ORGANIZATION OF REFLEX SYMPATHETIC INFLUENCES ON FREQUENCY AND FORCE OF CARDIAC CONTRACTIONS

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Autonomic nerves have generalized influences on all functions of the heart, reducing or increasing the frequency and force of its contractions and the velocity of conduction of excitation simultaneously. However, we know that stimulation of different branches of the cardiac nerves can lead to isolated responses of separate structures of the heart, or even of small areas of myocardium [2, 5, 8, 13, 14]. Meanwhile, stimulation of efferent nerves cannot shed any light on how nervous influences on different functions of the heart are organized during natural reflex responses. Influences of this kind have been analyzed only in isolated studies [10, 11], and they have yielded information to show that natural reflex effects on the heart likewise are not generalized but differentiated. However, we could find no publications in which an attempt was made to discover to what degree different parts of the autonomic nervous system – sympathetic and parasympathetic – can exert differentiated reflex influences on the heart.

The aim of this investigation was to study the effect of sympathetic nerves, which provide an abundant innervation both of the sinoatrial node and of the ventricular myocardium, on the chronotropic and inotropic functions of the heart.

EXPERIMENTAL METHOD

In experiments on 21 cats weighing 3-4 kg, animals with weak parasympathetic tone [9], under pentobarbital anesthesia (30-40 mg/kg body weight), and under open chest conditions, either cold blockade of the vagus nerves at 0°C (halting the flow of impulses along afferent fibers) [6, 12] or electrical stimulation of their central ends (always of the right nerve) after bilateral division of the vagus nerves in the neck (parameters: 10 Hz, 2 msec, amplitude selected on the basis of minimal response threshold) was carried out. To study the organization of reflex influences, factors acting on the rhythm and contractility of the left ventricle were studied after division of the inferior cardiac nerves (CN). To measure the pressure in the left ventricle and aorta, special measuring systems were used [1, 3], with a natural frequency of not less than 300 Hz. EMT-34, EMT-35, and P23XL manometric transducers, a 1187 polygraph ("O.T.E. Biomedica"), an original 10-digit a/d converter (discretization frequency 300-500 Hz depending on the experiment), and an eight-digit PK-8020 computer were used. To monitor the temperature in the superior vena cava we used a "Vygon" thermocatheter, and to monitor blood gases and pH, a "Corning 178" analyzer (USA). Changes in the chronotropic function of the heart were assessed relative to the heart rate (HR). Inotropic influences were assessed by means of contractility indices (CI), selected beforehand [1]. To rule out any influences of hemodynamic changes arising in the course of the test responses on CI, in each experiment control tests were carried out (by changing the lumen of the descending aorta), reproducing the analogous hemodynamic effects. If the amplitude of the change in CI during the nervous influences exceeded their changes in the control, it was considered that this response could not have been due to accompanying hemodynamic fluctuations, but was connected with a specific influence on contractility in the course of the test reflexes. The data were calculated and analyzed on PK-8020 and

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TABLE 1. Frequency of Discovery (in %) of Different Variants of Changes in CI and HR during Cold Block of Vagus Nerves and Electrical Stimulation of Their Central Ends

Parameter	Experimental conditions	
	blockade	stimulation
Change in CI, HR being stable	16,28±3,98	25,88±4,75
Change in HR, BP being stable	22,09±4,47	4,74±2,30
Opposite changes in CI and HR	12,79±3,60	2,35±1,64
Unidirectional changes in CI and HR	40,70±5,30	47,06±5,41
No response of CI or HR	8,14±2,95	19,77±4,29

TABLE 2. Comparison of Frequency of Appearance (in %) of Positive and Negative Chronotropic and Inotropic Responses of the Heart to Cold Block and to Electrical Stimulation of Afferent Fibers of Vagus Nerves

Experimental conditions	Response			
	positive		negative	
	chronotropic	inotropic	chronotropic	inotropic
Blockade				
Application	19,0±8,6	57,1±18,7*	81,0±8,6	42,9±18,7*
Removal	43,2±7,5	84,6±10,0*	56,8±7,5	15,4±10,0*
Stimulation				
Application	17,2±7,0	12,5±11,7	82,8±7,0	87,5±11,7
Removal	72,2±10,6	83,3±15,2	27,8±10,6	16,7±15,2

Legend. *$p < 0.05$: difference between frequencies of appearance of chronotropic and inotropic responses significant.

