MECHANISMS OF CUTANEO-CARDIAC CONNECTIONS

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There have been many investigations into the effect of cutaneous stimulation of the formation of ascending flows of impulsation from damaged somatic and visceral organs, and they have demonstrated effective interaction between exteroceptive and interoceptive afferent flows at different levels of the CNS [2, 6, 7]. The substrate of primary interaction between afferent systems is provided by the segmental apparatuses of the spinal cord, especially the substantia gelatinose, neurons of which, when excited during activation of fast-conducting fibers, can induce prolonged primary afferent depolarization and can block or substantially restrict ascending flows of impulsation at the level of the first central relay neurons [3, 4, 9, 10]. However, existing ideas virtually rule out any participation of the interorganic nervous system in the realization of inhibitory influences during cutaneous afferent stimulation. Meanwhile it is known that the intracardiac nervous system can regulate levels of afferent flows from the heart, and that blocking of afferentation may be connected with activation of parasympathetic efferents during cutaneous stimulation [5]. This concept has been least researched at the level of cutaneo-cardiac connections. The aim of this investigation was to study the neuronal mechanisms of the influence of cutaneous efferentiation on the formation of ascending flows of impulsation from the heart.

EXPERIMENTAL METHOD

Acute experiments were carried out on 25 cats weighing 2.5-3 kg, anesthetized with chloralose (40-50 mg/kg) and curarized. Bipolar stimulating electrodes were fixed to the zone of the sinoatrial node (SAN) of the heart, and to the skin surface in the scapular region. Testing stimulation consisted of application of square pulses of current with a duration of 0.3 msec and a strength of 10-15 mA to SAN, and conditioning stimulation took the form of stimulation of the skin (series of five square pulses of current: duration 0.5 msec, frequency 1000 Hz, strength 2-10 mA). In five experiments stimulation of the peripheral end of the divided right vagus nerve at the level of the thyroid cartilage (current strength 0.2-2 mA) was used as conditioning stimulation. The electrical stimuli were generated by means of an ÉSU-2 stimulator. The interval between testing and conditioning stimulation varied from 15-20 to 200-350 msec. Evoked potentials (EP) were recorded from the exposed surface of the rostral zones of the cerebral cortex. EP were amplified and recorded by means of a Neuroaverager average response computer (OTE Biomedica, Italy), with 10 presentations of the signal. In the course of the experiments a one-stage bilateral vagotomy was performed, using special neurotomes. Throughout the experiment the animals' body temperature was kept constant and the exposed surface of the cortex was irrigated with warm (37°C) physiological saline.

EXPERIMENTAL RESULTS

Single electrical stimulation of SAN led to the formation of positive-negative EPs in the cerebral cortex with a combined amplitude of the initial phases of 149.2 ± 7.7 μV. In animals with intact vagus nerves, conditioning stimulation of the skin, preceding testing stimulation of SAN by 350 and 300 msec, caused significant changes in the amplitude of EP (144.4 ± 8.6 and 151.9 ± 11.4 μV, respectively). Reduction of the interstimulus interval to 250 msec led to some reduction of amplitude of EP (130 ± 9.2 μV), and the same effect was observed if the interval was 200 msec (129.6 ± 19.3 μV). Further reduction of the interval between the testing and conditioning stimuli caused a significant decrease in the combined

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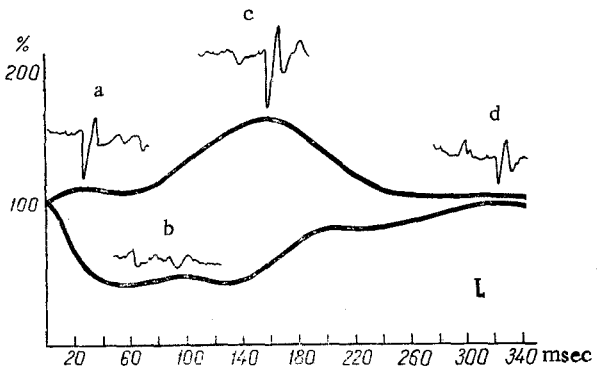

Fig. 1

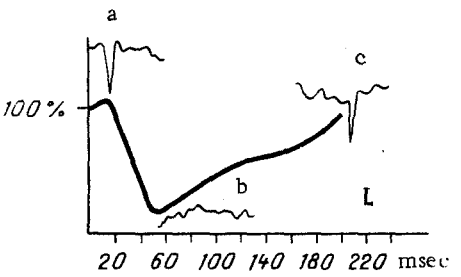

Fig. 2

Fig. 1. Combined stimulation of cutaneous zones and of SAN. Changes (in percent of initial level) in combined amplitude of 1st and 2nd phases of EP arising in rostral zones of the cortex in response to stimulation of SAN, with reduction of the interval between conditioning (cutaneous stimulation) and testing (stimulation of SAN) stimuli. 1) Bilateral vagotomy; 2) intact vagus nerves. a-d) EP for corresponding interstimulus interval. Here and in Fig. 2, calibration: 60 μV, 20 msec.

