ROLE OF THE VAGUS NERVES IN MECHANISMS OF MODULATION OF DUODENAL AFFERENT INFLUENCES

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Previous investigations [2, 3] showed that the spinal visceral afferent systems of the heart are subjected to modulating influences of hypothalamobulbar structures, realized through transmission of facilitatory or inhibitory bursts along the vagus nerves. It has also been shown that bilateral truncal vagotomy leads to enhancement of visceral afferent reactions [1, 3]. However, the concrete mechanisms of modulation of visceral afferentation that lie at the basis of physiological regulation of functions in the development of visceral nociception, and in the formation of "pathological systems" and "vicious circles" in the pathology of the internal organs have still received only little study. This applies most particularly to processes of modulation of afferent influences of the duodenum, the pathogenesis of most diseases of which is based on disturbances of mechanisms of regulation in the vagus nerve system.

The aim of this investigation was to study the nature of the modulating effects of the vagus nerves on duodenal afferentation.

EXPERIMENTAL METHOD

Acute experiments were carried out on 14-adult cats weighing 2-3 kg, anesthetized with chloralose (40-50 mg/kg), and receiving muscle relaxants and artificial ventilation. The investigation was carried out on fasting animals 12-14 h after the last meal. Bipolar stimulating electrodes and a catheter for injecting solutions were fixed on the duodenal bulb (DB). The right vagus was isolated at the level of the thyroid cartilage and divided; two bipolar stimulating electrodes were fixed to its central and peripheral segments. The animals were fixed in a stereotaxic apparatus and trephined to expose the surface of the cerebral cortex on the right side, and an active recording electrode was placed in the region of the sensomotor cortex. The reference electrode was fixed in the frontal sinuses. In the course of the experiments electrical stimulation (square pulses, duration 0.3 msec, amplitude 1-12 mA, frequency 0.1 Hz) was applied to the central and peripheral ends of the divided vagus nerves (CEVN and PEVN) and also to the region of DB. A method of paired stimulation was used. CEVN and PEVN were subjected to conditioning stimulation, DB to testing stimulation. The duration of the intervals between testing and conditioning stimuli varied from 20 msec to 1000 msec. Evoked potentials (EP) were recorded in the cerebral cortex (CC) in response to stimulation of DB, on a "Multibasis" universal system ("Biomedica," Italy). In some experiments one-stage bilateral truncal vagotomy was performed by means of special neurotomes. Solutions of naloxone (10-20 μg in a volume of 0.3 ml) and atropine (100-200 μg in a volume of 0.2 ml) were applied to the region of DB. These quantities of the drugs also were injected intravenously.

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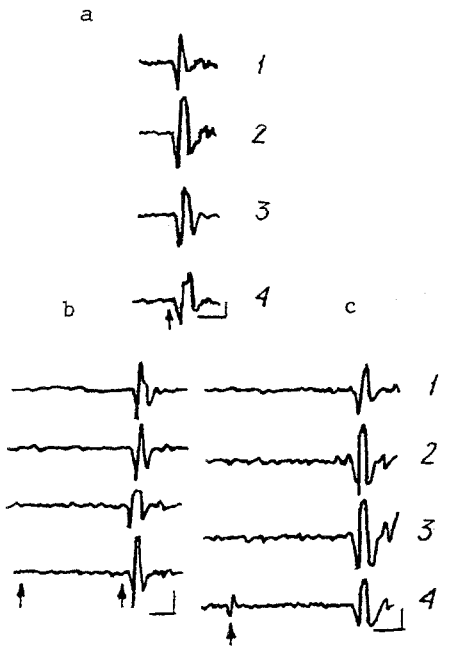

Fig. 1

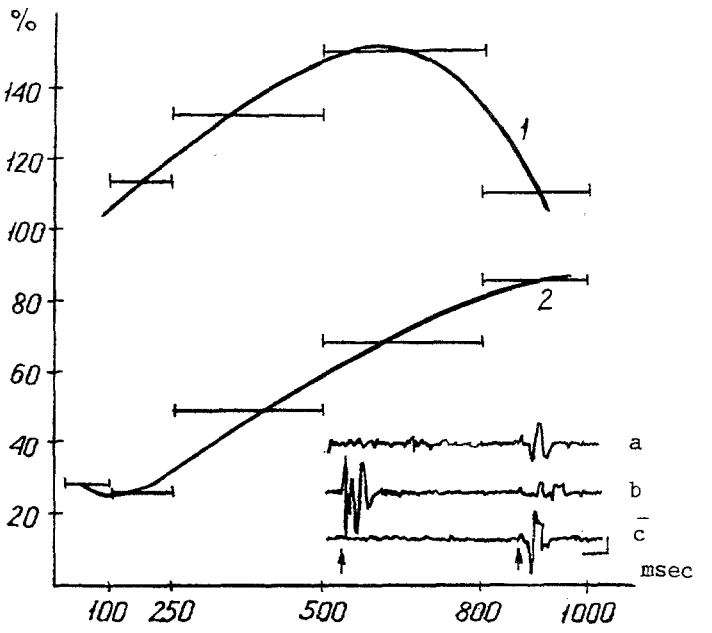

Fig. 2

Fig. 1. Evoked potentials (EP) recorded in CC to electrical stimulation of DB. a: 1) Initial data, 2) 20 min after bilateral truncal vagotomy, 3) 30 min after vagotomy, 4) 40 min after vagotomy; b: 1) initial data, 2) 10 min, 3) 20 min, 4) 25 min after application of atropine to DB; c: 1) initial data, 2) 10 min, 3) 20 min, 4) 25 min after application of naloxone to DB. Conditioning stimulation of PEVN. EP were recorded during 10 presentations of the signal. Calibration: 50 μV, 100 msec.

