CONTROLLED ATRIAL FIBRILLATION AND A POSSIBLE MECHANISM OF ITS ORIGIN

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KEY WORDS: vagus nerve; extrasystole; effective refractory period; potential self-excitation period; atrial fibrillation.

Fibrillation of the myocardium is traditionally explained [1, 4, 6, 12] by the appearance of ectopic foci of pacemaker activity in it or by the formation of closed pathways for the circulation of excitation. However, the prolonged coexistance of two alternative hypotheses indicates rather that fresh arguments are needed in support of both [1, 6]. This outcome, in turn, is largely dependent on the experimental and mathematical models used [1, 2, 7, 11, 13, 15]. The aim of the present investigation was to analyze fibrillation under conditions as close to natural as possible.

EXPERIMENTAL METHOD

In experiments on 20 cats anesthetized with chloralose and pentobarbital (75 ± 15 mg/kg) and artificially ventilated, the right vagus nerve (VN) was stimulated through platinum electrodes from an ÉSU-2 stimulator (2 msec, 40 Hz, 6 thresholds). Bipolar platinum probes were inserted into the right atrium through the jugular and femoral veins to record the ECG on an ÉLKAR-4 electrocardiograph and to stimulate the myocardium directly from a second ÉSU-2 stimulator (5 msec, 1, 5, and 10 thresholds). For visual monitoring of the events an S1-18 oscilloscope was used.

EXPERIMENTAL RESULTS

In eight experiments a frequency of contraction of 212 ± 8 beats/min (M ± m), 10-15% higher than the initial rate, was imposed on the heart, after which from 1 to 10 three-pulse

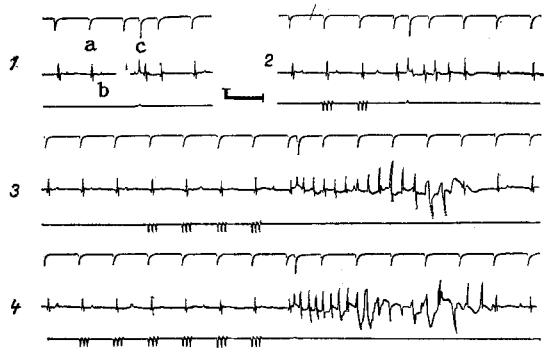

Fig. 1. Dynamics of ERP and arrhythmia-inducing effect during strengthening of the vagus effect on the heart. In each fragment, from top to bottom: marker of atrial stimulation, intra-atrial ECG, marker of stimulation of VN. 1, 2, 3, 4) Determination of ERP in the initial state and after 2, 4, and 6 volleys of stimulation of VN respectively. Minimal intervals between pacing and testing stimuli are given. a, b, c) P and R waves on the ECG and artefact of myocardial stimulation respectively. Calibration: 1 mV, 0.25 sec.

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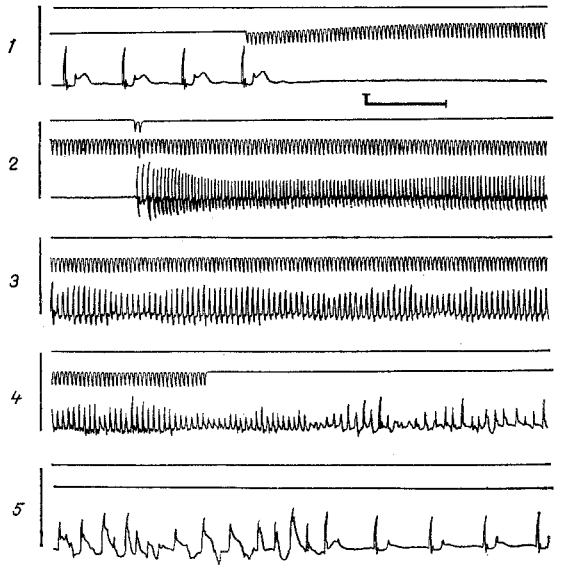

Fig. 2. Onset of AF in response to application of two testing stimuli to myocardium during vagal arrest of the heart. On each fragment from top to bottom: marker of atrial stimulation, marker of stimulation of VN, intra-atrial ECG (highest wave is P). 1, 2) Beginning of trace; 3) trace of 4th minute of fibrillation; 4, 5) end of trace at 6th minute. Here and in Fig. 3, calibration: 1 mV, 0.5 sec.

