Dromotropic Effects of Stellate Stimulation on the AV Node and Internodal Pathways[1] (37379)

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There are few data in the literature on the differential dromotropic influences of right and left stellate ganglion stimulation. Fogelson (1) observed (1929) that stimulation of the right accelerans nerve had minimal effect on A–V interval, but stimulation of the left accelerans nerve shortened it by 30–40 msec. Irisawa, Caldwell and Wilson (2) also concluded that the left stellate ganglion had a greater positive dromotropic effect. Unfortunately, the variability of their data (reported from only four dogs) makes this conclusion tenuous. Wallace and Sarnoff (3) in studying the effects of stimulation of the left stellate ganglion observed that the A–H subinterval was shortened by 50%. In view of the potential importance of neural influences upon excitability and conductivity phenomena, the present experiments were undertaken to investigate the absolute as well as comparative dromotropic influences of the right and left sympathetics on conduction along the crista terminalis and across the AV node of the intact, *in situ* canine heart. Measurements were made of conduction time between fixed points along the posterior and middle internodal pathways from SA to AV node, from inferior right atrium to His bundle (a–h interval), and from His bundle to superior portion of the interventricular septum (h–v interval) during right and left stellate ganglion stimulation.

Methods. Fourteen dogs, anesthetized with Sernylan (phencyclidine HCl; 2.0 mg/kg) and alpha-chloralose (80 mg/kg), ventilated by positive pressure and room air, were placed on total cardiopulmonary bypass following bilateral thoracotomy at the fourth interspace. Bipolar plaque electrodes with silver pickup points 1.0–1.5 mm apart were used to record localized activation at points along the crista terminalis and over the band of tissue between the coronary sinus and AV ring (see Fig. 1) which anatomically correspond to the posterior internodal pathway and a segment of the middle internodal pathway (4–6). One electrode was sutured over the cranial portion of the crista approximately at the caudal pole of the sinus node (CT_S); a second across the crista at the level of the limbus of the fossa ovalis (CT_L); and a third over the band of tissue between the coronary sinus and AV ring (PIN). The sutures were placed parallel to the crista and to the general fiber orientation. Thus, conduction along both the middle and posterior internodal pathways can be assessed by comparing the conduction time before and during stellate stimulation between the CT_S and CT_L sites which in turn can be compared to conduction over the segment of tissue between the electrodes CT_S and PIN which corresponds to a segment of the posterior internodal pathway.

Additional electrodes were sutured epicardially on the lateral surface of the right atrial appendage (RA) away from known specialized conductile tissue, and over the SA node (SA) for pacing.

For recording activation across the AV node, a His electrode of the Hoffman-type was utilized (HIS). The electrode was placed at the inferior-medial portion of the right atrium in tissue overlying the AV node and His bundle. Thus, the "a" component of the His bundle electrogram corresponds to the activation of atrial tissue overlying or

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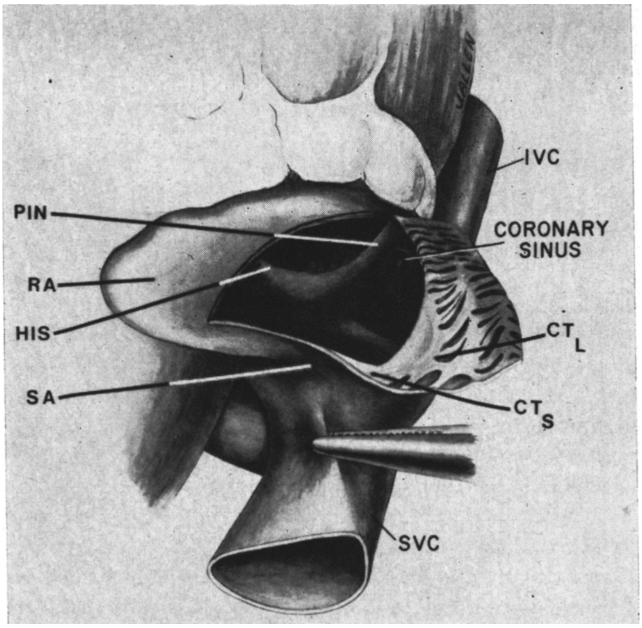

FIG. 1. A superior-lateral view of the heart illustrating the placement of the electrodes along the crista terminalis, over the posterior internodal pathway at the segment of tissue between the coronary sinus and AV ring, and over the His bundle. CT_S = the electrode site over the crista terminalis at the caudal pole of the sinus node. CT_L = site of the electrode over the crista at the level of the limbus of the fossa ovalis. PIN = electrode over the posterior internodal pathway as it passes through the segment of atrial tissue between the coronary sinus and AV ring. HIS = site of placement of the Hoffman-type electrode for recording the His bundle electrogram.

adjacent to the AV node and the His bundle, and the "h" component represents activation of the His bundle. The time interval between these two components (a–h subinterval) represents an approximation of the AV nodal conduction time (7, 8).

