MECHANICAL ACTION OF THE ATRIA DURING ATRIAL PACING ON SINU-ATRIAL NODE FUNCTION

T. M. Vinogradova, G. S. Sukhova,
É. A. Bogdanova, A. G. Smagin,
and M. G. Udel'nov

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The writers showed previously that if an artificial frequency of excitation is imposed on the atria, higher than the intrinsic pacemaker frequency, the operation of the latter may be modified [1]. Direct stimulation of the sinu-atrial node (SAN) by pulses with the same electrical parameters as during atrial stimulation caused no change in the frequency of its excitation. Investigation of the mechanism of the change in frequency of SAN during atrial excitation with imposed frequency showed that retrograde conduction of excitation cannot explain the phenomena observed [1].

Changes in the frequency of excitation of the pacemaker can be induced by electric currents generated by the atria in the surrounding medium, by mechanical activity of the atria, or by the influence of the intracardiac nervous system. The aim of this investigation was to examine these possible mechanisms and to discover the mechanism responsible for changes in the frequency of excitation of SAN during atrial pacing.

EXPERIMENTAL METHOD

Experiments were carried out on the frog's *(Rana temporaria)* heart. The sinus venosus was isolated together with the atria, everted in the form of a tissue slab, and placed in a humid chamber. Electrical potentials were recorded by suction electrodes with a tip not more than 100 μ in diameter. Electrical potentials were recorded on the ÉLKAR electrocardiograph. The atria were stimulated extracellularly with above-threshold pulses. Stimulating electrodes were silver wires 0.5 mm in diameter, and 2 mm apart. One electrode was grounded, square pulses 5 msec in duration from a "Physiovar" stimulator were applied through the other. The frequency of stimulation in all experiments exceeded the natural frequency of excitation of the preparation. Mechanical activity of the atria was recorded by means of strain gauge transducers. To block the ganglia of the intracardiac nervous system, a solution of arfonad was used in a concentration of 1 g/liter. Electrical and mechanical activity of the atria were uncoupled with the aid of a 0.7% solution of sodium citrate [3]. The experimental results were assessed by Fisher's accurate nonparametric method.

EXPERIMENTAL RESULTS

To study the role of the intracardiac nervous system, its ganglia were blocked in 10 experiments. For this purpose, a few drops of arfonad solution were applied to the surface of the preparation. The stimulating electrodes were located as usually on the atrial surface and above-threshold pulses of current were applied to them. Atrial pacing after arfonad application led to the same changes in SAN function as before its application. Hence it follows that the intracardiac nervous system evidently has no essential role to play in the mechanism of change of SAN activity during atrial pacing.

To study the bioelectrical effect of the atria on the sinus venosus, in 12 experiments the frog's heart was laid on a piece of filter paper, soaked in Ringer's solution, side by side with the isolated sinus venosus, and separated from it by a distance of 1-2 mm. In all experiments changes in the frequency of excitation of the isolated pacemaker were recorded. The change in frequency was significant ($P < 0.025$). Next, in eight experiments the conduct-

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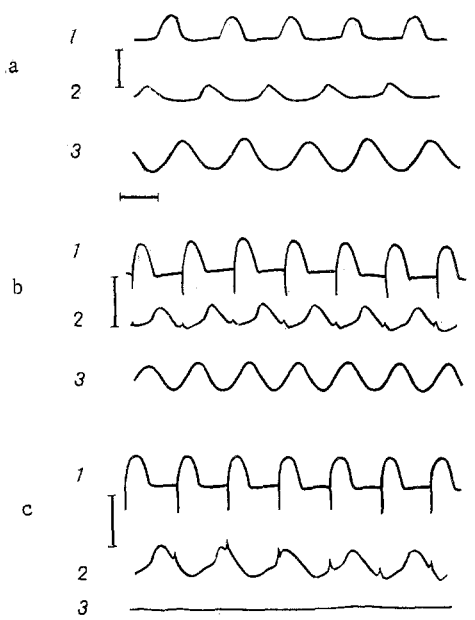

Fig. 1. Activity of SA node during atrial stimulation: a) before beginning of stimulation, b) during atrial stimulation (mechanical activity of atria preserved), c) during atrial stimulation after suppression of their mechanical activity. 1, 2) Extracellular action potentials of atria and sinus venosus, respectively, 3) mechanical activity of atria. Calibration: vertical 15 mV, horizontal 1 sec.

ing medium was grounded. Under these conditions, placing the whole heart side by side with the isolated pacemaker caused no change in the frequency of excitation of the latter. This is in agreement with the results of previous investigations [2, 4]. However, in the experiments with atrial stimulation, one of the stimulating electrodes was grounded. The change in the frequency of excitation of the pacemaker thus evidently does not take place under the influence of electric currents generated by the atria.