IBM PC/AT personal computers, using our own program package. Statistical analysis was carried out by Student's t test and Fisher's φ transformation. Results were statistically significant at the $p < 0.05$ level.

EXPERIMENTAL RESULTS

In the experiments of series I (11 cats, 86 procedures) the effects of complete cold block of the vagus nerves on chronotropic and inotropic functions of the heart were studied. In some reactions (51.2%) differentiated changes in HR and CI were observed: opposite deviations of their mean values or isolated changes in these parameters (Table 1). Even when these deviations were in the same direction (40.7% of responses) their time course could differ significantly. It will be clear from Fig. 1a that the interval between the beginning or ending of the procedure and the response to it, and the rate and time of attainment of the peak response, and the character of the return of these parameters to their initial background level differed for HR and CI. Evaluation of the effects of the nerve block on the cardiac rhythm and contractility showed that changes in these functions were heterogeneous (Table 2).

In the experiments of series II (10 cats, 85 procedures) responses of the heart to stimulation of afferent fibers of the vagus nerves were analyzed. Table 2 shows that the characteristics of chronotropic and inotropic effects did not differ significantly in these experiments. However, differential responses of these parameters were also found

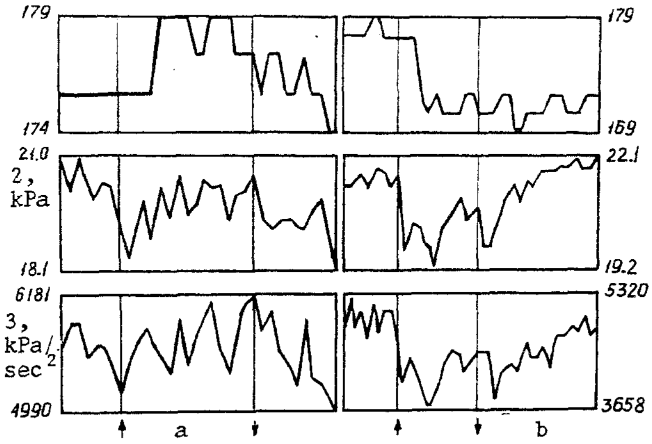

Fig. 1. Changes in HR (1), MSBP (2), and CI (3) during cold block (a) and electrical stimulation of vagal afferent fibers (b). Arrows indicate beginning and end of reflex procedures. The ratio of the maximum of the first derivative of ventricular pressure to the time taken for intraventricular pressure to reach a maximum (DP/PVP_{time}) taken as example of CI.

under these conditions (in 33.2% of cases, Table 1), and their time course during unidirectional deviations could differ significantly (Fig. 1b).

The differential reflex effects on cardiac rhythm and contractility could have been realized under these experimental conditions by the sympathetic nervous system, and for that reason, in the third series of experiments, effects of sympathetic nerve division on these reflexes were analyzed. To do this, those animals (nine cats) which exhibited distinct reflex influences on HR and CI in the course of the experiments were investigated.

Division of the right ICN (eight divisions altogether) always evoked a marked negative chronotropic effect. Division of the left ICN (in six experiments), however, slowed HR in two experiments, increased it in one, but had no effect on HR in three experiments.

Division of ICN in four of nine experiments (44.4% of cases) led to changes in reflex effects on the cardiac rhythm and contractility. We called this phenomenon "collapse of the cardiac reflex." This can be described as follows: against the background of divided sympathetic nerves one component of the cardiac reflex (chronotropic or inotropic) disappeared or was reversed; the other component may have undergone no significant change under these conditions. Results of this kind were obtained in experiments with both cooling and stimulation of the nerves (Fig. 2).

Experiments in which this phenomenon was discovered differed in the following respects (Fig. 3): 1) chronotropic responses to division of the left ICN were absent in these experiments only; 2) initial values of BP at the beginning of the experiments were significantly higher in the animals of this group than in the rest: mean systolic BP (MSBP) 146.5 ± 0.9 mm Hg (19.5 ± 0.1 kPa) and 106.9 ± 0.4 mm Hg (14.3 ± 0.1 kPa) respectively (whereas no differences were found with respect to the other hemodynamic parameters – HR, EDP).