The cervical vagi and stellate ganglia were decentralized to minimize reflex compensations during stellate ganglion stimulation. A Grass SD 5 stimulator was used for supramaximal stimulation of both right and left stellates using parameters of 10 Hz, 10 msec duration, and 5–7 V.

Individual electrograms were amplified using Grass P-511 amplifiers whose half-amplitude filters were set at 35 Hz for high pass and 10 kHz for low pass. With these filters there was a flat frequency response from approximately 200 Hz to 1 kHz. The outputs from the amplifiers were connected to the input of a Precision Instrument Model 6100 tape recorder operated in the direct mode. For analysis, the electrograms were played back through a Tektronics 565 oscilloscope and photographed with a Grass C4N kymographic camera at 500 mm/sec. However, the recordings chosen for figures were photographed on Polaroid film from the oscilloscope at 20 msec/div. Using playback at 500 mm/sec, conduction time could be accurately measured to 1.0 msec.

Conduction time, rather than absolute conduction velocity, was utilized in determining the influence of the right and left stellate ganglia on conduction along the crista terminalis. The absolute conduction velocity was not used because of uncertainty in accurately measuring distances between each pair of electrodes, particularly between the electrode at the level of the limbus (CT_L) and the one between the coronary sinus and AV ring (PIN). The conduction time (msec) from the electrode at the caudal pole of the sinus node (CT_S) to that over the crista at the level of the limbus (CT_L) and that from the CT_L to the electrode be-

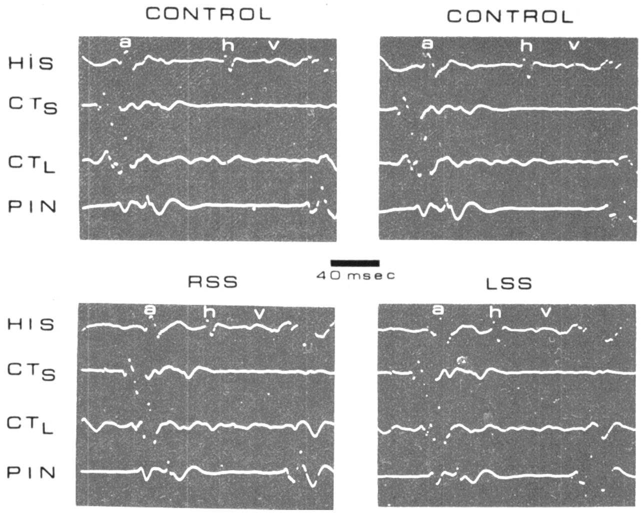

FIG. 2. An example of the control pulses and responses to stimulation of the right (RSS) and left stellate ganglion (LSS) with stimulation parameters of 10 Hz, 5 msec duration, and 5 V. (top) The respective control beats; (bottom) the responses to stellate stimulation. (HIS) His bundle electrogram (a) atrial component of His electrogram, (h) activation of the His bundle, and (v) activation of the ventricular septum. (CT$_S$) electrogram recorded from the crista terminalis at the caudal pole of the sinus node; (CT$_L$) electrogram from the crista terminalis at the level of the limbus of the fossa ovalis; (PIN) activation of the posterior internodal pathway as it passes between the coronary sinus and AV ring. The length of the bar equals a time interval of 40 msec.

tween the coronary sinus and AV ring (PIN) were compared before and during right and left stellate ganglion stimulation. Measurements were made from comparable components in the control and stimulation electrograms.

Results. Figure 2 shows the effect of stellate stimulation on conduction time along the crista terminalis as well as across the AV node itself, with pacing from the SA node at 300/min. The top portion of the figure shows the control activation for stellate stimulation while the bottom portion shows the corresponding responses to right (RSS) and left (LSS) stimulation. During the control period prior to RSS, the activation spread from CT$_S$–CT$_L$–PIN, thence across the node to the His bundle. The time interval between CT$_S$–CT$_L$ was 4 msec and that between CT$_L$–PIN 14 msec. The a–h subinterval was 80 msec. and H–V 34 msec. With stimulation of the right stellate (RSS) the time intervals between activation of the electrodes along the crista terminalis were unchanged. However, the a–h subinterval was shortened to 47 msec with the h–V subinterval remaining unchanged. Prior to stimulation of the left stellate ganglion, the time interval between activation at the CT$_S$ and CT$_L$ electrodes was 2 msec, and 12 msec for the interval between activation of the CT$_L$ and PIN sites. Left stellate stimulation (LSS) did not alter conduction time between the internodal pathway recording sites, while the a–h subinterval was shortened from 80 to 44 msec. Thus, using changes in the a–h subinterval as an index of AV nodal conduction time, left stellate stimulation had a greater dromotropic influence on the AV node than did the right stellate. In the absence of any dromotropic effect on the crista terminalis, it is concluded that there is no differential effect on conduction along the middle and posterior internodal pathways.

