# MECHANISM OF THE NERVOUS REGULATION OF THE CARDIAC ACTIVITY. EFFECT OF DIVISION OF THE VAGO-SYMPATHETIC TRUNKS ON CHANGES IN EXCITABILITY OF THE VENTRICLE OF THE FROG'S HEART

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Although the effects of the vagus and sympathetic nerves on the heart have been studied for over a century, contradictory results have been obtained, especially in the firld of the vago-sympathetic effects on the conductivity of the heart muscle. An important reason for this is the fact that until recently no account has been taken of the phase of the cardiac cycle in which the investigation of the conductivity was made. In the present investigation this objection was overcome by the use of a special method of studying the excitability of the heart in accordance with the phases of the cardiac cycle [7], developed in the department of pathophysiology of this institute.

## EXPERIMENTAL METHODS

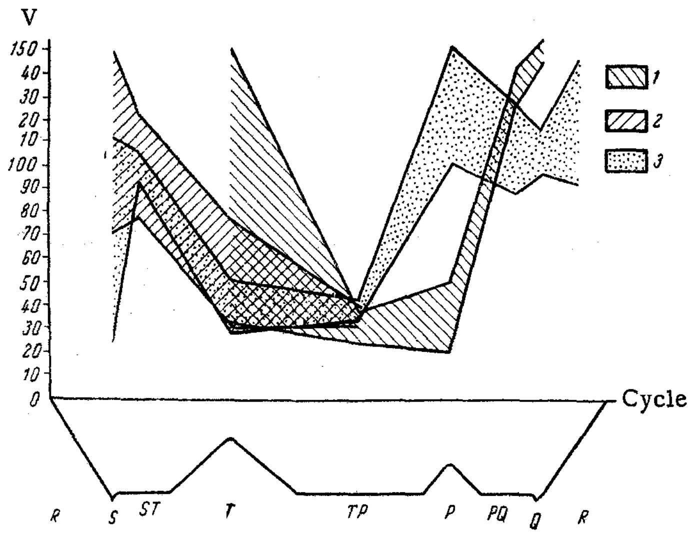
The principle of the method is that the action potentials of the heart for investigation are amplified approximately 40,000 times by means of an ink-writing electrocardiograph and led to a special electronic phasing device. This selects the R wave from the whole complex of the ECG, and by its means, switches on a special stimulator after an accurately measured time lag. This stimulator applies a rectangular pulse to the heart (in our investigations 1 millisec in duration and an amplitude uniformly controllable between 0 and 150 V) at a predetermined moment of the cardiac cycle.

All the experiments were performed on male frogs (Rana temporaria) weighing 30-35 g. The frog was immobilized by destruction of the spinal cord; the thorax was opened widely, the heart liberated from the pericardium, and a bipolar needle electrode connected to the stimulator was applied to the ventricle in the center of the heart. The two electrodes from the electrocardiograph were inserted into the myocardium in the direction of the cardiac axis. Needle electrodes were used with a view to applying the stimulating pulse to the smallest possible area of myocardium, so that a strictly determined area of the heart muscle (the smaller the area of the possible focus the greater the standardization of the experimental conditions) received local stimulation. A drawback of the needle electrode is that pulses of high amplitude (up to 150 V) must be used in the experiments.

The threshold of excitation of the ventricular myocardium was determined by the appearance of extrasystoles and was evaluated in volts. The investigation was carried out at the points R, S, ST, T, TP, P, Q and PQ of the cardiac cycle. After determination of the background curve of excitability in the frog, the right vago-sympathetic trunk was divided and the curve of excitability again determined. The left vago-sympathetic trunk was then divided and the curve of excitability determined a third time.

Altogether 35 animals were used in the experiments, including 10 controls, in which the excitability was determined not in the order given above, but immediately after unilateral or bilateral division of the vago-sympathetic trunks. These control experiments were performed in order to exclude any possibility of burning the myocardium during repeated stimulation, drying the preparation, or other incidental factors.

The numerical results were analyzed statistically and the changes observed were significant.




Effect of division of the vago-sympathetic trunks on excitability of the ventricle of the frog's heart. 1) Normal heart; 2) unilateral division; 3) bilateral division.

## EXPERIMENTAL RESULTS

The results are shown in the figure. The changes in the excitability of the myocardium of the ventricle are given in this figure, not by curves, but by polygons. This is because during statistical treatment two or three types of curves could be distinguished at certain points of the cardiac cycle (high and low thresholds of excitation). The upper border of each polygon corresponds to the uppermost threshold for the point, and the lower border to the lowest threshold (counting the duplicated mean error – probability 95.5%). The curves of the control experiments are not reproduced in the graph, for they were indistinguishable from the basic pattern.