To explain the effect of mechanical activity of the atria on the formation of the general pacemaker frequency, mechanical activity was blocked in 20 experiments by application of a few drops of sodium citrate solution to the atrial surface. About 30 sec later the atria ceased to contract and their mechanical activity was not recorded. Electrical activity both of the sinus venosus and of the atria under these circumstances remained almost unchanged. After cessation of mechanical contractions of the atria, atrial stimulation caused no change in the frequency of excitation of the sinus venosus. The difference between frequencies before and during atrial stimulation was not significant ($P > 0.1$). The results of one experiment of this series are given in Fig. 1. The initial frequency of contractions of the preparation was 37 beats/min (Fig. 1b, 1, 2). The frequency of mechanical contractions of the atria also was 43 beats/min (Fig. 1b, 3). After application of sodium citrate solution the atria ceased to contract (Fig. 1c, 3). In this case atrial stimulation with a frequency of 43 beats/min caused no change in the frequency of contractions of the sinus venosus, although the atria were excited with a frequency of stimulation of 43 beats/min and the sinus venosus continued to be excited with the original frequency of 37 beats/min.

To confirm the importance of the mechanical effect of atrial stimulation on activity of the sinus venosus, the atria of a preparation with blocked mechanical activity were stimulated. No change was observed in the frequency of excitation of the SA node in this case. Mechanical activity of the atria was then restored by application of a few drops of Ringer's solution with twice the normal Ca^{++} concentration to the atria. There were eight such experiments. Immediately after application of Ringer's solution with twice the Ca^{++} concentration mechanical activity of the atria was restored and, at the same time, the sinus venosus began to change

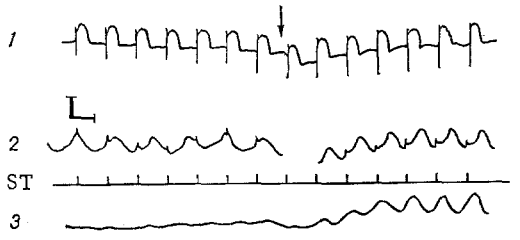

Fig. 2

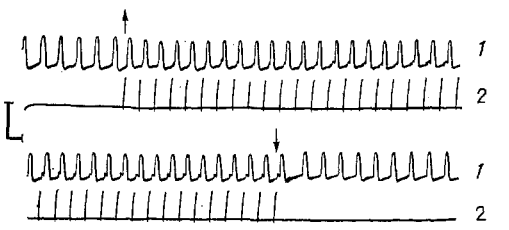

Fig. 3

Fig. 2. Changes in activity of SA node on recovery of mechanical activity of atria. 1, 2) Extracellular action potentials of atria and sinus venosus, respectively; 3) mechanical activity of atria. ST) Marker of atrial stimulation. Arrow indicates time of application of Ringer's solution with twice Ca^{++} concentration. Calibration: vertical 10 mV, horizontal 1 sec.

Fig. 3. Changes in activity of SA node during mechanical stimulation. 1) Extracellular action potentials of sinus venosus; 2) marker of stretching of sinus venosus. Arrows indicate beginning and end of mechanical stimulation.

over to the frequency of stimulation. The results of one such experiment in this series are given in Fig. 2. In a preparation with blocked mechanical activity atrial stimulation with a frequency of 43 beats/min caused no change in the frequency of excitation of the SA note: It continued (just as before the beginning of stimulation) to be excited with a frequency of 34 beats/min. Application of a drop of Ringer's solution with twice the normal Ca^{++} concentration led to restoration of atrial mechanical activity (Fig. 2, 3) and to a change by the SA node to the frequency imposed on the atria (Fig. 2, 2).

The results of the experiments in this series showed that an important role in the mechanism of the influence of the atria on the sinus venosus is evidently played by mechanical activity of the atria. It can be tentatively suggested that mechanical activity of the atria affects the process of formation of the general pacemaker frequency, by changing the rate of slow diastolic depolarization.

