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From the Third Medical Clinic of Kyoto University (Director: Professor M. Maekawa, M. D.)

**Experimental Studies on the Relationship between Electrical
and Mechanical Events in the Toad Heart (I)**

**ON THE RELATIONSHIP BETWEEN ELECTRICAL AND MECHANICAL EVENTS
IN THE TOAD VENTRICLE**

By

BUNJIRO ONO

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INTRODUCTION

A number of fundamental investigations had been offered as the foundation of the electrocardiographic study (Kölliker and Müller¹⁾, Marchand²⁾, Engelmann³⁾, Bayliss and Starling⁴⁾, Mary⁵⁾, Burdon-Sanderson and Page⁶⁾, and recording of the human electrocardiogram could be made for the first time by Waller⁷⁾. The invention of string galvanometer by Einthoven⁸⁾ provided a clue to analyse electrocardiogram and made it possible to put to practical use. On the other hand, in investigating the generation of bioelectricity, several theories, such as Hermann's negative hypothesis^{9,10)}, and Bernstein's membrane theory¹¹⁾ were proposed. The introduction of such theories on excitation into the electrocardiographic study has further offered several formulations, such as Schütz's difference theory¹²⁾, the theory of limited potential differences of Lewis¹³⁾, Craib's hypothesis of dipole^{15,16)} and Wilson's bipolar theory^{16,17)}. Especially Wilson has ingeniously applied the solid angle law to the hypothesis of dipole and developed the Bernstein theory into a new field, the so-called new-membrane theory which has been so far generally accepted.

In 1945, Prof. Maekawa^{18,19)} insisted on the chain-doublers theory which was dependent upon the unitary relationship between the electrical generation and the contraction of cardiac muscle. This chain-doublers theory has so far given an extremely satisfactory explanation to the electrocardiographic study¹⁸⁻²⁹⁾. Necessarily from this theory it would be surmised that the mechanogram of cardiac muscle is nothing but the integration curve of the monophasic action potential.

In the present study this supposition was experimentally tested. And the satisfactory results will be shown to support the theory under consideration.

METHODS

a) Preparation and Procedure: The toad hearts in the winter stage were used. The toad being fixed on its back, the chest wall and the pericardial sac were opened and the heart was exposed. The improved Straub's cannula was introduced through the truncus arteriosus. The heart provided was excised and perfused with Locke's solution (NaHCO₃ 0.01, CaCl₂ 0.02, KCl 0.02, NaCl 0.65, glucose 0.1, H₂O 100g.). Absorbent cotton moistened with Locke's solution was spread on a glass dish, and the excised heart was placed on it (Fig. 1). The perfusion pressure was maintained at 4 to 6 cm. H₂O during the contraction and 3 to 5 cm. H₂O during the relaxation. The total amount of the perfusate was 5 to 7 cc. The room temperature ranged from 3.0°C. to 12.0°C. A non-polarizable electrode of silver-silver chloride type was used. For recording the monophasic action current a different electrode covered with a 3 M-KCl solution soaked cotton gauze pad was put on the surface of the heart. The indifferent lead electrode was placed at the circumference of the glass dish. The integration curve was obtained by using a integrator circuit. The potential changes were observed and photographed on the electromagnetic oscillograph (Yokogawa, N-3 type, with H-type vibrator) after direct coupled 3 stage amplification. The mechanogram was recorded with a specially devised recorder which made use of an oscillator.

b) Mecanogram-recorder: Making use of the Hartley circuit, changes in the capacity of the condenser were rendered to a oscillatory current of the plate circuit. Any amplifier was not required for recording (Fig. 2). The condenser consisted of copper plates, $1.5 \times 5.0 \text{ cm}^2$ in dimensions, placing in parallel with each other. This equipment was available for recording the pulsation of the excised toad heart without disturbance.

c) Electrical integrator: An ordinary integrator circuit was used with a slight improvement. The circuit diagram is shown in Fig. 3. The potential to be obtained will be given by the following equation:

$$e_c = \frac{1}{CR} \exp\left(-\frac{t}{CR}\right) \int f(t) \exp\left(+\frac{t}{CR}\right) dt$$

In Fig. 4, the changes in the curves are presented at varied time constants with a constant pulse duration. Fig. 5 indicates that the pulse duration changes when the peak amplitude of the integration curve is kept constant. The integrator was available within the range of the time constant of 2 to 5 times the pulse duration. The time constant of 3 times the pulse duration is then considered to be suitable, the gain of the present amplifier being taken into consideration. Since the Q-T time in the present experiment is 2 to 3 sec., the time constant of 10 sec., the time constant of 10 sec. was adopted.

d) On occasion, as a reference, the triphasic curve by the epicardial direct unipolar recording, the mechanogram and the monophasic action cur-

Fig. 1. Schematic drawing of experimental arrangement.

Fig. 2. Schematic diagram of the mechanograph.

rent were simultaneously recorded.