After division of the right vago-sympathetic trunk, in the phases of the cardiac cycle corresponding to the areas S and ST of the ECG the refractoriness disappeared, the refractory zone shifted towards the beginning of the cardiac cycle (P, PQ, Q, R), and the upper and lower limits of the thresholds of excitation came together in the phase of the cardiac cycle corresponding to the descending limb of the T wave, shown in the graph by a narrowing of the polygon.

After bilateral division of the vago-sympathetic trunk refractoriness could be determined only in the descending limb of the R wave of the ECG. The limits, of the thresholds of excitation were even closer together in the region of the descending limb of the T wave. In the zones P, PQ, and Q these limits were wider than normal, and in the S zone they were wider than after unilateral division. By comparison with unilateral division, the limits of the thresholds of excitation in the ST interval were narrower. The threshold of excitation in the zones P, PQ, and Q rose above normal, and in the zone of the S wave it fell below the level after unilateral division. Division of the vago-sympathetic trunks had no visible effect on the excitability of the myocardium during diastole of the heart (middle of the TP interval).

Our results indicate that after division of the vago-sympathetic trunks the excitability of the myocardium of the ventricle is increased during the whole of the cardiac cycle. These phenomena were more marked after bilateral than unilateral division, probably on account of mutual reinforcement of the action of the two vagus nerves on the heart. The slight difference between the tendencies of the changes after unilateral and bilateral division may be attributed to the fact that the right and left vagus nerves act on different structures in the heart [4, 7].

A possible explanation of the findings is that after division of the vagus nerves a definite increase in the lability of the ventricular myocardium takes place as a result of the changes in the neurotrophic situation. This suggestion agrees with the hypothesis that parabiotic inhibition develops in the sinus node during stimulation of the vagus nerves [1], as a result of which inhibition may arise also (likewise parabiotic in character) in other parts of the heart. Since the refractory phase has a well marked parabiotic character, it may be assumed that stimulation of the vagus nerves must lead to an increase, and division of these nerves to a decrease, in refractoriness. This suggestion is confirmed by the work of I. A. Vetyukov [4], who showed that the myocardium of the atropinized heart is capable of contracting more strongly than normally in response to stimulation during the "absolute" refractory phase, and of V. B. Boldyrev [2], who found that an increase in the refractoriness of the myocardium takes place during vagal inhibition of the heart. Boldyrev also showed that an increase in the tone of the sympathetic nerve depresses the lability of the myocardium. Hence, the results of our investigation may be regarded as demonstrating an increase in the lability of the ventricular myocardium as a result of division of the nerve trunks conveying parabiotic impulses to the heart.

A special explanation is required for the widening and narrowing of the limits of the threshold of excitation observed in our experiments at certain points of the cardiac cycle. The electronic system used in the experiments possesses some degree of inertia, varying between 1 and 2 millisec. It is quite possible that points of the cardiac cycle separated by this interval possess different levels of excitability, thus giving the results a definite scatter. After division of the vago-sympathetic trunks an equalization of the thresholds of excitation evidently takes place at the end of the systole, shown on the graph by a narrowing of the polygons in the segments ST-T. Points in the cardiac cycle in the phase of the diastole (the TP interval) may in general possess equal excitability, which is not affected by division of the vago-sympathetic trunks. In the zones P, PQ, and Q, on the other hand, in which the onset of mechanical systole of the ventricle is displaced after division of the vagus nerves [5], in all probability a considerable dissociation of the thresholds of excitation takes place, depending on the time at which the stimulating pulse is applied, leading to the appearance of a definite scatter in the value of the thresholds of excitation and to a general elevation of their level. These results may be regarded as the result of the preferential action of the vago-sympathetic influences on the systolic part of the cardiac cycle.

## SUMMARY

A study was made of the changes in the excitation of the frog ventricular myocardium following division of the varo-sympathetic trunks at various phases of the cardiac cycle. In unilateral division of the vago-sympathetic trunks the refractory zone of the ventricular myocardium decreases and is shifted to the beginning of the cardiac cycle. In bilateral division the refractoriness continues only during the time corresponding to the descending slope of the R-wave. Definite changes of the threshold excitability level were noted following division of the varo-sympathetic trunks. The inference is that there were changes of the ventricular myocardium lability following division of the nerve trunks, the preponderant effect of the vago-sympathetic impulses on the systolic portion of the cardiac cycle was also noted.

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