Functional Distribution of Right and Left Stellate Innervation to the Ventricles:

PRODUCTION OF NEUROGENIC ELECTROCARDIOGRAPHIC CHANGES BY UNILATERAL ALTERATION OF SYMPATHETIC TONE

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■ Electrical stimulation of a variety of sites in the central nervous system of cats, dogs, and monkeys has been shown to produce electrocardiographic changes.[1-6] Clinical observations of patients with central nervous system lesions also suggest that the nervous system may play a role in the production of electrocardiographic changes in man.[8-16]

Electrocardiographic findings ranging from changes in ST-T wave form to a variety of cardiac dysrhythmias have been produced by the stimulation of many brain stem areas and some cortical areas in laboratory animals. Experiments by Manning and Cotton[1] have demonstrated that ectopic beats and idioventricular rhythms could be produced following electrical stimulation of the midbrain reticular formation and posterior hypothalamus of the cat. These dysrhythmias were abolished by bilateral vagotomy, vagal cooling, and cholingeric blocking agents, as well as following bilateral stellate ganglionectomy. Ueda et al.[2] produced changes in cardiac rate and rhythm by electrical stimulation of numerous areas throughout the midbrain and the diencephalon of the dog. "Ischemic-like" changes and dysrhythmias following stimulation of the hypothalamus in cats have been reported by Meville et al.[3] Korteweg et al.[4] reported from studies on cats that hypothalamic induced electrocardiographic changes, consisting of ectopic beats, idioventricular rhythms, and nonspecific changes of ST-T wave form, were abolished by cordotomy at the level of the second cervical spinal segment. Delgado,[5] using chronic monkey preparations, found rhinencephalic areas in which stimulation produced atrial and ventricular ectopic beats and other cardiac dysrhythmias.

In our laboratory, it has been demonstrated previously that electrical stimulation of the hippocampus in cats produced irregular idioventricular rhythms as well as nonspecific ST-T wave form changes.[7] It was considered likely that these electrocardiographic changes were the result of increased sympathetic activity acting on the ventricles. The appearance of form changes in the ST segment and T wave following hippocampal stimulation was independent of the level of vagal tone, but vagal activity was essential for the appearance of an idioventricular rhythm in those experiments where vagal slowing of the supraventricular rate was necessary to unmask a slower idioventricular rate.

Accumulating clinical evidence indicates that patients with central nervous system disease may have abnormal electrocardiograms in the absence of demonstrable heart disease.[9-13] The most common abnormalities are nonspecific ST-T wave form changes, but occasionally multiple premature beats and idioventricular rhythms are seen. One of the more characteristic ECG disturbances, seen in patients with cerebral vascular disease, consists of a prolongation of the Q-T interval, or an apparent

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Q-T interval prolongation resulting from a wide T-U fusion wave. Attempts have been made to correlate these changes with electrolyte abnormalities[9, 11] and subendocardial ischemia.[16] Similar changes have been observed acutely during neurosurgical procedures.[17] Our experimental laboratory data, as well as the studies of others, suggest that change in sympathetic tone is a likely primary factor in the production of neurogenic electrocardiographic form changes.

The purpose of the present study was to attempt to produce, in the dog, electrocardiographic changes similar to those reported in clinical studies of patients with central nervous system disease. Unilateral and bilateral stellate ganglion stimulation and ganglionectomy were performed in a series of experiments, and it was found possible to reproduce, in the dog, electrocardiographic changes similar to those reported in man. Furthermore, following these procedures, changes in the functional refractory periods of ventricular myocardium were recorded and could be correlated with the electrocardiographic form changes.

Methods

Healthy mongrel dogs of both sexes, weighing 10 to 15 kg were anesthetized by intravenous administration of thiopental (20 to 25 mg/kg) followed by sodium barbital (180 mg/kg). Under artificial respiration the chest wall was opened along the midsternal line and retracted to permit wide exposure of the heart. Bipolar stimulating electrodes were placed on the right atrial appendage so that the heart could be driven at fixed rates. In all experiments an electrocardiogram from a longitudinal lead was recorded by means of subcutaneous stainless steel needle electrodes placed in the neck and left hindlimb. Transverse leads between the right and left chest walls and between the forelegs as well as anteroposterior leads were employed in a few experiments but showed less striking changes in the open chest preparations employed in this study. Recordings were made with a Grass 5P polygraph.

