EPILEPTIFORM ACTIVITY IN THE SOMATOSENSORY CORTEX OF RATS WITH TRIGEMINAL NEURALGIA

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As previous studies showed, one of the basic pathogenetic mechanisms of trigeminal neuralgia (TN) is the formation of a generator of pathologically enhanced excitation (GPEE) in the caudal nucleus of the trigeminal complex [1, 2, 10]. During the formation of a GPEE, pathology, in the form of corresponding disturbances of CNS activity, develops if the CNS formation, modified to activity of the GPEE, exerts an effective influence on other parts of the CNS directly or indirectly connected with it, and involves them in the formation of a new pathological organization, or pathological system [3, 4]. It can be tentatively suggested that the somatosensory cortex, to which nociceptive stimulation from the hyperactive caudal nucleus of the trigeminal nerve is projected, is involved in the formation of such a pathological system in TN.

The aim of this investigation was to study electrical activity in the somatosensory cortex of rats with TN.

EXPERIMENTAL METHOD

Experiments were carried out on 37 male Wistar rats weighing 250-300 g. TN was produced in the rats by a method based on the formation of a GPEE in the nociceptive system [1]. To create a model of the central pain syndromes based on the appearance of a GPEE, various substances which either disturb inhibitory mechanisms in the neuron population forming the generator or which cause their depolarization, have been used to produce it [2, 10]. In our experiments we used penicillin, which, as an antagonist of the inhibitory mediator GABA, disturbs inhibition and affects neuronal membranes by blocking Cl-channels or by reducing the transmembrane Cl gradient [7-9]. A microinjection of 1 μl penicillin (100 U) into the right or left caudal nucleus of the spinal tract of the trigeminal nerve in the course of 2 min was given under short-term ether anesthesia, taking coordinates from Paxinos' atlas [11]. Rats of the control groups were given an injection of 1 μl of 0.9% NaCl into the nucleus. The behavioral reactions of the rats after creation of the GPEE in the caudal nucleus were assessed by the method developed previously [1]. The duration and frequency of painful paroxysms, the intensity of the motor response, and of vocalization during an attack, and the intensity of the response to stimulation of the trigger zone (10 control and 10 experimental rats) were estimated. In electrophysiological experiments (12 experimental and five control rats) the electrocorticogram (ECoG) of the somatosensory cortex of both hemispheres was studied in animals immobilized by a muscle relaxant, before and after creation of a GPEE in the caudal nucleus. Evoked potentials (EP) were recorded in response to electrical stimulation of the skin of the snout in the region of the infraorbital foramen (the pain projection zone) with square pulses of current 0.5 msec in duration and 0.2-10 mA in strength. Electrical activity was recorded by means of an oscillograph and tape recorder from "Nihon Kohden" (Japan).

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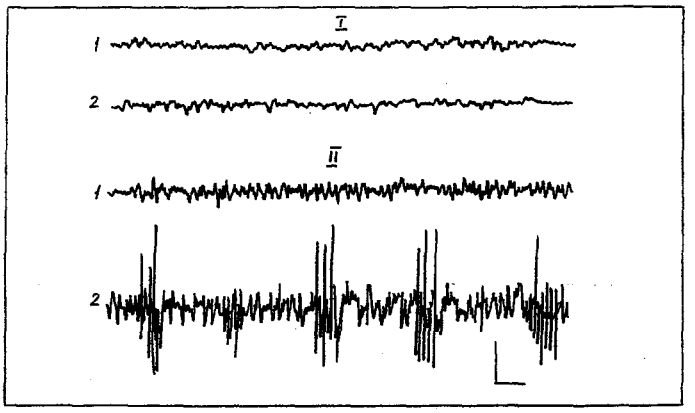

Fig. 1. Changes in electrical activity of somatosensory cortex of rat after creation of GPEE in right caudal nucleus of spinal tract of trigeminal nerve. ECoG before (I) and 40 min after (II) injection of penicillin into caudal nucleus of trigeminal nerve, leading to formation of a GPEE in that nucleus. ECoG of somatosensory cortex of right (1) and left (2) hemispheres. Calibration: 1 mV, 1 sec.