RESULTS

In Fig. 6, the mechanogram, the integration curve and the monophasic action current are shown from top downwards. For the monophasic action

current upward deflection indicates negativity, and for the integration curve the sign is the reverse. As is clear from this figure, the mechanogram is quite similar to the integration curve in the shape and the course, but the latter precedes the former by 0.25 sec. As a matter of course, the trough of

Fig. 3. The circuit diagram of the electrical integrator.

Fig. 4. Simultaneous recordings of integration curve (a) and impulse (b). In left figure (A), resistance (R): 2 MΩ, capacity (C): 2 μF, impulse duration (T): 2.2 sec, height of crest: 22.0 mm, CR=1.8 T and calibration: 10 mv. In right figure (B), resistance (R): 4 MΩ, capacity (C): 2 μF, impulse duration (T): 2.2 sec, height of crest: 23.0 mm, CR=3.6 T and calibration: 10 mv.

Fig. 5. Simultaneous recordings of integration curve (a) and impulse (b). In left figure (A), resistance (R): 2 MΩ, capacity (C): 2 μF, impulse duration (T): 0.9 sec, height of crest: 19.0 mm, CR=4.4 T and calibration: 10 mv. In right figure (B), resistance (R): 4 MΩ, capacity (C): 2 μF, impulse duration (T): 2.4 sec, height of crest: 19.0 mm, CR=3.3 T and calibration: 10 mv.

Fig. 6. Simultaneously obtained the mechanogram (a), the integration curve (b) and the monophasic curve (c). The mechanogram, the integration curve and the monophasic curve are shown from top downwards. Further description in text.

the integration curve was coincidental with the onset of the monophasic current, and rising phase of the integration curve corresponded to the plateau of the monophasic current. The crest of the integration curve was also in accordance with the end of the monophasic action current. In the simultaneous recording it was revealed that the rising phase of the mechanogram, the rising phase of the integration curve, the plateau of the monophasic action current and the S-T segment of the triphasic action current were all temporally in accordance with each other.

DISCUSSION

Before discussion for the present results will be made, the consideration on electrocardiogram proposed by Prof. Maekawa will be quoted here. This quotation will be available to make clear the purpose and significance of the present study. He states that³⁰⁾: "When one intends to explore the entity of electrocardiogram, it is nothing but grasping at the shadow and rejecting the substance that he assumes a rough causality between the physiological and anatomical informations and the corresponding changes in electrocardiogram. The action current is the electrical generation of the action of cardiac muscles. This is a confidence in physiology. This confidence or conception, however, seems to be too rough to the consideration at the present. And moreover, as mentioned earlier, it was revealed that the cell membrane, the epicardium and the pericardium also played important roles in generating the action potential as well as the cardiac muscle. Then, the question to consider is what the action of cardiac muscle is. It has been rather generally rejected that there is a direct re-

lationship between electrocardiogram and the contraction of cardiac muscles. Then what action of the cardiac muscle does it refer to the electrical generation? The answer has been an excitation. The excitation of cardiac muscle, however, has been considered to be the same meaning as the contraction. And the contraction has been so far experimentally indicated to have no relation to electrocardiogram. How queer is this argument? The current electrocardiographic study has been so far provided for a diagnosis of the function of hearts, depending upon such a ambiguous basis. Or to say in other words, the electrocardiographic study itself has been a vague and obscure conception.

The action current is a kind of electrical currents. And the muscle contraction is a mechanical work. In order to make the electrical current correspond to mechanical work, a dynamo should be required as an intermediation. The electrical current should be transformed into a magnetic field. No dynamo is found in the circuit of the action current. It means, therefore, nothing that an attempt is made for making the action current correspond to the contraction. It is a matter of course that there is no linear relation between them. Then the next question arises how the action current should be related to the contraction. It will be settled only by depending upon static electricity. And the Coulomb law must be introduced as an intermediation. The action current corresponding to the contraction, therefore, is not available in the form of electrical current but in the form of static electricity integrated with time".

Now considerations will be made on mutual relations in the mechanogram the integration curve and the monophasic action current obtained in the present experiment.

(1) Mechanogram: In general, there are two types of muscle contractions, iso-tonic and iso-metric. But it is actually difficult to obtain each of them as a pure type, separating one from the other. The classification of them must be made only with the feature manifested by the curve obtained, consideration being given to the experimental equipment. The curve obtained in the present experiment was apparently one of the isotonic contraction, and it indicated the intraventricular pressure. In simultaneous recording it was shown that the onset of the monophasic action current preceded the trough of the mechanogram by 0.25 sec., and the end of

the former preceded the summit of the latter by 0.25 sec. This temporal discrepancy between these two curves may be attributable to the inertia of the cardiac muscle and of the perfusion equipment by Ctraub's cannula. It should be also noted that the mechanogram is an expression in one dimension, while the contraction is a phenomenon in the three dimensions. Horwitz³¹⁾ described on the heart of the dog that the ejection curve showed an upward convex while the contraction curve was a straight line. Now, assuming the toad heart as a sphere, the relation between the surface area of the heart (F) and the perfusion pressure (H, fluid level in Straub's cannula) will be given as follows:

$$H = A - BF^{3/2}$$

where A and B are constants.