The stellate ganglia were exposed beneath the parietal pleura between the first and second ribs posteriorly. Stellate ganglionectomy was accomplished by cutting the rami communicantes and the ansa subclavia of the respective stellate ganglia. Stimulation of the stellate ganglia was accomplished by stimulating the intact ganglia or the distal ends of the cut ansa subclavia, by means of insulated electrodes connected to a Grass S4B stimulator. A 3- to 30-second train of repetitive rectangular pulses of 1.5 msec duration, at an amplitude of 10 to 20 volts and at a frequency of 10 to 20 stimuli per second was used routinely for stimulating the stellate ganglia.

MEASUREMENT OF FUNCTIONAL REFRACTORY PERIODS

The instrumentation for measurement of functional refractory periods is illustrated in figure

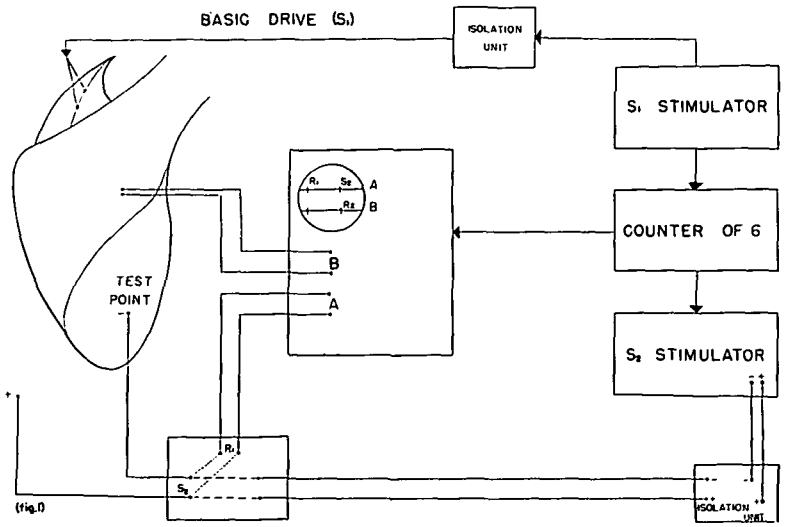

FIGURE 1

Diagram of instrumentation for measurement of the functional refractory period. See text for explanation.

1. The heart was driven at a constant rate from bipolar electrodes on the right atrial appendage connected through a stimulus isolation unit to a Grass S4 stimulator. The driving stimulus was called the basic drive (S1). To measure the functional refractory period (FRP) at an elected point on the epicardial surface, a unipolar electrode of nichrome wire, 200 micra in diameter, was secured to the epicardial surface. This test electrode was used to record the time of activation following a basic driving stimulus. The response to the basic drive at the test electrode was the R1 response, and was recorded on one channel (A) of a dual beam Tektronix 535 oscilloscope. The basic drive stimulator triggered a scale-of-six counter which, in turn, triggered the oscilloscope, such that every sixth R1 response could be aligned accurately with the left vertical axis of the oscilloscope scale. The scale-of-six counter also triggered a second Grass S4 stimulator to deliver a test stimulus (S2) to the test electrode on the epicardium at a variable delay after every sixth S1 stimulus. If the test stimulus did not fall within the refractory period of the preceding R1 response a premature ventricular response was elicited at the test site and was propagated to a pair of reference bipolar electrodes attached at some point distant from the R1-S2 test site. The response occurring at the reference electrodes was displayed on a second channel (B) of the oscilloscope. The stimulus artifact (S2) was also seen on channel A. By adjusting a variable delay, the S2 stimulus could be moved closer and closer to the preceding beat (R1) until the time when it first failed to elicit a propagated premature beat as indicated by the absence of a recorded response at the reference electrode site. This R1-S2 interval was defined as the FRP and could be measured directly from the oscilloscope scale. Estimates of the FRP were made using stimulus intensities of greater than three times diastolic threshold. After measurement of the R1-S2 interval the test electrode was switched to its recording electrode mode to insure constancy of position of the R1 response at the left vertical axis of the oscilloscope scale.

In some animals endocardial refractory periods were measured, using nichrome hook electrodes which were sleeved in fine polyethylene tubing except at the tip. This insured complete insulation throughout the thickness of the myocardium. The electrode with its sleeving was encased within an 18 gauge needle which was used to penetrate the wall of the ventricle. Once the electrode was hooked into the endocardial surface the needle was removed, leaving the electrode in place.