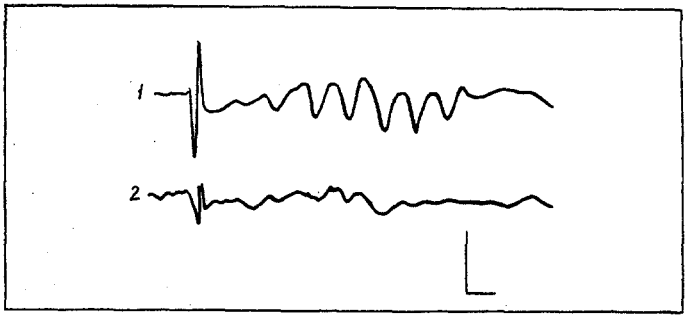

Fig. 2. Prolonged rhythmic after-discharge arising after primary EP in response to electrical stimulation of trigger zone of skin of rat snout in sensomotor region of right hemisphere after creation of GPEE in left caudal nucleus of trigeminal nerve. Responses recorded in right (1) and left (2) hemispheres during stimulation of skin of snout on that side. Calibration: 1 mV, 100 msec.

EXPERIMENTAL RESULTS

The first short attacks of a pain syndrome-with a frequency of 1-2/min began to appear 15-20 min after microinjection of penicillin into the animals' caudal nucleus, and they were accompanied by a cry and by scratching of the snout in the zone corresponding to the innervation of the infraorbital nerve. With the course of time the frequency of the episodes increased, to 4-7/min after 40-60 min. The attacks were paroxysmal in character, and with time they were easily provoked by application of a light tactile stimulus to the trigger zone. After 120 min the frequency and duration of the attacks decreased, and the paroxysms of pain became infrequent (one episode during 10-15 min). As previous investigations [5] showed, with the onset of TN, the animals began to develop microcirculatory disturbances.

In animals of the control group, none of the 10 rats developed attacks of Pain after injection of 0.9% NaCl into the nucleus.

In electrophysiological experiments the ECoG recorded from the somatosensory area of both hemispheres was monitored continuously before and after creation of the GPEE in the caudal nucleus. Spike-wave discharges began to appear 10-20 min after microinjection of penicillin into the caudal nucleus in the somatosensory region of

the contralateral hemisphere relative to the site of injection. These discharges became grouped into bursts after 20-30 min, each burst consisting of 4-6 discharges, with a duration of 1-2 sec. Changes in cortical electrical activity after penicillin microinjection into the caudal nucleus are shown in Fig. 1. In some cases 40-60 min after penicillin injection, spike-wave activity also was observed in the ipsilateral hemisphere. Epileptiform activity in the contralateral hemisphere was always greater in amplitude and duration.

In the control group, after injection of 0.9% NaCl into the caudal nucleus of the animals, changes in the ECoG in the somatosensory cortex described above were not observed.

In response to electrical stimulation of the skin of the snout, in the region of innervation of the infraorbital nerve on the side of penicillin microinjection, rhythmic after-discharges appeared in the cortex of the contralateral hemisphere, after EP, consisting of several waves (Fig. 2). Our results agree with those of other workers [6], who studied cortical electrical activity of patients with TN and showed that high-amplitude spikes were recorded from them, accompanied by hypersynchronization of activity.

As the present investigations showed, as a result of activity of a GPEE in the caudal nucleus of the trigeminal nerve, rats develop a pain syndrome with behavioral manifestations characteristic of trigeminal neuralgia, and epileptiform activity appears in the somatosensory cortex, and is particularly strong in the contralateral hemisphere. The onset of this activity reflects, on the one hand, activity of the GPEE in the caudal nucleus of the trigeminal nerve and, on the other hand, involvement of the somatosensory cortex, receiving stimulation from the hyperactive caudal nucleus, in the formation of the pathological pain syndrome of this form of trigeminal neuralgia.

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