FREQUENCY-DEPENDENT EFFECTS ON THE ISOLATED FROG HEART IN AN ALTERNATING ELECTRIC FIELD

É. A. Bogdanova, L. N. Plyashkevich, and A. G. Smagin

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KEY WORDS: electrical stimulation; resonance phenomena; sweeping; chrono-inotropism.

Electrical and mechanical responses of the heart to the action of an electric field [1] have not yet led to the creation of a model which is completely free from contradictions.

In this investigation, in order to stimulate the heart a method used in radio engineering was adopted: it is based on recording mechanical oscillations during a gradual change in the frequency of electrical stimulation (sweeping). Under these circumstances the conditions of excitation were almost the same as those used to excite electromechanical oscillating systems in engineering [6].

EXPERIMENTAL METHOD

Altogether 20 experiments were carried out on the frog (*Rana temporaria*) heart. The frog was immobilized and the chest opened. The membranes were removed from the heart and the organ isolated after division of the blood vessels, then placed in Ringer's solution (pH 7.2) in a special chamber. Mechanical activity of the preparation was recorded by means of special piezoelectric transducers, signals from which were led to the input of differential amplifiers, incorporating microcircuits of type 140UD8. Signals from the outputs of the amplifiers were led to the screen of a type SI-16 oscilloscope and recorded on tape by N338-1P and OM4-02 automatic writers. To observe mechanical activity of the heart visually, a binocular microscope was used. A television camera was mounted in one ocular of the microscope and signals from it were led to a videorecorder and examined on a VL-100 television receiver. The heart was excited by an alternating electric field under sweeping conditions, within a frequency range of 0.3-0.4 Hz. By using pulses of different polarity it was estimated that polarization phenomena and tissue damage near the electrodes would be minimized. Graphite rods, lowered into the Ringer's solution, were used as electrodes. A special device, based on a blocking generator, was used for electrical stimulation. The current between the electrodes was controlled within limits of 0.1-20 mA, both by incorporation of additional resistors in the loading circuit and by varying the distance between the electrodes.

EXPERIMENTAL RESULTS

In the low frequency region (0.3-0.6 Hz), to every change in direction of the current a mechanical response appeared (Fig. 1a), i.e., during one period of stimulation the preparation contracted twice. During a smooth increase in the frequency of stimulation the amplitude of the responses usually rose gradually, and then began to fall. As a result, spindle-shaped figures were produced, with ill-defined maxima (Fig. 1, region 5-30 sec). As the frequency of stimulation increased, a second, and sometimes a third, spindle-shaped change in ampliutde of the responses took place; the ratios between the frequency of stimulation (ω_{st}) and the frequency of responses of the heart preparation (ω_h) were different. Whereas at low frequendy $\omega_h \approx 2\omega_{st}$ (there were two contractions to one period of stimulation), for the second spindle $\omega_h \approx \omega_{st}$, and for the third spindle $\omega_h \approx {}^1/_2\omega_{st}$. Reduction of the number of responses by half was usually preceded by a gradual decrease in each second response, as could be clearly seen also by observation with the microscope and television camera (the phenomenon of mechanical alternation [1]).

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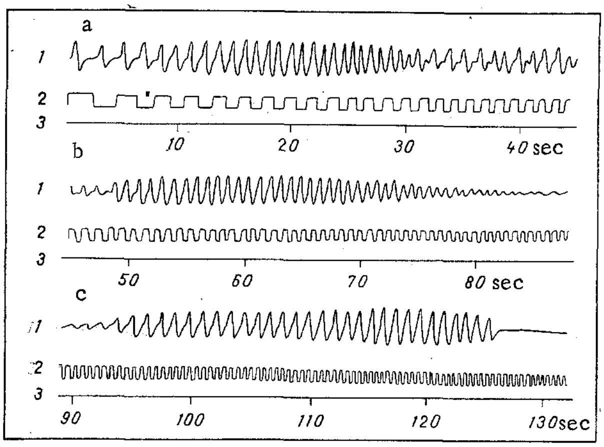

Fig. 1. Changes in mechanical responses of frog heart preparation during sweeping cycle: 1) contractions of preparation; 2) signals of stimulating current (4 mA); 3) time from beginning of stimulation (in sec). a, b, c) Consecutive cuts of sweeping cycle.