volleys of stimulation of VN were applied synchronously with the pacing stimuli (1.5 threshold). The effective refractory period (ERP) was determined simultaneously: it fell in response to stimulation by 1, 2, 4, 6, 8, and 10 volleys of stimulation from 127 ± 7 to 110 ± 6, 100 ± 8, 73 ± 7, 59 ± 6, 54 ± 6 and 52 ± 5 msec in the cycle immediately after the end of stimulation of VN. A regular feature of these experiments was the appearance of single or grouped extrasystoles during stimulation of VN by only 1 or 2 volleys (Fig. 1). As the stimulation increased, the arrhythmia was intensified and changed into atrial fibrillation (AF) if stimulation of VN was not stopped before determination of ERP. A characteristic feature of the arrhythmia described was shortening of the interval between spontaneous excitation during a decrease in ERP (Fig. 1). An increase in the interval between pacing and testing pulses by 30-40 msec compared with ERP prevented the development of AF whatever the level of activation of VN, and termination of its stimulation always terminated AF through a stage of slowing of the arrhythmia.

To rule out the role of the pacing pulses in the maintenance of AF, in 12 experiments VN was stimulated until complete cardiac arrest, after which two testing pulses were applied one after the other to the atrium. If the interval between them was shorter than ERP, the myocardium responded only by a single excitation, but as soon as the interval became equal to ERP, AF also arose (Fig. 2), and its duration depended on the effectiveness of stimulation of VN, from 3 to 8 min. Another typical feature of the AF observed was an initial rise of the frequency of excitation (up to 50 Hz, Fig. 2) followed by its stabilization at the 25-30 Hz level.

Analysis of the results revealed the following important facts: 1) participation of extrasystoles in the genesis of AF, observed by all workers, although neither extrasystoles nor stimulation of VN separately induced AF. Hence it follows that summation of vagal and extrasystolic effects are an essential condition for its appearance; 2) considering the unchanged principle of application of the testing stimulus, it can be postulated that the intensity of the arrhythmia-inducing effect is determined by the degree of vagal influence on the heart, and extrasystoles simply perform a triggering function [1, 12]; 3) since the degree of arrhythmia correlates with shortening of ERP, it is logical to suggest that the key factor in the development of AF is critical shortening of the action potential (AP) to a level at which it reveals the existence of one other parameter of myocardial excitability, namely the period of self-excitation (PPSE), which occurs simultaneously with ERP but ends a little earlier.

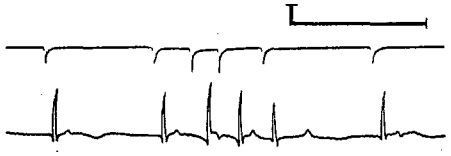

Fig. 3. Shortening of ERP during extra excitation of the myocardium. From top to bottom: marker of atrial stimulation, intra-atrial ECG. Minimal intervals between stimuli given, corresponding to background and extrasystolic ERP.

It can therefore be discovered only during the combined action of two or more factors which mainly shorten ERP and have a lesser effect on PPSE. In the case under discussion, these factors are an extrasystole (Fig. 3) and stimulation of VN; 4) premature activation of K-channels against the background of incomplete inactivation of Na–Ca-channels evidently corresponds to critical shortening of AP, and for that reason self-excitation of the contractile myocardium, which possesses latent pacemaker capacity [1, 14], becomes possible. But since the excitation thus arising is essentially also an extrasystole, with its inherent ability to shorten ERP [3], the arrhythmic process becomes self-maintained, and converts into AF, which is thus not identical with the true automatism of the nodal cells but is more reminiscent of the mechanism of burst excitation in a neuron [5].

If the point of view described above is accepted, certain fundamental facts can be explained.

1. The impossibility of AF when a single stimulus is applied to the myocardium, arrested by stimulation of VN, and the inevitability of its appearance when two stimuli are applied [9, 10], of which the second plays the role of testing pulse.

2. An increase in the frequency of myocardial excitation immediately after the onset of AF [1, 4, 11], which may be connected with summation of the extrasystolic effects of shortening of AP.

3. During hypothermia and exposure to certain other factors fibrillation is preceded, not by shortening, but by lengthening of AP, although this does not contradict the point of view expressed above. As we know [3, 8], cooling lengthens the plateau phase of EP by a greater degree than the repolarization phase, so that the difference between PPSE and ERP can be reduced to such a degree that any shortening of AP (extrasystole!) is sufficient to trigger pacemaking activity.

4. On the basis of the facts described above it can be tentatively suggested that a vulnerable period of myocardial excitability simply does not exist as such, but it arises with the first extrasystole, provided that the ERP thereby becomes shorter than PPSE.

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