CHANGES IN SENSITIVITY OF TISSUE RECEPTORS OF THE SMALL INTESTINE TO LACTIC AND CITRIC ACIDS PRODUCED BY POTASSIUM IONS

L. V. Filippova

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The sensitivity of interoceptors of the small intestine to intraarterial injections of KCl and lactic (LA) and citric (CA) acids was investigated in cats anesthetized with urethane. Threshold doses stimulating the receptors of the small intestine were 54 ± 6 μg/g for KCl, 16 ± 1 μg/g for LA, and 8.2 ± 0.9 μg/g for CA. Under the influence of potassium ions the thresholds were reduced to 8 ± 1 μg/g for LA and 6.0 ± 0.6 μg/g for CA.

Investigations [1, 3-5] have shown that potasstium ions and certain organic acids (lactic, citric) stimulate tissue receptors in doses corresponding to their concentrations under natural conditions.

On the basis of the published evidence [2, 8-16] that the concentration both of lactic (LA) and citric (CA) acids and of potassium ions rises simultaneously in blood flowing from a working organ, an investigation was carried out to discover the direction in which the sensitivity of the tissue receptors changes during the combined adminstration of these metabolites.

EXPERIMENTAL METHOD

Experiments were carried out on 52 cats anesthetized with urethane (1-1.2 g/kg). A loop of small intestine with its innervation and blood supply intact was placed in a constant-temperature bath filled with warm (37-38°C) Ringer-Locke solution. Solutions of LA in a dilution of 3.9-125 mM, CA in a dilution of 0.97-62.5 mM (in a volume of 0.2 ml), and KCl in a concentration of 22.4 and 16.8 mM (in a volume of 0.5-1 ml) were injected into the central end of one of the small intestinal arteries at a distance of not more than 10 mm from the bowel wall.

Afferent impulses were recorded in the peripheral segments of the intestinal nerves by means of bipolar silver electrodes, a cathode follower, and an amplifier with a transmission band of 75-2000 Hz and photographed from the screen of a cathode-ray oscilloscope. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS AND DISCUSSION

The sensitivity of the interoceptors of the small intestine to LA and its change under the influence of potassium ions was studied in 25 animals (54 segments of small intestine).

After injection of 70 μg LA (0.2 ml, 3.9 mM) a very slight increase in the intensity of the afferent impulse activity was observed in only five of the 16 cases. Injection of 140 μg (0.2 ml, 7.8 mM) produced an effect in 68% of the 63 cases. The mean threshold dose of LA stimulating the interoceptors of the small intestine was 16±1 μg rather less than described earlier [3].

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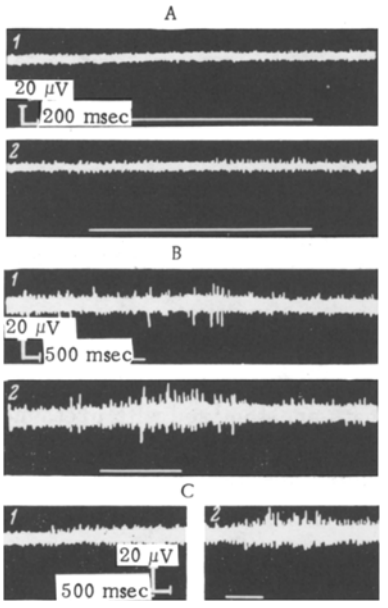

Fig. 1

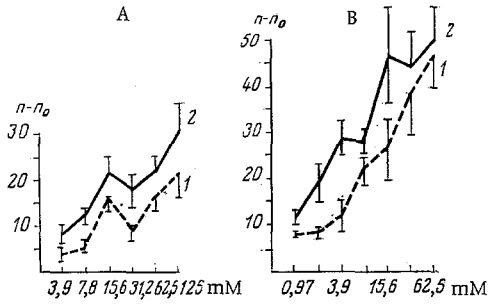

Fig. 2

Fig. 1. Afferent impulse activity in intestinal nerves evoked by LA before (1) and after (2) injection of KCl (1 ml, 16.8 mM), A, B, C) records of three experiments. Concentrations of LA: 3.9 (A), 7.8 (B), 31.2 (C) mM. From top to bottom: afferent impulse activity, marker of injection of acid. Calibration: vertical line – 20 μV, horizontal line – 200 msec (in A) and 500 msec (in B, C).