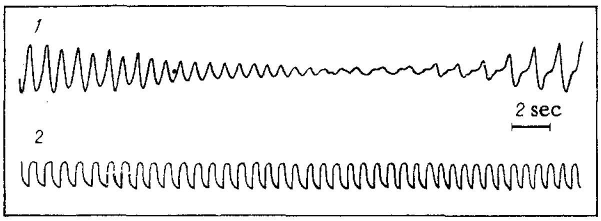

Fig. 2. Fragment of sweeping cycle. Legend as to Fig. 1.

Two or three spindles with maxima of amplitude at multiple frequencies appeared in the sweeping cycle from 0.25 to 2.5 Hz; ω_h in the zones of these maxima remained roughly constant as a result of multiplication or division of the frequency. In this particular example the zones of the maxima corresponded to 0.5, 1, and 2 Hz. The frequency of the responses in all three cases was about 1 Hz.

Symbols arising during the sweeping cycle differed somewhat in shape, and sometimes they were asymmetrical, with a gradual or abrupt decrease in amplitude of the responses — "collapse of the waves" (Fig. 1, 120-130 sec). In one of the periods of "collapse of the waves" several contracting regions could be seen under the microscope. Besides contractions of fairly complex shape, sinusoidal or sawtoothed signals, reminescent of FF flutter waves on the ECG, appeared (Fig. 2, left third of trace 1).

During a change in frequency in the opposite direction (from high to low frequencies) the principal distinguishing features of the trend of the responses still remained, although exact repetition of the picture of forward sweeping was not observed. During repeated sweeping cycles, complete identity likewise was not found in development of the responses, but the typical distinguishing features and characteristic details still remained.

In each experiment three or four values of stimulating current were tested (usually 2, 4, 6, and 8 mA). Dependence of the observed patterns on current amplitude was not confined simply to the "threshold" effect: with a change in strength of the stimulating current, the distinctness of the spindles, their shape, and their number in the sweeping cycle all changed. A decrease in amplitude of the responses was observed on a change to the highest strength of stimulating current (8 mA; Fig. 3). The response of the preparation became more uniform under these circumstances.

Changes in the amplitude of contractions of the preparation with an increase in frequency cannot be explained purely on the basis of traditional views on refractoriness. In extreme points of the frequency range (at high and low frequencies) contractions of equal frequency and amplitude appeared, whereas within a narrow range of the frequency scale contractions which differed sharply in amplitude appeared.

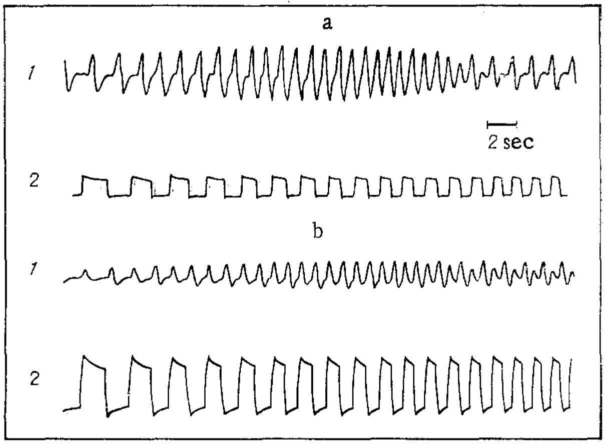

Fig. 3. Fragments of sweeping cycle during stimulation with equal frequencies but with different strength of current.

With an increase in the frequency of stimulation, immediately after the increase in amplitude of the responses mechanical activity was inhibited, which could signify that the limit of functional lability of the preparation had been exceeded. Nevertheless, at a higher frequency the amplitude of contractions increased once more. During reverse sweeping the enhancement of the responses at a high frequency was repeated and mechanical activity was reduced again at a lower frequency.

In the region of low frequencies (about 0.5 Hz) the response of the preparation likewise could not be explained purely by the duration of recovery processes: the frequency of contractions of the preparation was twice the frequency of stimulation.

These experiments thus revealed unique resonance phenomena. The amplitude of mechanical oscillations of the preparation was increased at multiple frequencies (for example, within the region of 0.5, 1, and 2 Hz), but during excitation there was a steadfast tendency toward maintenance of a definite frequency (about 1 Hz) at the harmonics, which was evidently the natural frequency of this particular oscillatory system.

