EFFECT OF ELECTRICAL STIMULATION OF THE PERIAQUEDUCTAL GRAY MATTER OF THE MIDBRAIN ON EXPERIMENTAL TRIGEMINAL NEURALGIA

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KEY WORKS: generator of pathologically enhanced excitation; trigeminal neuralgia; analgesia.

An extensive search is now in progress for ways of relieving pain through activation of the brain structures which constitute what is now distinugished as the antinociceptive system [1-3, 6, 7, 9-11]. Particular attention is being paid to analgesic effects arising during stimulation of the nuclei raphe, located in the midbrain and medulla [1, 3, 5, 8, 9]. Very few studies have been undertaken of the effect of electrical stimulation (ES) of brain structures on pain syndromes of central origin.

The aim of this investigation was to study the effect of ES of the periaqueductal gray matter of the midbrain on experimental trigeminal neuralgia induced in rats by the creation of the midbrain on experimental trigeminal neuralgia induced in rats by the creation of a generator of pathologically enhanced excitation (GPEE) in the caudal nucleus of the trigeminal nerve. For comparison the effect of ES of the above-mentioned structures was studied on physiological pain induced by nociceptive stimulation.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats. Physiological pain was induced by temperature stimulation (55°C) of the tail. To assess the effect of ES of the brain on physiological pain, the latent period (LP) of the pain response in rats was studied. Experimental trigeminal neuralgia was induced by creating a GPEE in the caudal nucleus of the spinal tract of the trigeminal nerve with the aid of tetanus toxin [4]. Behavioral responses of the animals were observed in a specially equipped chamber and the motor response (actogram) and localization (phonogram) were recorded. The technique of ES through implanted electrodes was described previously [1].

EXPERIMENTAL RESULTS

The control rats developed a pain response to nociceptive temperature stimulation after 0.97 ± 0.02 sec. During ES of the periaqueductal gray matter and dorsal nucleus raphe LP of the pain response was lengthened (Fig. 1). The analgesic effect was found to depend on the parameters of the stimulating pulses (Fig. 1). The first significant increase in LP was observed during ES of brain structures by pulses of current with an amplitude of 2-4 V and a frequency of 10-15 Hz. LP increased with an increase in both frequency and amplitude, to reach 13.90 ± 2.59 sec when the frequency was 45 Hz and the amplitude 14 V. If no pain response had appeared before 20 sec during ES of the brain, temperature stimulation was stopped to prevent burns. The optimal parameters of ES were a frequency of 25-30 Hz and an amplitude of 8-10 V; under these conditions a marked analgesic effect and absence of side effects in the form of a hyperactive motor reaction, sometimes observed during ES with a frequency of 45 Hz and an amplitude of 12-14 V, were found. Histological examination confirmed that the tips of all electrodes were located either in the dorsal nucleus raphe or in the ventral part of the periaqueductal gray matter. ES of the dorsal nucleus raphe gave a more marked analgesic effect than ES of the periaqueductal gray matter.

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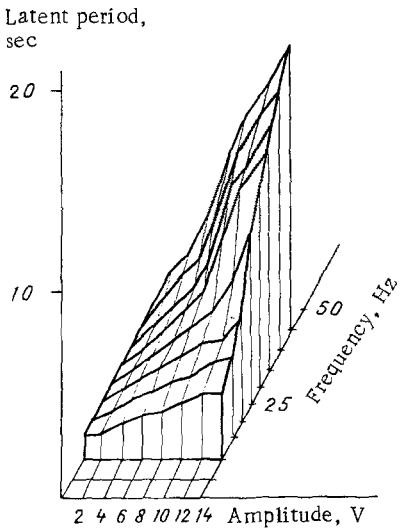

Fig. 1. Effect of ES of the central gray matter of the midbrain on LP of the pain response to nociceptive temperature stimulation.

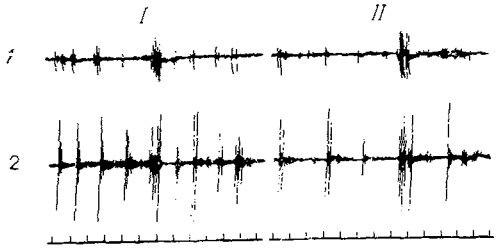

Fig. 2. Effect of ES of dorsal nucleus raphe on course of experimental trigeminal neuralgia in rats. I) Phonogram (1) and actogram (2) before ES; II) phonogram (1) and actogram (2) during ES (f = 25 Hz, A = 6 V).