Fig. 2. Change in spike frequency in intestinal nerves produced by injection of LA (A) and CA (B) before (1) and after (2) injections of KCl solution. Abscissa, concentrations of acid solutions (in mM); ordinate, $n-n_0$, where n and n_0 represent number of spikes per second during development of maximal effect and before injection of agents, respectively. Vertical lines show mean error (± m) of the means (M).

The data in the literature on the sensitivity of the receptors of the small intestine to potassium ions were obtained by perfusion of the organ [1]. The response of the blood pressure served as a measure of excitation of the receptors. The threshold concentration of KCl injected into the perfusion fluid in a volume of 1 ml was found to be 15.6 mM. In the present series experiments on 12 cats (21 segments of small intestine) showed that the threshold dose of KCl inducing excitation of the receptors of the small intestine when injected directly into the blood is 330 μg (0.2 ml, 22.4 mM). The flow of afferent impulses was increased in 62% of 24 cases. The threshold concentrations of KCl for receptors of the small intestine found in these experiments agree with those determined previously [1]. Expressed per gram tissue weight the mean threshold dose of KCl was 54 ± 6 μg/g.

The next series of experiments showed that after injection of doses of KCl which by themselves did not cause visible changes in the flow of afferent impulses, the sensitivity of the receptors to LA was modified. After injection of KCl in a concentration of 16.8 mM, for instance, the flow of impulses in response to injection of 70 μg LA (0.2 ml, 3.9 mM) was now increased in nine, and not five, of the sixteen injections, i.e., in 56% of cases; the effect itself on the frequency and amplitude of the spikes was greater. After injection of 1 ml KCl in a concentration of 16.8 mM a previously ineffective dose of LA (Fig. 1A, trace 1) now led to increased afferent activity in the same segment of the small intestine (Fig. 1A, trace 2). The response of the receptors to injection of large doses of LA also was considerably increased by potassium ions (Fig. 1B, C). Graphs showing changes in the frequency of spikes generated under the influence of LA solutions of different concentrations before and after injection of 1 ml KCl are shown in Fig. 2A. It is clear that after preliminary injections of KCl the intensity of the bioelectrical reaction increases.