Fig. 2. Combined stimulation of vagus nerve and SAN. Changes (in % of initial level) in combined amplitude of 1st and 2nd phases of EPs arising in rostral zones of the cortex in response to stimulation of SAN with reduction of interval between conditioning stimulus applied to peripheral end of divided right vagus nerve and testing stimulus (stimulation of SAN). a-c) EP and corresponding interstimulus interval.

amplitude of EP. For instance, when the interstimulus interval was 150 msec the amplitude of EP was 78 ± 11.8 msec ($p < 0.01$), whereas when the interval was 100 msec the amplitude was 77.4 ± 14.6 msec ($p < 0.01$). The strongest effect of inhibition of the testing EPs was observed with an interval of 50 msec between stimuli (61 ± 6.7 μV, $p < 0.001$). Shortening of the interval to 20 msec led to an increase in the amplitude of EP up to 101.7 ± 15.1 μV, compared with 138.5 ± 14.7 μV when the interstimulus interval was 15 msec ($p > 0.1$).

After the data described above had been recorded, one-stage bilateral vagotomy was performed on the animals at the level of the thyroid cartilage. The combined amplitude of the initial phase of EP during stimulation of SAN 25-30 min after division of the vagus nerves was 129.1 ± 12.3 μV. Conditioning stimulation of the skin with intervals of 350 and 300 msec between stimuli caused no significant changes in the amplitude of EP (126 ± 12.8 and 132.4 ± 14.5 μV, respectively, $p > 0.1$). Shortening of the interstimulus interval to 250 msec led to some increase in the combined amplitude of EP (138.8 ± 18.4 μV, $p > 0.1$), which was more marked when the interval was further shortened to 200 msec (179.3 ± 32.2 μV, $p > 0.1$) and to 150 msec (206 ± 37.2 μV, $p > 0.1$). With an interval of 100 msec between testing and conditioning stimuli the amplitude of EP was 160.6 ± 23.3 μV ($p > 0.1$), whereas when it was reduced to 50, 20, and 15 msec, it was virtually identical with data recorded without conditioning stimulation of the skin (134.4 ± 21.1, 135 ± 25.5, and 130 ± 12.3 μV, respectively).

In a separate series of experiments the peripheral end of the divided right vagus nerve was subjected to conditioning stimulation. The amplitude of potentials evoked by testing stimulation of SAN, with changes in the interstimulus interval, varied as follows: 176 ± 14.7 μV with an interval of 200 msec, 122.4 ± 11.5 μV for an interval of 140 msec ($p < 0.01$), 87.3 ± 10.2 μV for an interval of 80 msec ($p < 0.001$), 34.4 ± 5.5 μV for an interval of 60 msec ($p < 0.001$), and 197.6 ± 14.7 μV for an interval of 10 msec ($p > 0.1$). The combined amplitude of EPs recorded without conditioning stimulation in this series of experiments was 188.8 ± 12 μV. All the relationships described above are illustrated in Figs. 1 and 2.

The experimental results described above demonstrate facts known in principle previously. First, the appearance of EP in the rostral zones of the cerebral cortex during stimulation of myocardial nervous structures, and second, inhibition of EP by competitive cutaneous stimulation [1, 3, 9]. However, these two phenomena have not yet been examined in connection with

each other. In addition, CNS structures have been unambiguously defined as the substrate for viscerosomatic interaction, and the principal neuronal mechanism of its interaction is presynaptic inhibition [4, 5, 8, 11]. In the first series of experiments we showed that the most effective interaction of cutaneous and cardiac afferent flows is manifested when the interval between testing and conditioning stimuli lies between 50 and 150 msec. The smooth rise (not earlier than after 20 msec) and the long duration (not less than 150 msec) of inhibitory influences of conditioning stimulation suggest that the principal factor involved in the development of depression of potentials evoked by testing stimuli is the mechanism of presynaptic inhibition [5]. However, it is impossible on the basis only of these data to answer the question: in which parts of the nervous system do the phenomena described above take place? We know that presynaptic inhibition is one of the basic mechanisms of intracardiac regulation of cardiac afferentation [5]. Comparison of these facts with results obtained in the present investigation suggests that processes of cutaneo-cardiac interaction take place not only within the CNS, but also at the periphery — at the level of the intracardiac nervous system. In the present experiments bilateral vagotomy not only led to the exclusion of inhibitory influences by conditioning stimulation, but also led to some facilitation of cardiac afferentation, manifested as an increase in the combined amplitude of EP. In our view, these data are sufficiently weighty arguments in support of the following assertions: electrical stimulation of the skin induces increased activity in the afferent fibers of the vagus nerves, giving rise to tonic depression of cardiac afferentation by mechanisms of presynaptic inhibition at the level of the intracardiac nervous system. This is also proved by the results of experiments in which stimulation of the peripheral end of the divided vagus nerve is used as conditioning stimulation. Analysis of the mechanisms of development of facilitation of cardiac afferentation during electrical stimulation of the skin lies outside the aims of this present investigation, but it can be postulated that these effects are to some degree brought about by the relative asympathicotonia developing after bilateral division of the vagus nerve. Our results can evidently be usefully taken into account in the clinical application of methods of electrical stimulation of the skin in patients with pathology of the heart, for an increase in tone of the vagus nerves can provoke the development of various kinds of complications, such as disturbances of the cardiac rhythm.

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