EFFECT OF ATROPINE BLOCKING OF THE VAGUS NERVES ON THE EXCITABILITY OF THE LEFT VENTRICLE IN THE GUINEA PIG

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The influence of the vagus nerves on the excitability of the myocardium has not yet been adequately investigated, and the results of its study have proved contradictory. Some authors [4-6, 10], for instance, consider that stimulation of the vagus nerves increases the excitability of certain parts of the heart, while others have obtained the opposite results [2, 7]. Contradictions such as these may arise as a result of inconsistent experimental conditions and also because of the fact that the excitability of the heart and the character of the vagal influence on it vary in the course of the cardiac cycle.

During the study of the effect of division of the vago-sympathetic trunks on the excitability of the ventricular myocardium of the frog's heart, the authors observed that this division causes a considerable shortening of the effective refractory period and that the vagal influences act on the excitability of the myocardium mainly during systole.

In the present investigation the effect of atropine on the excitability of the myocardium of the left ventricle of the guinea pig was studied in situ.

EXPERIMENTAL METHOD

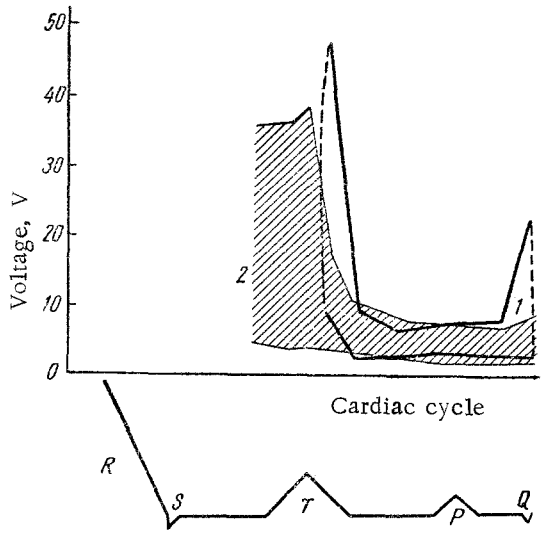
The guinea pig was lightly anesthetized with ether and maintained on artificial respiration. A unipolar electrode, insulated from the surrounding tissues, was sutured to the animal's left ventricle. The wound was closed hermetically, and the investigations were carried out on the 7th day after the operation. This electrode, and a second (the indifferent) electrode introduced beneath the skin of the dorsal region, were connected to a stimulator by means of which a single rectangular impulse, 1 msec in duration and with an amplitude which could be controlled smoothly within the range of 0-50 V, was applied to the heart. As a result of the use of a special synchronizing device [1] the impulse was applied to the heart at an accurately predetermined phase of the cardiac cycle. The excitability was measured at the moments of the cardiac cycle corresponding to the Q, R, S, T, and P waves, and in the S-T, T-P, and P-Q intervals of the ECG. The background excitability curve and the excitability curve 10 min after injection of atropine sulfate in a dose of 10 μg/100 g body weight were investigated.

Altogether 26 experiments were performed. Statistical analysis was used to determine the significance of the results obtained.

The threshold of excitability was taken to be the minimal voltage of the stimulating current to cause the appearance of an extrasystole on the ECG.

EXPERIMENTAL RESULTS AND DISCUSSION

The changes in excitability were presented not as curves (see figure), but as polygons, for statistical analysis revealed two types of curves corresponding to the high and low thresholds of excitability. The upper limit of each polygon passed through the means of the high thresholds (plus twice the mean error); the lower limit through the means of the low thresholds (minus twice the mean error). This scatter of the results may be explained as follows.



Effect of atropine on excitability of the myocardium. 1) Excitability of the intact myocardium; 2) excitability of myocardium against the background of atropinization. Explanation in text.

The heart is a heterogeneous system. According to existing data [9], three types of fibers are present in the myocardium of the guinea pig: P, V_1, and V_2, and the amplitude of their action potential bears a different relationship to the magnitude of the hyperpolarizing current. Although an attempt was made, when the electrode was sutured to the heart, to implant it in the same area of the myocardium, some displacement of the electrode could certainly have taken place in the different experiments, and the number of fibers of the different types lying beneath it could also have varied, and these factors evidently led to the appearance of the scatter.

It is clear from the figure that the intact heart in situ was excitable during that part of the cardiac cycle which corresponds to the segment from the upper third of the descending limb of the T wave to the end of the P-Q interval. During the remainder of the cardiac cycle (corresponding to electrical systole) the heart was in a refractory state. Ten minutes after the injection of atropine the effective refractory period was shortened S-T interval). As the figure shows, the excitability of the myocardium during diastole showed no special changes under the influence of atropine. In some phases of the cardiac cycle a narrowing of the polygons occurred, i.e., the excitability of neighboring areas of the myocardium tended to become equalized.

Atropine shortened the effective refractory period of the heart in situ. This result becomes understandable in the light of the findings described by Burn [3]. This worker showed that the excitability and the contractile power of the myocardium are functionally dependent on parallel metabolic processes constantly resynthesizing acetylcholine in the myocardium. In the conditions of the denervated heart atropine had a dissociating action on the cholinergic structures of the myocardial cells themselves, thereby lowering their excitability. In the intact organism, the action of atropine was composed of items: an action on the cholinergic structures of the myocardial cells and an action on the synaptic formations of the vagus nerve, liberating acetylcholine which was exogenous in relation to the myocardial structures. Blocking the second component had the stronger effect, expressed as an increase in the excitability of the myocardium. The present findings support Burn's view that the pharmacological effect of acetylcholine is dependent on which tissue structures synthesize it, and with which tissue formations it comes directly into contact.

It is difficult to say what is the direct mechanism of the influence of atropine on the excitability of the heart muscle, for "the threshold of stimulation depends on the level of the membrane potential...., and also on the electrical characteristics of the fiber...., on the fraction of the stimulating current which penetrates through the membrane" [8]. However, by virtue of the fact that atropine equalizes the excitability of neighboring areas of the heart muscle, it may be suggested that it modifies the functional heterogeneity of the myocardium, existing as a result of the uneven distribution of cholinergic neural structures in the contractile muscle of the ventricles.

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