Fig. 2. Changes in combined amplitude of initial phases of EP (in % of initial data, taken as 100%), recorded in CC during stimulation of DB, with conditioning stimulation of right CEVN (2 and b) and PEVN (1 and c). a) Initial data recorded after right-sided vagotomy. Calibration: 50 μV, 100 msec.

EXPERIMENTAL RESULTS

Stimulation of DB led to recording of EP in CC with a focus of maximal activity in the region of the cruciform sulcus in the first sensomotor area. The most stable phases of EP were the first and second – the initial positive-negative fluctuation of potential. The combined amplitude of the first and second phases at the beginning of all experiments averaged 136 ± 12.6 μV. An increase in amplitude of EP to 193 ± 16.2 μV was observed ($p < 0.01$) 3-5 min after bilateral truncal vagotomy. This phenomenon continued for 25-35 min, after which the amplitude of EP returned to its initial values (144 ± 14.8 μV), falling after 35-50 min to 108 ± 10.4 μV (Fig. la). In the course of each experiment of this and subsequent series the intensity of the electrical stimuli applied remained constant.

In a separate series of experiments EP were recorded to testing electrical stimulation of DB after right-sided vagotomy. CEVN and PEVN were subjected to conditioning stimulation alternately. Stimulation of CEVN with an intensity sufficient to form an EP in CC (threshold intensity) led to inhibition of the test EP. The degree of depression of amplitude of EP depended on the duration of the intervals between stimulations, with maximal manifestation of the effect from 20 msec to 500-800 msec (Fig. 2; Table 1). An increase in the intensity of stimulation of CEVN caused a uniform increase in the degree of depression of the test EP and facilitated lengthening of the inhibitory effects of 1000 msec or more, whereas a change in the intensity of stimulation of PEVN in some cases led to loss of the facilitatory influences or even to their reversal.

TABLE 1. Amplitude of EP in CC in Response to Change in Duration of Intervals between Testing and Conditioning Stimulation and in Connection with Application of Atropine and Naloxone Solutions to Stimulated Region of DB

Duration of intervals between stimuli, msec	Amplitude of EP in response to stimulation of DB, μV, conditioning stimulation of vagus nerve, peripheral end			
	central end, μV and %	application of solutions of		
		atropine	naloxone	
Initially	136±12,6 100 %			
25th minute of application of preparation			110±10,8 81 %	214±21,6* 157 %
20—100	38±3,4* 28 %			
100—250	36±1,2* 27 %	154±14,9 113 %		
250—500	68±6,3* 50 %	180±12,3* 132 %	179±12,4* 132 %	157±14,2 115 %
500—800	94±11,2* 69 %	208±18,1* 146 %	196±11,8* 144 %	169±13,6 124 %
800—1000	118—14,3 87 %	151—14,2 111 %		

Legend. *$p < 0.01$ indicates data differing significantly from general initial result, taken to be 100%.

After stable reproduction of these phenomena, in a separate series of experiments a solution of atropine was applied to the region of DB. The amplitude of EP was reduced 25 min after injection of the preparation. Conditioning stimulation of PEVN under these conditions led to a significant increase in amplitude within the effective range of intervals between stimulations (Fig. 1; Table 1).

In a special series of experiments naloxone solution was applied to DB, leading to a marked increase in amplitude of the test EP after 25 min. Conditioning stimulation of PEVN after application of naloxone did not lead to facilitation of duodenal afferentation but, on the contrary, facilitated some degree of depression of the amplitude of EP (Fig. 1; Table 1). Intravenous injection of atropine and naloxone in the doses tested did not affect facilitation and inhibition of duodenal afferentation when conditioning stimulation was applied.

The experimental results are proof that the vagus nerves are involved in modulation of afferent duodenal influences. They demonstrate the essential importance of the duodenal intramural systems in the regulation of central descending influences and in the processes of formation of visceral afferent control. This applies in particular to the reaction of facilitation of duodenal afferentation which was found to conditioning stimulation of PEVN, development of which is blocked by application of naloxone to DB. It can be tentatively suggested that the type of afferent response of the duodenum is determined mainly by the opiate system of the organ, and that centrogenic modulation of spinal afferentation is realized through the opiate-containing neurons of the vagus nerves. Cholinergic reactions evidently have an indirect effect on regulation of the afferent functions of the duodenum, although this does not rule out the participation of systems with a different type of "ergy" in these processes. Our previous findings [2], indicating inhibition of cardial afferentation during conditioning stimulation of PEVN, in our view, do not contradict the phenomena described above, if allowance is made for differences in responses of the heart and the digestive organs to an increase in tone of the vagus nerves.

LITERATURE CITED

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