Prolongation of Ventricular Action Potential
Due to Sympathetic Stimulation

Masahiro Murayama, M.D., Kenichi Harumi, M.D.,
Saburo Mashima, M.D., Katsuro Shimomura, M.D.,
and Satoru Murao, M.D.

SUMMARY

The changes of monophasic action potential durations due to stellate stimulation for the period of 3 sec were studied in dogs with suction electrodes from the anterior surface of the right ventricle and the posterior surface of the left ventricle. Prolongation of monophasic action potential duration was observed from the period of 2 to 3 sec during stimulation to that of 10 to 20 sec after the termination of stimulation. Prolongation of monophasic action potential duration due to right stellate stimulation was predominant in the right ventricle and that due to left stellate stimulation was predominant in the left ventricle. The transient T wave change in the surface electrocardiogram occurring immediately after the beginning of stellate stimulation could be explained by this local difference in prolongation of ventricular repolarization. Since the onset of prolongation of monophasic action potential duration preceded increase in blood pressure following stellate stimulation, this prolongation of monophasic action potential duration did not result from the hemodynamic changes and could be a primary effect of the sympathetic nerve stimulation.

Additional Indexing Words:
Monophasic action potential  Sympathetic nerve  T wave  QT interval

It has been well documented that T wave changes can be induced in experimental animals by stimulation of the cardiac sympathetic nerves. It has also been reported from our and other laboratories that there are different effects on T wave form with stimulation of right as compared to left cardiac sympathetic nerves. The changes in T wave form associated with long period of stimulation of right or left cardiac sympathetics is explicable on the basis of localized changes in refractory period measurements associated with unilateral sympathetic stimulation. It was noted in our laboratory that the initial change in T wave form during sympathetic stimulation was in opposite direction to the change in T wave form seen after the stimulation.

From the Second Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Hongo 7, Bunkyo-ku, Tokyo 113, Japan.

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Autenrieth and associates have also reported a biphasic course of T wave changes during intracoronary and systemic isoproterenol infusion. Early during infusion at the time of the initial change in T wave form suction potential recordings from some ventricular sites shortened while those from others were unchanged. Later the polarity of T wave form change reversed and at this time there was shortening of suction potential duration at all sites sampled in the perfused areas. Comparable studies of the biphasic course of T wave changes seen with sympathetic stimulation have not been previously reported. This report concerns serial change in form of suction potential recording during and after brief periods of intense unilateral stimulation of the cardiac sympathetics.

**Methods**

Ten mongrel dogs weighing 9 to 20 Kg were anesthetized with intravenous administration of sodium pentobarbital, 30 mg/Kg. Additional doses of 5 to 10 mg/Kg were given to maintain anesthesia. The trachea was cannulated and respiration maintained with a pump respirator. The right and left stellate ganglia were isolated and bipolar steel hook electrodes attached. The chest was opened through a sternal splitting incision and the heart suspended in a pericardial cradle. A bipolar steel hook electrode was attached to the right atrial appendage, the sinus node crushed and the atrium paced at a fixed rate. The pacing rate was fast enough to maintain control of drive during sympathetic stimulation. Since, in 6 preliminary experiments, there were no differences in the effect of stimulation of the intact stellates or stimulation of the peripheral cut ends of the stellates on T wave form, the stellates were left intact in this study. The stimuli were 2 msec rectangular pulses at frequencies of 20 to 50 CPS and intensities of 20 to 30 V. These were delivered to the right or left stellate for periods of 3 sec. Stimulation of the right stellate was done in 8 animals and that of the left stellate in 10 animals.