Analysis concentrated on experiments with an initially raised BP in the animals (MSBP 161.2 ± 0.5 mm Hg, or 21.4 ± 0.07 kPa) showed that in all these experiments, the "collapse of the cardiac reflex" phenomenon developed after division of ICN, but not all cases of division of the left ICN were accompanied by changes in HR. In experiments with a normal initial BP (MSBP 106.1 ± 0.2 mm Hg or 14.1 ± 0.03 kPa), however, this phenomenon was observed in only 16.7% of cases, and 75% of all divisions of the left nerve evoked chronotropic effects.

Thus: a) a change in afferent impulsation along the vagus nerves leads to differential reflex effects of the sympathetic nervous system on the cardiac rhythm and on left ventricular contractility; b) the right ICN has undoubtedly stronger tonic chronotropic effects on the heart. However, for the reflex effects of the sympathetic nervous system on HR to be realized, both ICN are necessary, for after division of one of them, the chronotropic component

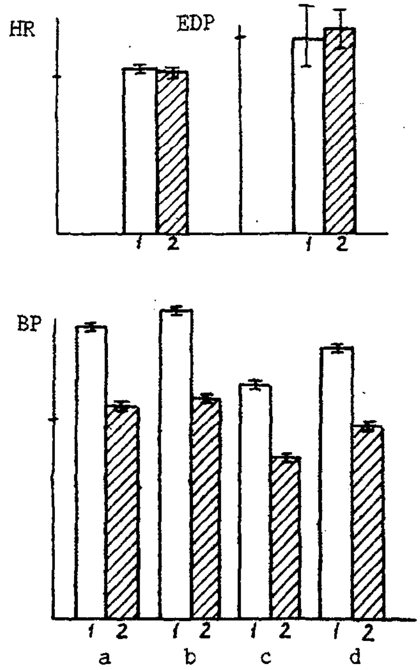

Fig. 2. Comparison of original hemodynamic parameters in cats with manifestation of the "collapse of the cardiac reflex" phenomenon (1) with corresponding parameters for remaining animals (2): a) MSBP, b) systolic BP, c) diastolic BP, d) mean BP. Calibration: HR 150 beats/min, EDP 0.27 kPa (2 mm Hg), BP 13.3 kPa (100 mm Hg).

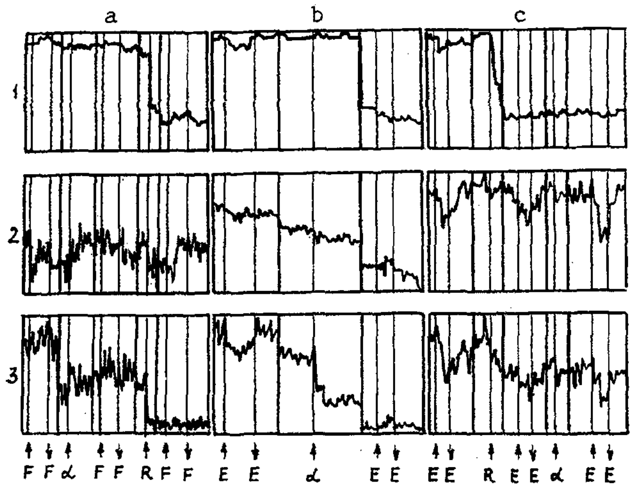

Fig. 3. "Collapse of cardiac reflex" in different experiments (a, b, c). 1) HR, 2) MSBP, 3) CI, BP/PVP_{time}. Arrows indicate beginning and end of procedures; F) cold block of nerves, E) electrical stimulation of nerves, R) division of right ICN, L) division of left ICN. Ranges of changes of parameters: HR 118-177 (a), 142-180 (b), 144-177 beats/min (c), MSBP 18.0-23.6 (a), 9.2-15.7 (b), 18.6-23.4 kPa (c); CI 2739-5659 (1), 1418-4809 (b), 2669-5304 kPa/sec^2 (c).

of the reflex can be transformed. On the other hand, both right and left ICN are important for the organization of reflex sympathetic influences on left ventricular contractility, for division of the left nerve may lead to abolition or reversal of the inotropic component of the reflex. Involvement of both ICN in sympathetic reflex regulation of the inotropic and chronotropic functions of the heart depends on the initial BP level of the animals.

These results do not contradict the known facts concerning differences in functional specialization of the right and left cardiac nerves [14]. The different properties of the cardiac nerves can evidently be utilized by the sympathetic nervous system to organize the integrated fine structure of its influence on heart rate and ventricular contractility. These patterns of organization of sympathetic reflex influences on the different functions of the heart may perhaps be the most valuable in the concrete conditions under which the circulatory system functions.

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