EFFECT OF EXTIRPATION OF THE ORBITOFRONTAL CORTEX ON DEVELOPMENT OF REFLEX ANALGESIA

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KEY WORDS: orbitofrontal cortex; nociception; electroacupuncture

We now know that the cerebral cortex and, in particular, its somatosensory and orbitofrontal regions, are involved in the formation of the complex system of sensations linked with pain. As many investigations have shown, the functional role of the orbitofrontal cortex (OFC) and sensomotor cortex in the perception of pain signals differs [1, 3, 5, 11]. The functional development of these cortical regions also is preserved in the development of reflex analgesia. The writers showed previously [2] that cooling the somatosensory cortex and, in particular, the second somatosensory area, prevents the development of reflex analgesia, evidence of the activating effect of this cortical region on the antinociceptive system of the brain, which plays a leading role in the development of reflex analgesia. Meanwhile blocking of the functions of OFC in acute experiments did not interfere with the development of the analgesic effect after electroacupuncture (EAP). It is also known that OFC has an inhibitory effect on activity of nonspecific brain-stem structures [7], which participate in the regulation of nociceptive sensitivity [1, 3, 5].

It was accordingly decided to study the influence of OFC on the development of reflex analgesia in unrestrained animals.

EXPERIMENTAL METHOD

Experiments were carried out on 11 adult unrestrained cats, kept in an experimental chamber. Nociceptive electrical stimuli were applied as bursts of pulses (frequency of pulses in the burst 5 Hz, pulse duration 1 msec, burst duration 1 sec) through bipolar electrodes, inserted into the dorsal aspect of the forearm of both forelimbs. The intensity of stimulation was increased stepwise from 100 mV to 100 V. The orbitofrontal zones of the cerebral cortex were removed bilaterally by electrocoagulation under hexobarbital anesthesia (30 mg intraperitoneally). The region of coagulation included the anterior pole of the precentral and coronal gyri, the gyrus proreus, and the anterior part of the orbital gyrus. Before extirpation of the cerebral cortex all the animals were tested to determine the profile of their response to pain on a conventional scale, reflecting the thresholds of nociceptive sensitivity of the animals, from the primary sensory response to the stimulus to generalized emotional-affective manifestations of pain. The most characteristic features of the behavioral responses for each of the five levels on the conventional scale were described by the writers previously [4, 6]. In addition, changes in the profile of nociceptive sensitivity of all the animals were determined after EAP, which was applied to one forelimb in the region of application of the nociceptive stimuli, through steel needles, to which a pulsed current with a frequency of 3 Hz was applied for 30 min. The duration of each pulse was 1 msec. The strength of the stimulating current was limited by the appearance of local muscle contractions and it was always below the threshold of the nociceptive response. After extirpation of the cortical areas, testing of the animals began on the 8th day. The significance of the results was determined by Student's t test. At the end of the investigations the brain was removed to verify the accuracy of the destructive lesions.

EXPERIMENTAL RESULTS

Testing of the animals before extirpation of OFC demonstrated the stability of the thresholds of the response to increasing nociceptive stimulation at all levels of the conventional

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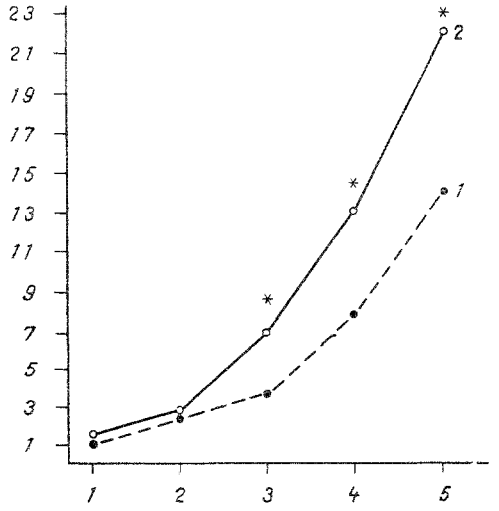

Fig. 1

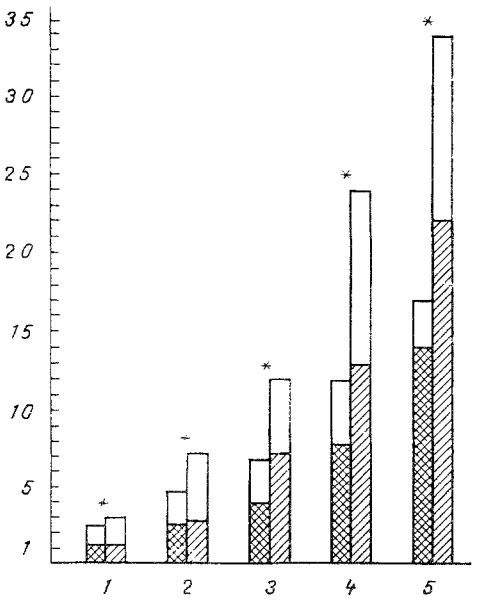

Fig. 2

Fig. 1. Changes in pain response profile of animals after extirpation of OFC. 1) Profile of pain response in intact animals, 2) after extirpation of OFC. Here and in Fig. 2: abscissa, levels of nociceptive response; ordinate, intensity of stimuli applied (in thresholds); *$p < 0.05$.