Ventricular monophasic action potentials were recorded with bipolar suction electrodes. The electrode assembly was a plastic cup with an outside diameter of 3 mm, and a height of 5 mm. There was a 1 mm diameter silver electrode in the center of the cup which touched the surface of the injured myocardium when −60 to −70 mmHg suction was applied. The other pole of the recording system was a 1 mm wide ring attached to the circumference of the suction cup. Monophasic action potentials were recorded simultaneously from a site on the anterior surface of the right ventricle and the posterior surface of the left ventricle. Recordings were taken at a paper speed of 250 mm/sec. The recordings were considered satisfactory if the downstrokes were smooth and the amplitudes exceeded 50 mV. A Y lead was also recorded using the triaxial dog lead system. Blood pressure was continuously recorded from the carotid artery with a Nihon Kohden MPU-0.5 pressure transducer. Durations of monophasic action potentials were measured from recordings obtained at 1 sec intervals during and for 10 sec after termination of sympathetic stimulation, and from recordings obtained at 5 sec intervals for an additional 30 sec. Durations of monophasic action potentials were measured at
the point where the downstroke was 20% of the maximal height. This time will be referred to as the 80% repolarization time.

Observations were repeated 3 to 4 times. Data were expressed as the mean±SD and were analyzed using Student's t-test.

RESULTS

I. Right stellate stimulation

The atrial pacing rate was 155±27/min. During control periods the 80% repolarization times of right ventricular monophasic action potentials averaged 184.3±19.4 msec and those of left ventricular monophasic action potentials averaged 177.0±24.7 msec. Right stellate stimulation produced prolongation of the 80% repolarization time in the right ventricle of all dogs. An example is shown in Fig. 1. In 7 of 8 dogs prolongation of the 80% repolarization time occurred at 3 sec after the onset of stellate stimulation and in the other dog it occurred at 1 sec after the termination of stimulation. Prolongation of the 80% repolarization time persisted for 10 to 20 sec after the termination of stimulation, and was maximal at 2 to 8 sec after the termination of stimulation. The magnitude of the maximal prolongation in the 80% repolarization time ranged from 6 to 18 msec with an average of 10.0±4.7 msec in the right ventricle. The 80% repolarization time was always less prolonged in the left ventricle than in the right ventricle on monophasic action potentials recorded simultaneously during and after right stellate stimulation. The magnitude of the maximal prolongation in the 80% repolarization time ranged from 0 to 8 msec with an average of 4.5±2.6 msec in the left ventricle. There

![Fig. 1. Example of changes in monophasic action potential following right stellate stimulation. Prolongation of 80% repolarization time at 5 sec after the termination of stimulation in the right ventricle (7 msec longer than the control state), while no prolongation was observed in the left ventricle. Shortening of 80% repolarization time at 20 sec after the termination of stimulation occurred in the right ventricle (5 msec shorter than the control state). R-R interval was kept constant at 356 msec.](image-url)
Fig. 2. Example of the serial changes of 80% repolarization time of monophasic action potential following right stellate stimulation.

was a statistically significant difference in the effects of right stellate stimulation on right and left ventricular monophasic action potential duration at the p<0.01 level.

The serial changes in 80% repolarization time prior to, during and after stimulation of 1 dog’s right stellate are graphed in Fig. 2. As shown in the figure, after the initial prolongation, 80% repolarization time shortened to less than control durations. Prolongation of the monophasic action potentials resulting from right stellate stimulation occurred prior to increase in blood pressure.