An attempt was made to simulate mechanical action of the atria on the SA node. For this purpose, in 10 experiments the isolated sinus venosus was secured on one side in a frame, and on the other side it was attached to the core of a relay. Under the influence of pulses applied to the relay, its core was deflected by an assigned value, thereby stretching the sinus venosus. The preparation was stretched through 10-15% of its initial length in the transverse direction. To obtain a greater effect, the preparation was stretched with abrupt pulses [5]. The frequency of mechanical stimulation in all experiments was higher than the initial frequency of excitation of the sinus venosus.

In all experiments mechanical stimulation caused a change in the frequency of excitation of the sinus venosus. If the frequency of mechanical stimulation exceeded the intrinsic frequency of the sinus venosus by not more than 10%, in most experiments the sinus venosus switched to the frequency of mechanical stimulation. The time taken to switch to the frequency at which the pacemaker was stretched varied from a few seconds to 1 min. As an example, the results of one experiment of this series are illustrated in Fig. 3. The frequency of contraction of the sinus venosus was 40 beats/min. Rhythmic stretching of the sinus venosus with a frequency of 46 beats/min led to switching of the sinus venosus to this frequency. After the end of stimulation the sinus venosus returned to its initial frequency of 40 beats/min.

External repetitive mechanical stimulation can thus modify the process of formation of the general pacemaker frequency. This approximate model of the mechanical action of the atria of the sinus venosus showed that, in principle, it is possible to change the general pacemaker frequency through the application of external mechanical forces. This means that the change in pacemaker frequency during atrial stimulation may be largely due to mechanical activity of the atria.

Under natural conditions the frequency of atrial contractions is determined by the frequency of pacemaker excitation. It can therefore be postulated that under adequate physiological conditions the reciprocal effect of mechanical activity of the atria on the pacemaker can

be reduced to stabilization of the frequency of its spontaneous excitation. This improves atrial function, making it more regular.

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MYOCARDIAL HYPERTROPHY IN YOUNG AND OLD ANIMALS WITH EXPERIMENTAL HYPERTENSION

G. V. Kopylova and L. P. Cherkasskii

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Clinical investigations have shown an increase in mortality with age among patients with hypertension accompanied by marked myocardial hypertrophy [10]. One reason for this may be narrowing of the range of adaptive and compensatory powers of the heart muscle in old age [5, 7] as a result of slowing of protein synthesis, a decrease in the RNA concentration and a decrease in its renewal in the cardiomyocytes [4, 8]. These data have been obtained in experiments on a model of acute hemodynamic overloading of the heart (coarctation of the aorta). The character of possible structural changes in the old heart in chronic hypertension has virtually not been studied morphologically.

The aim of this investigation was, by using morphological and graphic methods, to supplement the information obtained by physiological studies [1] by studying the morphogenesis of the "hypertensive" heart in old animals and to compare it with young animals with chronic hypertension.

EXPERIMENTAL METHOD

Renal (renovascular) hypertension was induced in rabbits of two age groups (6-10 months and 3.5-4.5 years) by bilateral operations (with an interval of 2-3 weeks) to produce stenosis of the renal arteries by 1/3-1/4 of their initial diameter, by Gorev's method [2]. The control group consisted of nine old and 14 young animals, the experimental group of nine old and 16 young animals. Control and experimental rabbits with hypertension (4 months after the second operation) were killed by air embolism. After autopsy of the animal, the heart and its parts were weighed separately [3]. Samples of tissue from the left ventricular myocardium for electron microscopy were treated in the usual way. Longitudinal and transverse sections of heart muscle were cut on an LKB ultramicrotome, stained with uranyl acetate and lead citrate, and examined in the IEM-100B electron microscope. For light microscopy, heart tissue was fixed in neutral 10% formalin, paraffin sections were stained in the usual way with hematoxylin and eosin, and the diameter of muscle fibers of the circular layer of the myocardium was measured with an MOV-15 ocular micrometer under a magnification of 700 (100 fibers in each case).

EXPERIMENTAL RESULTS

The results showed that the rabbit's heart undergoes hypertrophy with age. This was shown by the increase in the weight of the heart, the cardiac index (the ratio of the weight of the heart to body weight), and also the ratio of the weight of the left ventricle to body weight in the old animals (Table 1). Corresponding to the increased weight of the heart there

Laboratory of Pathophysiology, Institute of Gerontology, Academy of Medical Sciences of the USSR, Kiev.

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