Effects of Cardiac Sympathetic Nerve Stimulation on Conduction in the Heart

By Andrew G. Wallace, M.D. and Stanley J. Sarnoff, M.D.

There is general agreement that sympathetic agents enhance impulse transmission through the A-V node, but reports differ concerning their influence on specialized conduction tissue and ventricular muscle. Recently several investigators have suggested that catecholamines may result in a more synchronous contraction of the heart, resulting possibly from a change in the sequence of ventricular activation. In the experiments described in this report, we have examined the effects of direct cardiac sympathetic nerve stimulation on the manner of ventricular activation, on conduction in ventricular muscle and Purkinje tissue, and on A-V nodal transmission. A preliminary report of these observations has appeared elsewhere.

Methods

Mongrel dogs weighing 14 to 21 kg were anesthetized with pentobarbital sodium (25 mg/kg). Ventilation was maintained with a Jefferson pump and rectal temperature was monitored and kept between 37.5° and 39.0°C with external heating pads. Arterial pressure was measured with a Statham strain gauge transducer.

After the chest had been opened through a midsternotomy, intracardiac recording electrodes each containing five surface contacts, were placed at two positions during separate periods of total venous occlusion (fig. 1). Each period of occlusion averaged two minutes. One electrode was implanted at the base of the right anterior papillary muscle through a 2 to 3 cm right ventriculotomy. The second electrode was implanted directly over the bundle of His through a right atriotomy. Additional recording electrodes were placed sometimes on the epicardial surface of the ventricles and the heart was paced through an electrode sutured to the right atrium. Estimated blood losses were corrected with donor blood or dextran.

The left stellate ganglion was isolated by cutting all central rami and stimulated through a bipolar electrode using a Grass impulse generator and isolation unit. In two animals the right stellate ganglion was surgically removed. Experimental observations in these two animals did not differ quantitatively from the other studies and they are, therefore, not considered separately. Bilateral vagotomy was performed in all animals.

In other experiments conduction in muscle was evaluated by a technique similar to that described by Moe and Mendez and Swain and Weidner. An electrode was sutured to the wall of the right ventricle and oriented parallel to the anterior descending branch of the left coronary artery (fig. 2). The electrode contained several (four to eight) bipolar contacts spaced...
Stimulating electrodes

FIGURE 2
Electrode implanted on the right ventricle for measurement of conduction velocity in epicardial muscle.

at intervals of 2.5 to 4.5 mm. The first set of contacts was used to pace the ventricle at a constant rate and activity was recorded from each higher position. Conduction time from stimulus to recorded activity was plotted against the distance between the pacing site and each recording contact. The slope of such a time distance plot reflected conduction velocity in muscle parallel to the electrode. The pacing stimulus was a 10- to 15-volt pulse of 2 to 5 msec duration. Records from contacts within 5 mm of the point of stimulation were frequently distorted by the pacing artifact and were not included in the measurements.

Silver wires from each electrode contact were connected to a switch box designed to permit selection of any two from each electrode. Bipolar signals were amplified with Tektronix 122 preamplifiers and the outputs displayed on a Tektronix 502 dual beam oscilloscope. Frequencies below 80 cycles/sec and above 1000 cycles/sec were filtered out to sharpen the desired signals which were photographed with a DuMont Type 321 camera at a paper speed of 1200 inches/min.

Results

Interpretation of electrograms recorded from intracardiac and epicardial surface contacts has been discussed in detail by Stuckey, Hoffman and their associates. Figure 3 shows a typical record and illustrates the nomenclature used to describe the tracings. The tracings were obtained from electrodes implanted over the His bundle (His), right Purkinje papillary muscle junction (PPJ) and the epicardial surface of the left ventricle (Ventricle). The electrode over the bundle of His recorded activity from three structures, the atrium subjacent to the electrode (A), the bundle of His (H), and the base of the underlying interventricular septum (S). The PPJ electrode recorded activity from two structures, a spike from the underlying band of Purkinje tissue (P) and a later complex from the base of the papillary muscle (PM).

At the recording speed of 1200 inches/min, (ipm) intervals could be measured reproducibly to the nearest 0.4 msec. In any given animal at constant heart rate, interelectrode intervals did not vary more than 0.4 msec during consecutive cardiac cycles.

The effect of stellate ganglion stimulation on the interval between complexes recorded

<table>
<thead>
<tr>
<th>EP#39</th>
<th>A</th>
<th>H</th>
<th>S</th>
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<tbody>
<tr>
<td>HIS</td>
<td></td>
<td></td>
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<tr>
<td>PPJ</td>
<td>P</td>
<td>PM</td>
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<td>Ventricle</td>
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FIGURE 3
Recordings from His bundle (upper beam), right Purkinje papillary junction (middle beam) and epicardial surface of left ventricle (lower beam). A = atrium, H = His bundle, S = basal interventricular septum, P = Purkinje, PM = papillary muscle and V = ventricle.
from the atrium and His bundle was examined in 52 experiments on 12 animals. Heart rate was held constant in each experiment. In all animals sympathetic stimulation shortened the A-H interval. The average change was a decrease of 31.1 msec or 49.8% (range 12.0 to 65.0 msec). The data are summarized in table 1 and tracings from one such study are shown in figure 4.

