INTEROCEPTIVE AND NOCICEPTIVE PRESSOR REFLEXES TO THE ACTION OF POTASSIUM CHLORIDE ON TISSUES OF THE HIND LIMB

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The graph of amplitude of pressor reflexes against logarithm of KCl concentration consists of two S-shaped curves. By analogy with the reflexogenic zone of the small intestine studied previously, it is postulated that the first branch of the curve, in the KCl concentration region from 15.6 to 62.5 mmoles/liter, is due to excitation of receptors, while the second branch (62.5-500 mmoles/liter) is due to direct excitation of afferent fibers. The threshold KCl concentration for interoceptive reflexes is 8-10 mmoles/liter, which is the same as the threshold concentration of K ions for membranes of the heart and the small intestine. Threshold concentrations for nociceptive reflexes from the tissues of the hind limb are higher than for other zones. The increase in threshold to 62.5 mmoles/liter for the reflexogenic zone farthest from the heart is regarded as confirmation of the hypothesis that signals giving information about nociceptive stimuli are transmitted by a flow of synchronized impulses.

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The graph of amplitude of pressor reflexes in response to the action of potassium ions on receptive zones of the small intestine and membranes of the heart, expressed as concentration–effect curves, consists of two branches [1, 6]. Reflexes to the action of potassium ions in relatively low concentrations reflect excitation of receptors, while those produced by high concentrations reflect their action on sensitive fibers [2]. More powerful reflexes (nociceptive) are evidently due to synchronized discharges of microbundles of non-medullated fibers [5]. It follows from this concept of the peripheral mechanism of nociceptive effects that discharges of these bundles, synchronized at the point of origin, may undergo partial or complete desynchronization during conduction of the impulses to the brain, because fibers, even of a group serving the same function, differ in their conduction velocity [8]. Other conditions being equal, the degree of desynchronization must increase with an increase in the length of the afferent fibers [2, 6, 8].

These considerations suggest that the threshold of nociceptive reflexes, reflected by the threshold concentration of the substance concerned, must depend on the distance between the reflexogenic zone and the spinal cord. If this is so, the shorter the afferent pathway from a given zone to the spinal cord, the lower the concentration of chemical stimulus which will be sufficient to evoke a nociceptive reflex.

This hypothesis was tested by studying the relationship between the amplitude of pressor reflexes and the potassium ion concentration during the action of these ions on the receptive zone farthest away from the spinal cord–the distal part of the hind limb. It was intended to compare the results obtained with the characteristics of zones in the intestine [1, 5] and membranes of the heart [6] studied previously.

EXPERIMENTAL METHOD

The pressure in the carotid artery of cats anesthetized with urethane (1.5-2 g/kg) was recorded by a mercury manometer. The KCl concentration was doubled with each stimulation between the range of 15.6

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TABLE 1. Quantitative Characteristics of Pressor Reflexes in Response to the Action of KCl on Distal Part of Hind Limb

Threshold concentration (in mmoles/liter)	Amplitude of threshold reflexes (in mm Hg)	Concentration threshold for nociceptive reflexes (in mmoles/liter)	Amplitude of threshold nociceptive reflexes (in mm Hg)	Amplitude of reflexes at concentrations of 500 moles/liter (in mm Hg)	Concentration corresponding to maximum amplitude of reflex (in mmoles/liter)	Maximum of amplitude of reflex (in mm Hg)
A. Perfusion with Ringer–Locke solution						
15,6	3	31,2—46,8	20	41	0,75	47
15,6	4	46,8—62,5	12	34	1	46
15,6—23,4	4	62,5—93,7	14	26	1	29
23,4—31,2	3	93,7—125	16	36	0,75	40
15,6—23,4	8	125—250	20	22	1	24
15 6	2	125—250	18	18	1	28
23,4—31,2	2	125—250	10	28	0,75	35
15,6—23,4	4	125—250	14	25	1	36
15,6	2	125—250	23	26	1	42
15,6	7	125—250	40	58	0,5	58
Mean values	3,8±0,6	—	18,7±2,6	31,4±3,6	—	38,5±3,2
B. Injection into anterior tibial artery						
		31,2—62,5	26	32		
		62,5—97,3	14	33		
		62,5—100	54	110		
		62,5—125	22	38		
		62,5—125	17	46		
		62,5—125	58	80		
		93,7—125	20	50		
Mean values		—	30,1±6,8	55,6±9,9		

