NOCICEPTIVE PRESSOR REFLEXES AND NERVE IMPULSE ACTIVITY IN RESPONSE TO INTRADERMAL INJECTION OF POTASSIUM CHLORIDE IN CATS

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The dose–effect curves of the pressor reflex from the skin, by analogy with those from reflexogenic zones of certain organs studied previously, consisted of two parts: interoceptive and nociceptive reflexes. The latter appeared in response to the direct action of high concentrations of KCl (125-250 mM) on nerve fibers. Synchronization of excitation in the fibers, which is considered to be the special code of pain, could not be detected on the neurograms.

There are two views regarding the nature of the peripheral mechanism of pain. One regards pain as the result of excitation of a specific receptor system [13]. The second postulates that the same peripheral nervous structures are responsible for painful and painless sensations, and that "excitation of nerve endings by ordinary stimulation cannot give rise to a sensation of pain, but this can take place in response to stimulation which acts on the nerve fiber itself" [12].

The view that direct stimulation of nerve fibers takes place when a painful stimulus is applied has been confirmed experimentally only in the last decade [1, 2, 4-7, 9-11]. These workers showed that certain afferent nerve fibers of the intestine, the membranes of the heart, and the tissues of the lower limbs possess a dual function: they conduct impulses from receptors when these are stimulated in the usual way, and they act as direct "receptors" of nociceptive stimuli. This conclusion was based on the analysis of the relationship of pressor reflexes arising during the action of chemical stimuli and, in particular, of K ions.

If this is true for nerves of all organs, similar results would be expected in response to injection of KCl into the fluid perfusing an area of skin. The present investigation was carried out to study this problem.

EXPERIMENTAL METHOD

In experiments on cats under urethane anesthesia the skin of the hind limb was perfused with Ringer's solution by the method described earlier [8]. KCl was injected into the perfusion fluid in concentrations of between 15.6 and 1000 mM, and in a volume of 1 ml. Recording electrodes connected to a UBP 1-01 amplifier were placed on the medial branch of the saphenous nerve running from the perfused area of skin. Potentials were recorded on a loop oscillograph. The pressure in the carotid artery was recorded by a mercury manometer on a kymograph.

EXPERIMENTAL RESULTS AND DISCUSSION

Injection of KCl into the perfusion fluid of the area of skin evoked a pressor reflex. The threshold concentration of KCl was 15.6 mM. The amplitude of the threshold reflexes did not exceed 3 mm Hg. With

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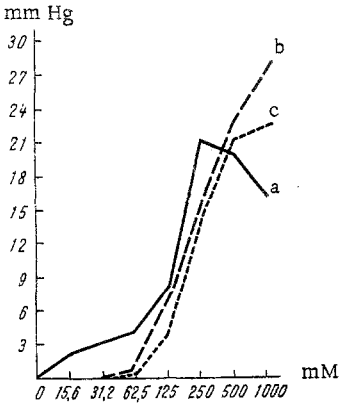

Fig. 1. Amplitude of pressure reflex as a function of KCl concentration: a) injection of KCl into saphenous artery, receptive field of skin flap intact (mean results of 14 experiments); b) injection of KCl into saphenous artery, receptive field of skin flap isolated (mean results of nine experiments); c) central end of divided saphenous nerve bathed in KCl solutions (mean results of 12 experiments). Abscissa, KCl concentration (in mM); ordinate, amplitude of reflexes (in mm Hg).

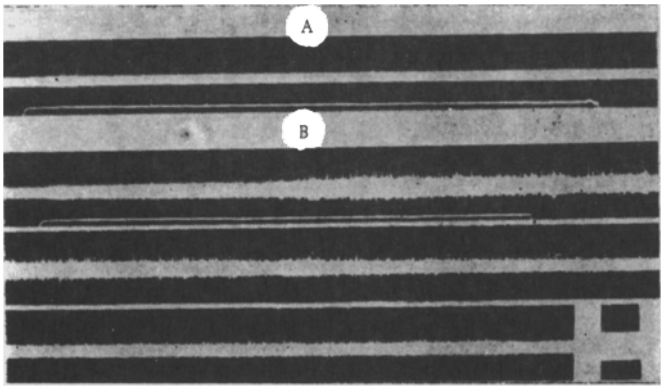

Fig. 2. Impulses recorded in fibers of saphenous nerve after injection of KCl into blood vessels of skin in concentrations of 31.2 (A) and 250 (B) mM. Time marker 10 Hz, calibration 20 μV.

an increase in concentration, the amplitude of the pressor reflex gradually increased. After injection of KCl in a concentration of 125-250 mM, a much greater reflex effect on the blood pressure was produced than with smaller concentrations. A further increase in the KCl concentration evoked reflexes of the same order (Fig. 1a).

Reflexes to small concentrations of KCl arising in response to excitation of receptors [9] were called reflexes of the first order. Pressor reflexes to high concentrations of KCl, accompanied by hyperpnea and movements of the animal, were called reflexes of the second order. They arise by the action of KCl directly on the nerve fibers. Concentrations evoking reflexes of the second order are nociceptive or painful [2, 9].

To verify the excitatory action of KCl on the nerve fibers, experiments were carried out on which the compounds were injected into the perfusion fluid after complete isolation of the receptive field. In these experiments the genicular branch of the saphenous nerve and all the blood vessels of the skin flap were ligated.

The threshold concentrations of KCl in these experiments was 62.5 mM. However, pressor reflexes to high concentrations of KCl were of the same order as those in the experiments with an intact receptive field (Fig. 1b).

To confirm the direct excitatory action of large concentrations of KCl on nerve fibers, a series of experiments was carried out in which the central end of the divided saphenous nerve was bathed in KCl solution of different concentrations [10].

The result was a dose–effect curve which was almost identical with that obtained in the experiments of the previous series (Fig. 1c). In half of the experiments the first (already nociceptive) pressor reflexes were obtained by the action of KCl in a concentration of 250 mM. When the nerve was bathed in KCl solutions with concentrations of 15.6-125 mM, no pressor effect was obtained. In 35% of the experiments the initial concentration causing elevation of the blood pressure was 125 mM, and in 15% of experiments it was 62.5 mM.

The reflexes of the first and second orders differed in their genesis and character. Clearly the impulse activity in the nerve fibers evoking these two types of reflexes could not be identical. It has been postulated that nociceptive concentrations of KCl evoke synchronized discharges in thin afferent fibers, and that these are the special code of pain [9]. Synchronization of impulses of excitation in the fibers could be detected on a neurogram as high-voltage integral potentials. To test this hypothesis, activity of the medial branch of the saphenous nerve was recorded during injection of KCl in various concentrations.

Neurograms after injection of KCl in subnociceptive and nociceptive concentrations are shown in Fig. 2. KCl in a concentration of 31.2 mM evoked very slight low-voltage spike activity at the beginning of injection (Fig. 2A), while in a concentration of 250 mM it evoked prolonged and well-marked impulse activity (Fig. 2B). Initially, low-voltage spikes were recorded, but in the middle of the injection these changed to high-voltage. However, it was impossible to judge from the character of this activity whether synchronization of excitation occurred in the fibers, or to determine which group of fibers conducted the impulse. It can be postulated that low-voltage impulse activity is characteristic of group C fibers, and high-voltage activity of group A fibers [3]. The possibility is not ruled out that synchronization of impulses in group C fibers is masked by the high-voltage discharges in the group A fibers.

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