Fig. 2. Effect of EAP on structure of nociceptive response of animals before and after extirpation of OFC. Cross-hatched columns — thresholds of nociceptive response before extirpation of OFC; obliquely shaded columns — thresholds of nociceptive response after extirpation of OFC; unshaded part of columns — changes in thresholds of nociceptive response after EAP.

scale, so that the profile of nociceptive sensitivity of each animal could be established. EAP caused a significant rise of the thresholds of response at all levels of the conventional scale, evidence of changes in both perceptual and emotional–affective components of pain. Extirpation of OFC raised the thresholds of response mainly at the 4th and 5th levels of the conventional scale, reflecting emotional–affective manifestations of pain. The primary sensory threshold and the pain threshold (levels 1 and 2), under these circumstances, were virtually unchanged (Fig. 1). These data confirmed an earlier conclusion, namely that extirpation of OFC in animals or division of connections between the frontal cortex and thalamus in man induce, initially, suppression of complex emotionally-negative components of the nociceptive response without any disturbance of the sensory-discriminative components of pain [1, 8].

EAP in animals with extirpation of OFC revealed a significant rise of the thresholds of the pain response at all levels, but especially at levels 4 and 5. This elevation of the thresholds of response after EAP obtained in animals with extirpated OFC differed significantly from that in intact animals (Fig. 2). The more marked development of reflex analgesia which we observed in animals after extirpation of OFC compared with intact animals thus suggests stimulation of activity of the antinociceptive system of the brain in the absence of OFC.

These results are in good agreement with those of other investigations which demonstrated potentiation of the antinociceptive action of β-endorphin after destruction of the frontal cortex in rats [10]. Lowering of the excitability of neurons in the corpus striatum and substantia nigra, belonging to antinociceptive structures, induced by stimulation of the frontal cortex, also has been reported in the literature [9]. Thus, the data given above indicate the presence of an inhibitory effect of OFC on activity of the brain antinociceptive system. Inhibitory influences of OFC on the antinociceptive system predominate under these circumstances over the inhibitory manifestations of these cortical regions on nonspecific structures of the brain stem, which conduct nociceptive impulses. This hypothesis is confirmed, in our opinion, by the results of the present investigation and it is connected with strengthening of the

analgesic effect observed after EAP in animals with extirpation of the orbitofrontal cortex and with elevation of the thresholds of the nociceptive response at levels 3, 4, and 5 after destruction of OFC.

By contrast, as our previous investigations showed [6], extirpation of the second somatosensory area of the cortex led to lowering of the thresholds of the nociceptive response at all levels of the conventional scale, and also prevented the development of reflex analgesia [4, 5], on account of reduced activity of the antinociceptive system of the brain.

Comparison of our previous results, pointing to an activating effect of the somatosensory cortex and, in particular, of its second somatosensory area, on the antinociceptive system of the brain, with the results of the present investigation thus suggests that the development of the analgesic effect in the case of reflex stimulation will depend on functional interaction between the somatosensory and orbitofrontal areas of the cortex, with their opposite influences on activity of the antinociceptive system of the brain.

LITERATURE CITED

1. A. V. Val'dman and Yu. D. Ignatov, Central Mechanisms of Pain [in Russian], Leningrad (1976)
2. R. A. Durinyan, M. L. Kukushkin, and V. K. Reshetnyak, Patol. Fiziol., No. 1, 63 (1984).
3. L. V. Kalyuzhnyi, Physiological Mechanisms of Regulation of Nociceptive Sensitivity [in Russian], Moscow (1984).
4. M. L. Kukushkin, V. K. Reshetnyak, and R. A. Durinyan, Byull. Éksp. Biol. Med., No. 6, 650 (1986).
5. V. K. Reshetnyak, Progress in Science and Technology. Series: Human and Animal Physiology [in Russian], Vol. 29, Moscow (1985), pp. 39-103.
6. V. K. Reshetnyak and M. L. Kukushkin, Byull. Éksp. Biol. Med., No. 12, 645 (1986).
7. V. N. Chernigovskii, S. S. Musyashchikova, M. S. Sinyaya, and A. A. Mokrushin, Habituation in Visceral Systems [in Russian], Leningrad (1980).
8. W. P. Chapman, A. S. Rose, and H. C. Solomon, Am. J. Phychiat., 107, No. 3, 221 (1950).
9. L. Chavez-Noriega, P. Patino, and M. Garcia-Munoz, Brain Res., 379, No. 2, 300 (1986).
10. S. Itoh and G. Katsuura, Peptides, 6, 237 (1985).
11. W. D. Willis, Phil. Trans. R. Soc. London, B-308, No. 1136, 253 (1985).

EFFECT OF LATERALIZED ELECTRICAL STIMULATION OF THE BRAIN ON AUDIOGENIC CONVULSIONS IN RATS

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KEY WORDS: audiogenic convulsions; lateralized electrical stimulation

The phenomenon of audiogenic convulsions in rats is frequently used to analyze the physiological and biochemical mechanisms of epilepsy and in the search for methods of preventing and treating this disease. We now know that audiogenic convulsive sensitivity is reduced by systematic application of sound [4], by a raised level of biogenic amines [3, 5, 8] and opiates [10] in the brain, and also by an increase in the ratio of the level of inhibitory amino acids to the level of the activating kind [9].

It is important to study the possibility of using physical procedures as ways of protection against audiogenic epilepsy. We know, for example, that stimulation of the brain by an alternating electric current, as in the case of "electrosleep," has a beneficial effect on the state of the human nervous system [6]. It is logical to analyze the effect of electrical

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