As a physical analogy, we can examine a self-oscillating system under the influence of an inducing force [2], in this case electrical stimulation. Within the region of frequencies and amplitudes of the stimulating current investigated to maintain self-oscillations, and mixing of the two periodic systems — self-oscillating and induced — arises. The situation resembles the phenomenon discovered by L. I. Mandel'shtam and N. D. Papaleksi, which they called resonance of the n-th type [3]; when a periodic external EMF with frequency ω acts on an oscillating contour with natural frequency of ω_0 (ω is close to $n\omega_0$, where n is a whole number), under certain conditions powerful oscillations with a frequency of ω/n are excited. This analogy requires further experimental and theoretical clarification.

The question arises: are the resonance phenomena we have found due to the kinetics of chemical reactions lying at the basis of contraction and relaxation of heart muscle? Experimental data show that different effects of chrono-inotropic dependence (Bowditch's staircase," poststimulation potentiation, effects of paired stimulation, etc.) are linked with dependence of the supply of Ca^{++} to the myofibrils on the preceding movement of these ions, i.e., on the "prehistory of the contractions " [4]. The participation of calcium in muscular contraction is a complex enzyme-forming process. It has been shown [5] that enzymatic reactions possess resonance properties over a wide band of frequencies, and that with an increase in amplitude of a periodic disturbance they begin to react not only at the natural frequency, but also at multiple frequencies. Under these circumstances nonlinearities appear and resonance peaks become hysteresis-like in character. Although concrete comparison of these data and of the results of the present experiments demands a special examination, with more accurate temporal and amplitude parameters, the mere possibility of such an explanation of the resonance phenomena observed on the heart preparation is very interesting in principle.

LITERATURE CITED

1. E. B. Babskii and L. S. Ul'yaninskii, Electrical Stimulation of the Heart [in Russian], Moscow (1961).

2. K. K. Belya, Nonlinear Oscillations in Automatic Regulation and Control Systems [in Russian], Moscow (1962).
3. G. S. Gorelik, Oscillations and Waves [in Russian], Moscow (1959).
4. V. Ya. Isakov, A. K. Tsaturyan, and V. A. Shidlovskii, in: Problems in Cybernetics [in Russian], No. 36, Moscow (1977), p. 53.
5. E. E. Sel'kov, "Kinetics of open polyenzyme systems," Doctoral Dissertation, Pushchino (1979).
6. A. G. Smagin, Piezoelectric Resonators and Their Application [in Russian], Moscow (1967).

DETERMINATION OF DOUBLE BONDS OF THE BLOOD PLASMA LIPID FRACTION BY THE ADS-4M APPARATUS IN BURNED PATIENTS

V. K. Sologub, N. A. Olyunina, D. M. Lisitsyn, V. A. Lavrov, and Yu. E. Babskaya

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Double bonds (DB) between two carbon atoms in blood lipids are characteristic of unsaturated fatty acids (USFA), whose biological significance has been inadequately studied. Research in the last 10 years has shown the important role of USFA in the formation of highly active substances in the body, among which arachidonic acid, a precursor of the prostaglandins, and linoleic and linolenic acids deserve particular attention. As polyenic compounds, these acids have very high ability to participate in addition reactions or to split at the double bond.

We know that in burns the fatty-acid spectrum and concentration of USFA in the plasma change, and these changes apply both to free fatty acids and to acids of a lipid complex [3, 4]. Correlation has been found between the severity of the condition of a burned patient and the character and degree of changes in the spectrum and concentration of USFA, and the latter have been shown to be influenced by therapeutic measures. The importance of the study of the concentration and spectrum of USFA to the evaluation of the state of patients and effectiveness of their treatment has thus been demonstrated and the high sensitivity of an investigation of this type has also been observed. However, determination of the fatty acid spectrum by a chromatographic method is hardly suitable for regular monitoring of the patient's state because of the long time taken by the investigation and its complexity. The present writers have used a method of quantitative determination of DB in the lipid fraction of blood on an instrument known as a double bond analyzer (the ADS-4M), designed by the Institute of Chemical Physics, Academy of Sciences of the USSR [1].

The velocity of interaction of ozone with DB is several orders of magnitude greater than the velocity of its interaction with other functional groups, so that the analysis is highly selective [2]. This method has not been used hitherto in clinical practice.

In this investigation the diagnostic scope of the method of determination of DB in the blood lipid fraction in order to assess the state of burned patients and to monitor the effectiveness of their treatment, when used as an express method of detecting changes in the above parameters of USFA, was studied.

EXPERIMENTAL METHOD

Repeated tests were carried out on 25 patients aged from 18 to 50 years with thermal burns of the IIIA + B to IV degree, affecting from 7 to 80% of the body surface. Blood plasma

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