The contraction of cardiac muscle, therefore, should be more linear than the mechanogram obtained here.

(2) Integration curve: Recently the integrator circuit has been occasionally used in order to show the ventricular gradient³²⁾. But the integrator circuit used in the present experiment had somewhat different purposes. According to the theory of chain doublets, the potential in volume conductor at distance R from the center of the charged layer can be approximately given by the formula

$$\phi = \frac{1}{4\pi\lambda} \cdot \frac{\bar{T} \cos \theta}{R^2}$$

where $\bar{T} = \int |\dot{\tau}| \cdot d\nu$

This equation indicates that the monophasic action potential obtained by the injury of the cell membrane results from the differentiation form of the electrical generation in the cardiac muscle. The integrator circuit used here thus provided not to estimate the total amount of electricity generated but to observe the electrical generation in the cardiac muscle as a function of time. It is interesting to note that Schaefer³³⁾ has recently explained the electrical generation of the cardiac muscle in the form of the integration phenomenon. The theory of chain doublets more closely relates to Schaefer's theory than to the neo-membrane theory.

(3) Monophasic action current: For recording the monophasic action current, several methods have been used, such as physical methods (cooling, heating, pressure, suction), chemical methods (KCl, alcohol, drugs) and internal recording methods³⁵⁻⁴²⁾. And recently direct currents have been applied

to record the monophasic action current. All these methods provided to observe potential changes at the point where recording was going without any disturbance from the electrical generation of other parts. For the theoretical interpretation of the monophasic action current, Bernstein's membrane theory or the neo-ionic theory by Hodgkin and Katz has been generally accepted. Prof. Maekawa⁴⁸⁾, however, has already pointed out a fallacy upon which these theories were dependent.

The theory of chain doublets has also undergone several changes in the interpretation of the monophasic action current. When Prof. Maekawa^{29, 49)} proposed the theory of chain doublets for the first time, the positive monophasic wave led off monopolarly from the injured region has once been interpreted as the downstream phenomenon of the propagated excitation. Recent investigations, however, presented that the entity of the electrical generation of the muscle was closely related to the intramolecular transformation of myosin. The interpretation of the monophasic action current was thus improved, and the plausible cause was attributed to the diffusion of cations out of the injured region and the accumulation of anions in the cell.

The reason why 3 M-KCl solution was used to obtain the monophasic action current in the present experiment were as follows:

(a) Under the application of 3 M-KCl solution the monophasic action current could be recorded undisturbed over long periods.

(b) 3 M-KCl solution had almost no effect on the mechanogram and the triphasic action current. It was also revealed in a recent investigation⁴¹⁾ that the monophasic action current recorded with intracellular electrodes was not essentially different from the monophasic action current obtained by the KCl injury in the toad heart. It has been recently found that the monophasic action current obtained by the KCl injury was suppressed by the addition of NaCl solution⁵⁰⁾. It is of interesting that Na ions show a counteraction with K ions in the generation of the monophasic action current.

Much interesting has been so far had in studying on the relationship between electrical events and mechanical events. And several methods have been adopted in order to find relations between these two events, such as indirect methods (arterial blood pressure tracing, venous pressure tracing, phonocardiogram, ballistocardiogram, cardiogram),

semi-direct methods (electrokymogram^{55, 56, 57, 58}), roentgenkymogram^{59, 60}), dielectrocardiogram⁶¹⁻⁶³) and direct methods (intraventricular pressure curve^{64, 65}), epicardial contraction curve after opening of the thorax³¹), high-speed cinematograph after opening of the thorax⁶⁶). Electrocardiogram relating to the mechanical events has been observed by the standard limb lead, the semi-direct lead and the direct lead. The analysis of the wave of electrocardiogram, however, has been so far made mostly on the triphasic wave and on rare occasions made on the monophasic action current. Considerations on the relation between the integration curve of monophasic action current and the mechanogram have thus escaped the notice of previous investigators. This attempt was for the first time made by Prof. Maekawa.

It has been generally prevailed up to the present time that there is no essential relation between electrical events and mechanical events in the cardiac muscle. This fallacy resulted from that previous investigators searched after a mutual relation between the mechanogram and the triphasic action current which was itself a distorted record. Prizmetal has recently demonstrated with a high-speed cinematograph that the contraction of the dog heart was inseparable from the electrical events, supporting Eyster's opinion^{71, 72}). Schaefer also insisted on the concomitancy of the mechanical events with the electrical events, introducing the conception of integration into the action current. The hypothesis proposed by Prof. Maekawa on the relation between the contraction and the electrical generation was experimentally verified by Fukuda⁷³) on strip of the cardiac muscle. And the results obtained by Tanaka⁷⁴) in skeletal muscle fibers were also in good agreement with Maekawa's hypothesis.

CONCLUSION AND SUMMARY

The mechanogram, the integration curve and the monophasic action current were simultaneously recorded in the excised toad heart perfused with Locke's solution. The mechanogram was in accordance with the integration curve in the temporal course. This concomitancy was in good agreement with the results expected by the theory of chain doublets.

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