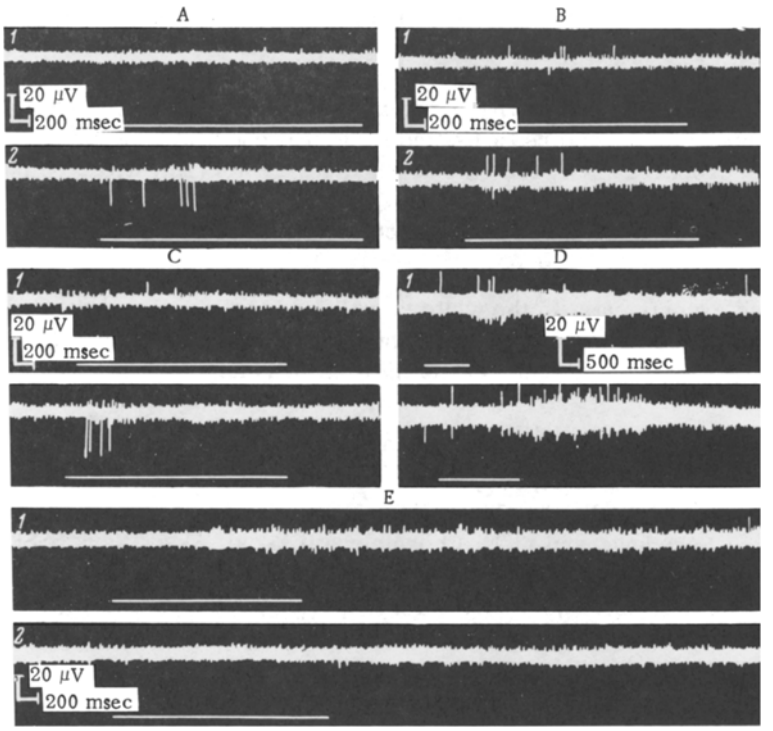

Fig. 3. Spike activity in intestinal nerves evoked by CA before (1) and after (2) injection of KCl (1 ml, 16.8 mM): A, B, C) records of one experiment; D, E) of two others. Concentrations of CA; 0.97 (A), 1.95 (B), 3.9 (C), 31.2 (D), and 62.5 (E) mM. From top to bottom: afferent activity, marker of injection of acid. Calibration: vertical line 20 V, horizontal line 200 msec (in A-C, E) and 500 msec (in D).

The results thus show that the sensitivity of interoceptors to LA is increased by potassium ions. The mean threshold dose of LA under these conditions was halved (from 16 ± 1 to 8 ± 1 μg/g).

A similar relationship was observed in the experiments to study the effect of potassium ions on CA reception. In experiments on 17 cats (30 segments of small intestine) receptors in eight of the 30 segments were found to respond by a slight increase in spike activity to injection of CA in a dose of 40.5 μg (0.2 ml, 0.97 mM). Strictly speaking this dose cannot be taken as the threshold, for a response occurred in only 26% of cases. This agrees with results obtained by other workers [4] who observed responses to the same dose of CA under the same experimental conditions in 31% of 13 cases. In the present experiments the mean threshold dose of CA stimulating the receptors of the small intestine was 8.2 ± 0.9 μg/g. After preliminary injections of KCl into the intestinal vessels, the receptors of 17 of the 30 segments now responded by increased activity to injection of 40.5 μg CA, i.e., in 57% of cases. The threshold dose of CA under these conditions was lowered to 6.0 ± 0.6 μg/g. After injection of CA in concentrations increasing on a logarithmic scale the effects of an increase in sensitivity of the tissue receptors under the influence of preliminary injections of KCl were manifested more clearly still (Figs. 2B and 3A-D). In some experiments with higher concentrations of CA (31.2-62.5 mM) not an increase but, on the contrary, inhibition of the response was observed (Fig. 3E).

During muscular work potassium ions leave the cells to enter the tissue fluid and blood [13]. The potassium ion concentration in blood flowing from an actively working muscle may increase to 7-8 mM and in the intercellular space to 14-30 mM. Consequently, the KCl concentrations used in this investigation correspond to those formed in blood and tissue fluid during normal activity of the animal.

Repeated experiments have shown that during muscular work, simultaneously with liberation of potassium ions, there is an increase in the blood concentration of other compounds, especially CA and LA [2, 8-12, 14-16]. It was shown 30 years ago [11, 15] that the LA concentration in human blood increases to

12-13 mM after running. Since in the present experiments the interoceptors were stimulated by LA in a concentration of 7.8 mM, it must be concluded that the excessive amounts of LA formed in the working organ were detected by tissue receptors. If it is remembered that during work potassium ions are liberated simultaneously, increasing the sensitivity of the interoceptors to LA, it must be accepted that the sensitivity of the small intestinal receptors to LA under natural conditions is high. Assuming that the resting muscle constantly produces LA at the rate of 11-15 μg/g/min [16], it can be postulated that the asynchronous "spontaneous" activity recorded in the peripheral segments of the intestinal nerves was produced to some degree by the response of the tissue receptors to the constant fluctuations in the concentration of this metabolite in the tissues.

The results of these experiments, in the writer's opinion, confirm the views developed by Chernigovskii [6, 7] and Lebedeva [3, 4] on the existence of chemoreceptors responding to slight changes in the concentration of tissue metabolites in the tissues of the internal organs.

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