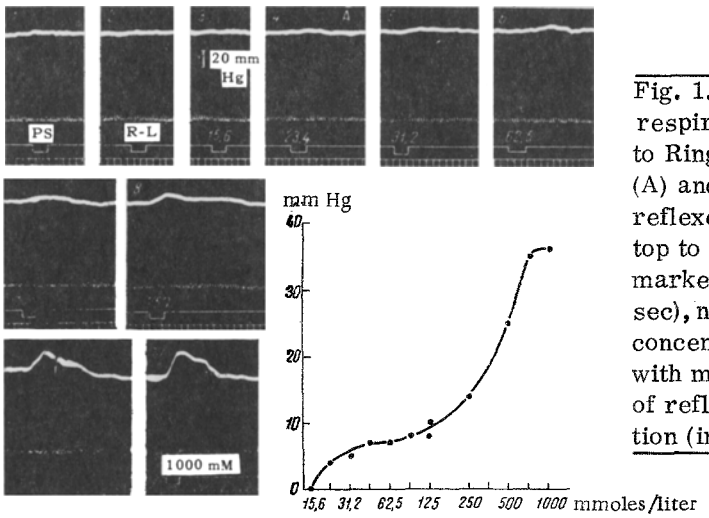

Fig. 1. Reflex responses of arterial pressure and respiration to stimulation of tissues with KCl added to Ringer–Locke solution used to perfuse hind limb (A) and curve of concentration against amplitude of reflexes (B) in one experiment of series I. a) From top to bottom: arterial pressure, respiration marker, of stimulation (30 sec), time marker (15 sec), numbers above marker of stimulation show KCl concentration (in mmoles/liter); zero line coincides with marker of stimulation. B) Ordinate–amplitude of reflexes (in mm Hg); abscissa–KCl concentration (in mmoles/liter).

mmoles/liter and 1 mmole liter. In experiments on 10 animals (series I) the tissues of the leg and foot, remaining connected with the rest of the body only through the sciatic nerve [7], were perfused with Ringer–Locke solution (37-38°). Solutions of KCl, in a volume of 2 ml, were injected into the perfusion fluid. Since the KCl solutions thus injected were diluted, to determine the threshold concentration in the experiments of series II (12 animals) prolonged perfusion was carried out with solutions containing an increased KCl concentration. In experiments of series III (7 animals), 1 or 2 ml of KCl solution injected were into tissues supplied with blood from the anterior tibial artery. For this purpose, the artery was clamped and KCl solu-

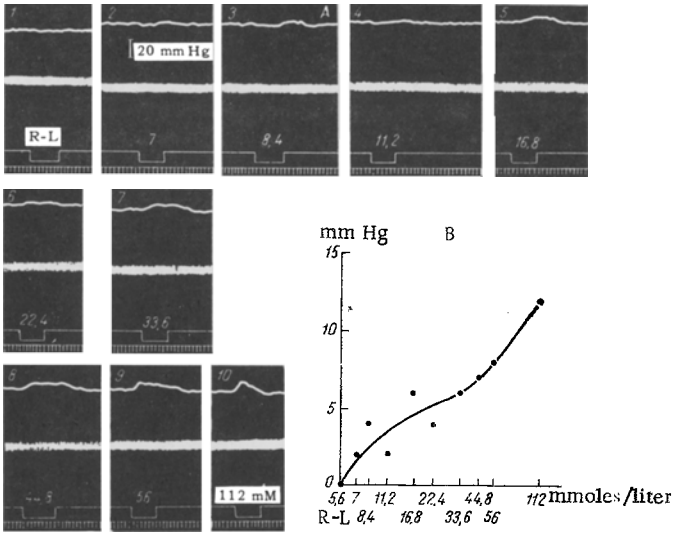

Fig. 2. Reflex responses of arterial pressure and respiration during perfusion of hind limb tissues with Ringer–Locke solutions enriched with K ions (A) and graph showing amplitude of pressore reflexes as a function of KCl concentration (B). A) From top to bottom: arterial pressure, respiration, marker of stimulation, time marker (5 sec); remainder of legend as in Fig. 1A. B) Ordinate–amplitude of reflexes (in mm Hg); abscissa (logarithmic scale)–KCl concentration (in mmoles/liter).

