulation which are functionally connected with nociception.

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