The dromotropic influence along the crista terminalis under paced conditions with stellate stimulation is summarized in Table I. The mean differences in conduction time between electrode sites are expressed in milliseconds. Independent of pacing site, right and left stellate stimulation had no effect

TABLE I. Summarizes the Effect of Right (RSS) and Left (LSS) Stellate Ganglion Stimulations on Conduction Along the Crista Terminalis and Posterior Internodal Pathway.[a]

	Mean differences in conduction times with sympathetic stimulation			
	RSS (msec ± SE)	Significance	LSS (msec ± SE)	Significance
		Pace SA ($N = 13$)		
$\mathrm{CT_S}$–$\mathrm{CT_L}$	−0.08 ± 0.04	NS	−0.08 ± 0.04	NS
$\mathrm{CT_L}$–PIN	0	NS	0	NS
		Pace RA ($N = 12$)		
$\mathrm{CT_S}$–$\mathrm{CT_L}$	0	NS	−0.09 ± 0.09	NS
$\mathrm{CT_L}$–PIN	−0.09 ± 0.09	NS	0	NS

[a] The values are the mean difference, ±SE, from control in conduction time observed in 14 dogs with pacing from the sinus node (SA) and right atrial appendage (RA). N = the number of observations from each pacing site. $\mathrm{CT_S}$–$\mathrm{CT_L}$ = activation of the segment of the crista terminalis from the caudal pole of the sinus node to the level of the limbus of the fossa ovalis. $\mathrm{CT_L}$–PIN = the interval between activation of the electrode on the crista at the level of the limbus and that over the distal segment of the posterior inter–nodal pathway (PIN).

on conduction time between sites on the middle and posterior internodal pathways. Similarly, norepinephrine (0.5 μg/kg) failed to change conduction times along the crista terminalis (data not included in table).

In comparison, the influence of supramaximal right and left stellate stimulations on AV nodal conduction expressed in terms of changes in a–h subinterval is shown in Table II. LSS shortened the a–h subinterval by 35% in the unpaced preparation while RSS shortened this subinterval by only 9%. During pacing from either the sinus node or right atrial appendage, a 27% decrease in conduction time across the AV node was observed with LSS while the decrease was 17% during RSS. The differences in effect of LSS and RSS on AV nodal conduction were highly significant ($p < 0.001$).

There was no significant influence of either right or left stellate ganglion stimulation upon the duration of the h–v interval of the His electrogram. RSS shortened the h–v interval from 56 ± 4.2 (SE) to 55 ± 4.2 msec and LSS changed this subinterval from 54 ± 5.0 to 51 ± 5.0 msec. None of these changes were statistically significant. Therefore, while there was a significant positive dromotropic influence of both right and left sympathetic stimulation upon conduction from the inferior portion of the right atrium to the His bundle, no such effect was observed on conduction from the His bundle to the upper portion of the interventricular

TABLE II. Compares the Effects of Right and Left Stellate Ganglion Stimulation on AV Nodal Conduction Indicated by a Decrease in the a–h Subinterval of the His Bundle Electrogram.[a]

Unpaced					Paced				
N	Control (msec)	LSS (msec)	Change (msec)	% Change	N	Control (msec)	LSS (msec)	Change (msec)	% Change
9	77	50	−27 ± 10.2	−35	26	70	58	−21 ± 4.0	−27
		RSS					RSS		
13	65	59	−6 ± 3.9	−9	23	76	63	−13 ± 3.12	−17

[a] The left portion of the table gives the mean, ± SE, a–h subintervals for the respective controls and stimulations in the unpaced preparation, while the right gives the corresponding values with pacing. The results of pacing from the sinus node and right atrial appendage are combined. N = the number of observations.

septum.

Discussion. Since an increase in heart rate can itself result in lengthening of the AV nodal conduction interval, the differential dromotropic influence of sympathetic stimulation should be studied under paced conditions (7, 8). Also, non-nodal supraventricular pacemaker shifts accompanying stellate stimulation produce changes in atrial activation and possible activation patterns at the AV node (9, 10). Thus, in ascertaining the influence of sympathetic stimulation on conductive time along the crista terminalis, the pacemaker site must be known so that a pacemaker shift producing a change in the activation pattern of the atrium does not appear as a change in conduction time. Since no differences appeared in the data resulting from the two pacing sites (SA node or RA appendage) the results are combined in Table II.