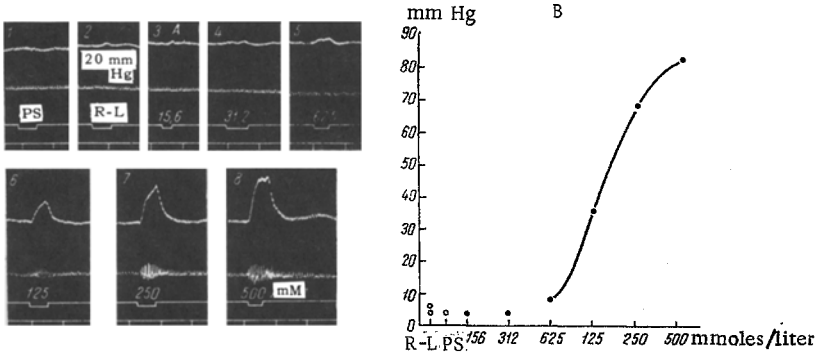

Fig. 3. Reflex response of arterial pressure and respiration to injection of KCl into anterior tibial artery (A) and curve of amplitude of pressor reflexes against KCl concentration (B). A) Order of curves as in Fig. 1A. Time marker 30 sec. B) Ordinate–amplitude of reflexes (in mm Hg); abscissa–KCl concentration (in mmoles/liter).

tion injected against the blood flow through the peroneal artery, given off distally to the point of occlusion. The clamp was then removed.

EXPERIMENTAL RESULTS AND DISCUSSION

In all experiments injection of KCl solutions into the distal part of the limb evoked only pressor reflexes. They disappeared after division of the sciatic nerve. This result is in agreement with those obtained previously [4, 7]. The points on the curve (Fig. 1B) fall approximately on two S-shaped curves. By analogy with the results of experiments on the reflexogenic zone of the small intestine [1] it can be postulated

that the first of these curves reflects the action of KCl on the tissue receptors of the limb, while the second is the result of direct excitation of afferent fibers. Correspondingly, reflexes in the region of the first curve must be regarded as interoceptive, and those in the region of the second curve as nociceptive (Table 1A).

In the 8 experiments of series II, the concentrations adequate to cause the appearance of threshold pressor reflexes were 8-10 mmoles/liter (Fig. 2A, B), as they were also for the receptive zone of the small intestine [1, 5] and membranes of the heart [6].

In 8 of the 10 experiments of series I, KCl concentrations at the threshold level for nociceptive reflexes were higher than 62.5 mmoles/liter, while in 6 experiments they were between 125 and 250 mmoles/liter (Table 1A). The corresponding KCl concentrations for the receptive zone of the small intestine were more constant and, significantly, they were between 31.2 and 62.5 mmoles/liter [1, 3]. However, it must be borne in mind that isolation of the limb for subsequent perfusion is more prolonged and traumatizing procedure than isolation of the small intestine. It requires deeper anesthesia, and this may be related to the higher threshold of the nociceptive reflexes.

The effect of depth of anesthesia is shown by the fact that, during repeated measurements in two experiments of series I, the thresholds of the nociceptive reflexes were reduced: in one case from 125-250 to 62.5-125 mmoles/liter, and in the second from 125-250 to 62.5-93.7 mmoles/liter. So as to exclude the influence of this factor as far as possible, in the experiments of series III the KCl solutions were injected into the anterior tibial artery without isolation and perfusion of the limb (Fig. 3A, B). Under these conditions the threshold KCl concentrations for nociceptive reflexes were lower—between 62.5 and 125 mmoles/liter (Table 1B). Nevertheless, just as in the experiments of series I, they were higher than the corresponding thresholds for receptive zones of the small intestine and membranes of the heart. This confirms the hypothesis that threshold concentrations of nociceptive reflexes are dependent on the distance between the receptive zone and the spinal cord.

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