Similar ES of midbrain structures was carried out in rats during the development of pathological pain (experimental trigeminal neuralgia). From 1.5 to 2 h after micro-injection of tetanus toxin (1-3 MLD for rats in 1 μl) into the caudal nucleus of the spinal tract of the trigeminal nerve the animals began to scratch particular areas of skin of the face. After 3-4 h the attacks increased in frequency, the rats cried, and they began to scratch the same region of the face vigorously. Paroxysms became more frequent and were readily provoked by stimulation of the zone of scratching, which became the trigger zone of facilitated evocation and increased in size with the passage of time. Attention must be drawn to a particular feature of this part of the investigation. Trigeminal neuralgia is a syndrome of severe pain, and the animal's general condition never permitted all the tests (64 versions of ES) to be carried out on the same rat. During development of the syndrome in each animal an increase in the number and total duration of the attacks was observed. In the early stages, during an interval of 2 min from two to ten attacks with a total duration of 6 to 25 sec were recorded whereas in the later stages of experimental trigeminal neuralgia the number of attacks in an interval of 2 min was 11-17 and their total duration was 31-50 sec. Localization of the trigger zone in the experimental rats in the region of innervation of the skin of the face by the second branch of the trigeminal nerve depended on localization of the GPEE in the caudal nucleus, evidence of the existence of topographic representation in that nucleus.

During ES the intensity of the attacks declined: their number and duration decreased. A 2-min recording of the motor response (actogram) and vocalization (phonogram) of a rat with an experimental pain syndrome is shown in Fig. 2: Before stimulation nine attacks were recorded in a 2-min interval and their total duration was 15 sec; during ES of the dorsal nucleus

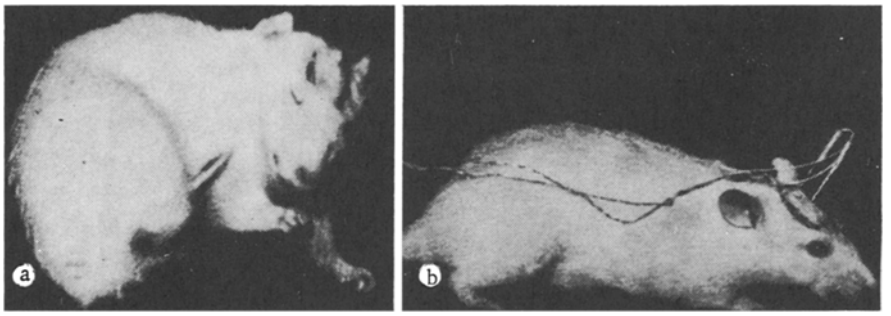

Fig. 3. Effect of ES of dorsal nucleus raphe on course of experimental trigeminal neuralgia in rat. a) Animal during an attack, b) animal in a state of rest, attack terminated by ES (f = 30 Hz, A = 10 V).

raphe the number of attacks and their duration were reduced almost by half (5 and 8 sec respectively). Sometimes during ES the syndrome completely disappeared and the animal remained quiet during ES for 2 min (Fig. 3). A significant reduction in the intensity of the syndrome was observed during stimulation under the following conditions: f = 15 Hz, A = 13 V; f = 20 Hz, A = 14 V; f = 25 Hz, A = 6-14 V; f = 30 Hz, A = 4-14 V. ES with a current of f = 15-45 Hz and A = 12-14 V induced not only analgesia in the animals, but also a number of undesirable side effects: restlessness, a hyperactive motor response, jumping. The histological control showed that the tips of the implanted electrodes were located in the ventral part of the periaqueductal gray matter and in the dorsal nucleus raphe.

ES of the dorsal nucleus raphe and ventral part of the periaqueductal gray matter thus depressed both physiological and pathological pain. One particular feature deserved notice: According to previous investigations [1, 3], nociceptive responses and pain syndromes connected with the creation of a GPEE in the dorsal horns of the lumbar segments of the spinal cord were completely suppressed, whereas trigeminal neuralgia, as the above data show, was not completely suppressed. These differences in the character of depression of nociceptive pain responses at the spinal level and of experimental trigeminal neuralgia suggests that in the first case activation of the serotoninergic inhibitory system (dorsal nucleus raphe) plays an essential role in the analgesic effect, whereas other systems, especially noradrenergic, evidently take part in the depression of pain sensitivity connected with the trigeminal nerve.

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