The lack of significant change in conduction time along segments of the middle and posterior internodal pathways agrees with results reported from atrial muscle by Hoffman and Cranefield (11). They and others (12–15) concluded that in those experiments in which a change in conduction velocity occurred, the effect was secondary to changes in extracellular potassium. The possibility of changes in atrial conduction velocity reported during sympathetic stimulation was based on the shortened duration of the P wave of the ECG (16). However, P wave duration is now recognized to be a poor criterion, since pacemaker shifts, either within the sinus node or to other non-nodal supraventricular sites, have an important affect on P wave morphology (9, 17, 18).

Comparison of conduction velocity of specialized atrial tissue with nonspecialized tissue has shown that atrial propagation is not uniform. In the mapping studies of Spach *et al.* (19, 20) and Goodman, Van Der Steen and Van Dam (21), conduction velocities were higher in regions corresponding to Bachmann's bundle and the crista terminalis (anterior, middle, and posterior internodal pathways of James) than in surrounding tissue. Holsinger, Wallace and Sealy (22) also found conduction velocity along the middle and posterior internodal pathways to be between 0.8 and 0.9 m/sec, compared to 0.2 to 0.4 m/sec in atrial muscle. Wagner *et al.* (23) noted that conduction velocity over Bachmann's bundle was higher (0.9–1.9 m/sec) than in adjacent tissue in the left atrium (0.4–0.5 m/sec). Others have implied that sympathetic stimulation has a positive dromotropic effect on ventricular Purkinje fibers producing an increase in ventricular synchrony or decrease in ventricular temporal dispersion (16, 24–26). The present experiments demonstrate that stellate stimulation has no dromotropic influence on the middle and posterior internodal pathways other than the indirect effect associated with pacemaker shifts.

The differential dromotropic effects of right and left stellate ganglion stimulation presumably represent variations in the functional distribution of sympathetic nerves to the region of the AV node. Thus, the greater influence of the left sympathetics upon the a–h interval may be interpreted to indicate that more fibers are distributed to the upper portions of the AV node than from the right. Similar reasoning has been applied to the greater chronotropic action of the right sympathetics with resultant inference that the SA node receives its predominant supply from the right side. It is also of interest that the left sympathetics generally have greater inotropic influences, particularly with respect to the left ventricle and to the augmentation in systemic arterial pressure responses (27), thus suggesting a primarily ipsilateral distribution of nerves from the sympathetic system. There is some indication this relative distribution pattern is not applicable to the sympathetic components of the cervical vagosympathetic trunks (28). Failure of either right or left sympathetic stimulation to significantly change the H–V interval must be interpreted to indicate a paucity of nerve endings in or immediately around the His bundle–major bundle branch complex. This observation is in agreement with those of Wallace and Sarnoff (3) who found only minor sympathetic influences upon conduction velocity along the Purkinje system to the base of the right papillary muscles. Hoffman and Cranefield (11) were also unable to detect important neural influences upon the ventricular conductile system. However, Alanis *et al.* (7, 8) reported a 13% shortening in h–v interval as a result of infusion of exogenous norepinephrine in the isolated, paced canine heart preparation.

Summary. The dromotropic effects of supramaximal stimulation of the right (RSS) and left (LSS) stellate ganglia on segments of the middle (MIN) and posterior (PIN) internodal pathways of James and across the AV node were studied in the anesthetized, open chest dog maintained on cardiopulmonary bypass. Contiguous bipolar electrodes were sutured over the sinus node and on the lateral surface of the right atrial appendage for pacing, and at three points along the MIN and PIN for measuring conduction time. One electrode was placed over the crista terminalis at the caudal pole of the SA node; a second across the crista at the level of the limbus of the fossa ovalis; and a third bipolar electrode over the PIN as it courses between the coronary sinus and AV ring. Conduction time through the AV node was assessed by alterations in the a–h subinterval of the His electrogram which was recorded with a Hoffman-type electrode sutured over the His bundle. With pacing from either the sinus node or lateral surface of the right atrial appendage at rates sufficient to maintain capture, no significant change in conduction time along segments of the MIN or PIN were observed during either RSS or LSS, or following injections of 0.5 μg/kg NE. Significant differences in the effects of RSS and LSS on conduction through the AV node were noted. Expressed in terms of percentage change from the control a–h subinterval, LSS shortened this interval 27% while RSS shortened it by only 17% ($p < 0.001$). However, there was no significant dromotropic influence of either right or left stellate ganglion stimulation on the h–v subinterval.

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