In eight of the above twelve animals, 31 observations were made of the effect of sympathetic stimulation on the interval between His bundle activity and complexes recorded from Purkinje tissue at the base of the right anterior papillary muscle. The average change with stellate stimulation was a decrease of 0.7 msec or 2.4% (range 0.0 to 3.0 msec). The observations are summarized in table 1 and figure 4 illustrates records from one such experiment.

The influence of sympathetic stimulation on ventricular activation was evaluated by two separate techniques. First, changes of the interval between excitation of the right anterior papillary muscle and the base of the interventricular septum were considered indicative of the magnitude of changes in total ventricular activation time. Second, the pattern and time-sequence of activation of the epicardial surface of the ventricles was mapped before and during stellate stimulation. The interval between activation of the right papillary muscle (PM) and the basal interventricular septum (S) was measured in 25 experiments in eight animals. Measurements of the PM-S interval averaged 41.1 msec during control periods and shortened in all animals with sympathetic stimulation (fig. 4). The average decrease of the PM-S interval was 2.4 msec or 5.8% (range 1.0 to 4.0 msec). In ten animals experiments were performed to determine if sympathetic stimulation altered the time sequence of epicardial activation. Electrograms were recorded from multiple positions on the surface of the ventricles and local activation was timed in relation to a fixed reference electrode. An attempt was made in each experiment to place the recording contacts at positions depolarized early, intermediate, and late in the normal course of epicardial excitation. Stellate ganglion stimulation had no major or consistent influence on the sequence of epicardial activation. One such experiment is presented in figure 5. At eight of the nine recording positions, stellate stimulation had no measurable effect while at one position the interval decreased by 1.1 msec.

In eight other animals the heart was paced from the right ventricle and electrograms recorded from several sets of paired contacts at fixed distances from the pacing site.

### TABLE 1

<table>
<thead>
<tr>
<th>Intervals (msec)</th>
<th>A-H (52)</th>
<th>H-P (31)</th>
<th>PM-S (25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>62.4 ± 2.6</td>
<td>29.5 ± 1.1</td>
<td>41.1 ± 1.4</td>
</tr>
<tr>
<td>Stellate</td>
<td>31.3 ± 0.9</td>
<td>28.8 ± 1.2</td>
<td>38.7 ± 1.4</td>
</tr>
<tr>
<td>Change %</td>
<td>-49.8 ± 2.0</td>
<td>-2.4 ± 0.1</td>
<td>-5.8 ± 0.2</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

The number of observations in each group is indicated in parenthesis beside each interval. The mean and standard error are given for each interval during control periods, during stellate stimulation and for the change resulting from stellate stimulation. The per cent change refers to the change of the means. The significance of the changes are indicated by the P values. Msec = milliseconds.
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EPICARDIAL ACTIVATION

FIGURE 5
The effect of stellate stimulation on epicardial activation. Earliest recorded activity was used as reference. Intervals between reference and recording points are given in msec. Control measurements are above and stellate measurements below the line. RV = right ventricle, LV = left ventricle. Heart rate = 188. Left stellate stimulation 8 volts, 6/sec.

Discussion

Considerable interest has been focused on the functional characteristics of the A-V node which account for delay of impulse transmission from atrium to ventricle. Hoffmann and Cranefield 17, 18 reviewed their own work 17, 18 as well as the observations of other investigators.10, 20 They concluded that the normal atrioventricular delay results from slow conduction through a narrow zone at the atrial margin of the node. Intracellular recordings from that zone reveal low resting membrane potentials and action potentials characterized by low amplitude, slow rate of rise and notches or slurs on the upstroke.4 These features of the action potential are thought to be responsible for diminished conduction velocity.21

Matsuda et al.21 have shown that adrenaline increases the resting potential of A-V nodal fibers, diminishes slurs on the upstroke and increases the amplitude and rate of rise of the action potential. These changes would be expected to result in enhanced conduction. In this study the interval between atrial activity and potentials recorded from His bundle reflected predominantly conduction time through the A-V node.22 The A-H interval shortened an average of 50% with sympathetic stimulation. This finding is consonant with previous reports which showed that intravenously administered catecholamines enhance conduction through the A-V node,17, 18 and with the observation that stellate stimulation shortens the P-R interval of the electrocardiogram23 as well as the interval between atrial and ventricular systole.24

The normal pattern of ventricular excitation has been studied extensively by Scher and his associates.25-27 According to their observations activity is recorded from the region of the right anterior papillary mus-