II. Left stellate stimulation

During these observations the atrial pacing rate averaged 150±22/min. During control periods the 80% repolarization times of right ventricular monophasic action potentials averaged 191.9±23.1 msec and those of left ventricular monophasic action potentials averaged 183.7±27.0 msec. An example of right and left ventricular monophasic action potentials, recorded prior to and after left stellate stimulation is shown in Fig. 3. In all 10 dogs the 80% repolarization time of left ventricular monophasic action potentials prolonged at 2 sec after the onset of left stellate stimulation and persisted for 10 to 15 sec after the termination of stimulation. The maximal prolongation of the 80% repolarization time occurred at 1 to 8 sec after the termination of left stellate stimulation and ranged 6 to 18 msec with an average of 11.7±3.8 msec. During left stellate stimulation the 80% repolarization time was always less prolonged in the right ventricle than in the left ventricle on monophasic action potentials recorded simultaneously. The magnitude of the maximal prol-
Fig. 3. Example of changes in monophasic action potential following left stellate stimulation. Prolongation of 80% repolarization time at 5 sec after the termination of stimulation in the left ventricle (18 msec longer than the control state) was greater than that in the right ventricle (9 msec longer than the control state). Prolongation of QT interval (20 msec longer than the control state) was observed. Shortening of 80% repolarization time at 25 sec after the termination of stimulation occurred in the right and left ventricle (3 msec and 4 msec shorter than the control state, respectively). R-R interval was kept constant at 356 msec.

Prolongation in the 80% repolarization time ranged 0 to 9 msec with an average of 5.1±2.7 msec in the right ventricle. The difference of prolongation between left and right ventricular monophasic action potentials, resulting from left stellate stimulation, was statistically significant at the p<0.01 level.

The QT intervals of Y lead electrocardiogram measured in 4 animals prolonged after left stellate stimulation, corresponding to the prolongation of monophasic action potential following left stellate stimulation.

Fig. 4. Example of the serial changes of 80% repolarization time of monophasic action potential following left stellate stimulation.
left ventricular monophasic action potentials in timing, as shown in Fig. 3. The maximal QT prolongation ranged from 8 to 20 msec with an average of 14.0±4.5 msec.

The serial changes in duration of right and left ventricular monophasic action potentials of 1 dog prior to, during and after left stellate stimulation are graphed in Fig. 4. As shown in the figure, shortening of monophasic action potentials occurred following the initial prolongation. As during right stellate stimulation, prolongation of left ventricular monophasic action potentials during left stellate stimulation preceded increase in blood pressure.

**Discussion**

The electrocardiographic changes produced by electrical stimulation of the cardiac sympathetic nerves have been reported by a number of authors since Rothberger and Winterberg in 1910. But most of the reports were concerned with the long-lasting T wave changes and the transient T wave changes preceding it was not fully studied. Since Yanowitz and Kralios used the long period of stimulation, the transient changes of T wave occurring immediately after the beginning of stimulation was obscured. The brief period of stimulation for 3 sec was used in this study. The stimulus artifact did not disturb recordings of monophasic action potentials during stimulation with suction electrodes used in this study. The analysis of serial changes of monophasic action potential durations following right or left stellate stimulation was possible with this technique.

Our results indicate that the transient prolongation of monophasic action potential duration was produced by the sympathetic nerve stimulation. Prolongation of monophasic action potential duration due to right stellate stimulation was more remarkable in the right ventricle than in the left ventricle and that due to left stellate stimulation was more remarkable in the left ventricle than in the right ventricle. Yanowitz and associates demonstrated that the left stellate innervation was predominant over the posterior wall of the left ventricle and the right stellate innervation dominated the anterior wall of the right ventricle. The difference of the grade of prolongation of monophasic action potential durations due to right or left stellate stimulation between the right and left ventricle was in agreement with local difference in sympathetic innervation. Shortening of monophasic action potential durations occurred at the late phase of poststimulation period was consistent with decrease of ventricular refractory period shown in Kralios' report. Since prolongation of monophasic action potential duration occurred at 2 to 3 sec after the beginning of stimulation when there was no increase in blood pressure, hemo-
dynamic effect could not be the major factor influencing the changes of monophasic action potential duration. This prolongation of monophasic action potential duration at the early phase of the sympathetic stimulation could be a primary effect of the sympathetic nerve.

The initial transient T wave change in the surface electrocardiogram following stellate stimulation corresponded to prolongation of monophasic action potential duration in timing and can be explained by the local difference in the sympathetic innervation. This change of ventricular repolarization in the local area seemed to be reflected also in prolongation of QT interval in the surface electrocardiogram.

**References**