FIGURE 6
Time-distance plot during right ventricular pace. Conduction time from stimulus to each recording contact is plotted on horizontal axis in msec. Distance from stimulus to each recording contact is plotted on vertical axis in mm. Solid circles = control. Open circles equal stellate stimulation. dD/dt equal slope of time-distance plot. Stellate stimulation 8 volts, 6/sec. Heart rate = 173.
cle within the first 5 to 10 msec of ventricular activation. The latest region of the heart to be activated is the basal interventricular septum. In this study potentials were recorded from the right papillary muscle and the basal septum and the PM-S interval was considered an index of changes in total ventricular activation time. This interval averaged 41.1 msec during control observations and shortened by 2.4 msec or 6% during stellate ganglion stimulation. These data suggest that sympathetic stimulation produces a small, but consistent decrease of ventricular activation time and support the conclusions of previous authors who have noted that the duration of the QRS complex of the electrocardiogram may decrease slightly with catecholamine infusions or stellate ganglion stimulation.

The interval between His activity (H) and the Purkinje spike (p) at the base of the papillary muscle, reflected conduction velocity in the segment of specialized tissue between the recording points. The H-P interval did not change in 30% of the stellate stimulations and the average decrease was only 0.7 msec or 2%. This finding does not exclude the possibility that conduction may have increased in more peripheral Purkinje tissue or in junctional zones between Purkinje tissue and ventricular muscle.

Impulse transmission in ventricular muscle was studied by a technique similar to that described by Moe and Mendez and later modified by Swain and Weidner. Time-distance plots on the epicardial surface of the right ventricle described a straight line for 15 to 30 mm from the point of stimulation. The average slope of this line was 490 mm/sec, a value consistent with previous estimates of conduction velocity in muscle. The slope of time-distance plots varied considerably between animals. This variation was not surprising since it was not possible to be certain of the orientation of the electrode relative to the longitudinal axis of fibers and since conduction velocity parallel to fiber orientation may be as much as ten times greater than that perpendicular to the fibers. In any given animal, however, the slope of the time-distance plot increased during stellate stimulation; the average increase was 8%. This finding indicates that sympathetic stimulation enhances conduction velocity in ventricular muscle.

Conduction velocity appears to be related to the amplitude and rate of rise of the cardiac action potential, and it is currently thought that amplitude and rate of rise are determined by the resting membrane potential. Hyashi and Azuma reported that adrenalin increases both the resting potential and amplitude of the action potential in toad ventricular fibers. However, others have not observed this effect in warm-blooded species. Trautwein and Schmidt showed that adrenalin increases both the amplitude and rate of rise of the action potential only if the resting potential also increases. These authors demonstrated that adrenalin does not influence either the rate of rise or amplitude if the resting potential is clamped at a constant level. It appears from these in vitro studies that for adrenalin to exert an influence on those properties of the fiber which are related to conduction velocity, it must alter the resting membrane potential.

The observation that stellate ganglion stimulation enhanced conduction in muscle suggests that sympathetic stimulation increased resting membrane potential. Such an interpretation implies that under the conditions of the experiment, some or all fibers were not at maximal resting membrane potential during the control period.

The earliest points of epicardial activation were consistently recorded from the anterior right ventricle, near the apex and adjacent to the septum. Activation then spread in a direction from apex to base (fig. 5). The general pattern and time sequence of epicardial excitation were not altered by cardiac sympathetic nerve stimulation. If it is assumed, as seems likely, that the pattern of epicardial excitation is determined primarily by the manner of Purkinje activation of the subendocardium, then it is not surprising that sympathetic stimulation failed to alter the sequence of epicardial activity.

These experiments have shown that stimulation of the cardiac sympathetic nerves...
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reduces markedly atrioventricular transmission time. In contrast to its effect on the A-V node, sympathetic stimulation produces little alteration of conduction in the specialized Purkinje system or in the general pattern or sequence of epicardial activation of the ventricles. Conduction velocity in muscle appears to be enhanced slightly which may account for the 2 to 3 msec decrease of total ventricular activation time. These observations do not indicate that stellate ganglion stimulation produces major changes of ventricular excitation. If changes in the synchrony of ventricular contraction occur as a result of sympathetically stimulation, they do not appear to be the consequence of altered activation.

Summary

The influence of cardiac sympathetic nerve stimulation on certain aspects of ventricular excitation was examined in dogs at constant heart rate. Bipolar electrodes were used to record electrical activity from atrium, His bundle, right Purkinje papillary muscle junction, basal interventricular septum and the epicardial surface of the ventricles. Stimulation of the left stellate ganglion reduced markedly the A-V nodal delay, but produced little or no change of conduction velocity in the Purkinje system or in the pattern of epicardial depolarization. Conduction in muscle was enhanced slightly by stellate stimulation and appears to account for the observed decrease of 2 to 3 msec in ventricular activation time. These data indicate that cardiac sympathetic nerve stimulation does not result in major changes in the sequence of ventricular excitation.

Acknowledgment

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