Results

I. ELECTROCARDIOGRAPHIC CHANGES FOLLOWING STELLATE GANGLIONECTOMY

The electrocardiographic form changes following stellate ganglionectomy are illustrated in figure 2. In most animals there was a de-

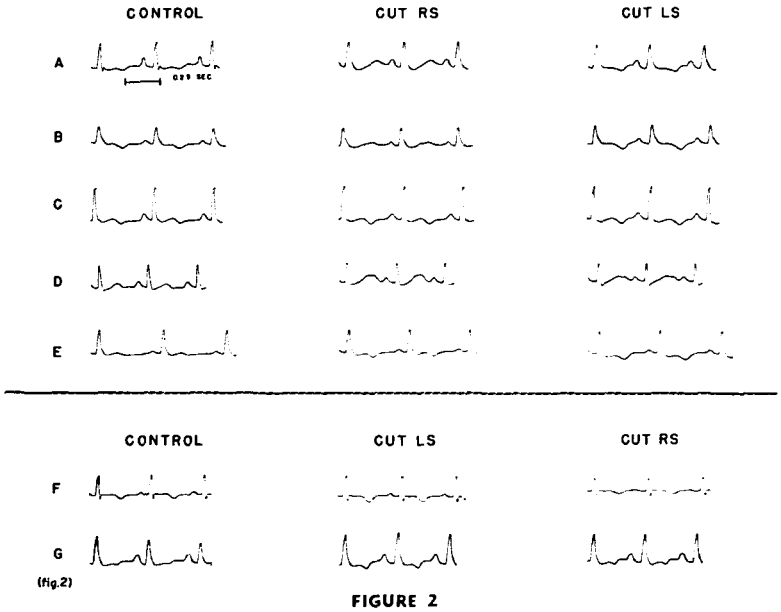

FIGURE 2

Electrocardiographic changes following stellate ganglionectomy. Records labeled A-E are from animals in which the right stellate ganglion (RS) was removed prior to removal of the left stellate ganglion (LS). Records labeled F and G are from animals in which the left stellate ganglion was removed prior to removal of the right stellate. Time line is 0.25 second.

crease in rate following ganglionectomy. To eliminate any possible form change resulting from rate change alone, the hearts were routinely driven at fixed rates from bipolar stimulating electrodes placed on the right atrial appendage.

Records A-E in figure 2 are five examples of results from twelve preparations in which the right stellate ganglion (RS) was removed prior to removing the left stellate ganglion (LS). Electrocardiographic changes, consisting of T-wave alterations and prolongations of the Q-T interval, appeared in 1 to 15 minutes following RS section. Once a form change appeared, it persisted for the duration of the experiment or until the experimental situation was altered. In figure 2 the initial T waves were negative in experiments A and B. Cutting RS reversed the polarity of the T waves and prolonged the Q-T intervals. Record C shows an initial biphasic T wave which did not change following RS section, but the Q-T interval was prolonged by 30 msec. Only the terminal phase of the T wave was altered in D, resulting in a prolongation of the T wave or a possible T-U fusion wave. In E the terminal phase of the T wave inverted in association with a prolongation of the Q-T interval.

Thirty to sixty minutes after removing RS, the left stellate (LS) ganglion was removed. Very often the form of the electrocardiogram changed in a direction toward the control situation. Thus, in experiments A and B, following LS removal, the T waves changed from positive to negative, approximating the form of the control tracing. It is to be noted, however, that there was no further significant change in the Q-T interval. In E the T wave remained negative with no change in Q-T duration. In passing, it may be noted that the P-R intervals often increased following stellate ganglionectomy, indicating prolonged A-V conduction time. The prolongation was usually more marked following LS removal than following RS removal. However, this parameter was not subject to special study in our experiments.

Records F and G are two examples of results from six experiments in which LS removal preceded RS removal. In these experiments the initial T waves increased their negativity when the left stellate was removed. Following subsequent RS removal the T waves returned to their control form. The Q-T intervals remained unchanged, or increased only slightly.

Figure 3 illustrates the change in the Q-T interval following stellate ganglionectomy. To measure Q-T intervals a polygraph paper speed of 100 millimeters per second was routinely employed. Q-T intervals were measured with calipers; the end of the T wave was taken as the point of return to the isoelectric line. Although errors are inherent in this method of measurement, the Q-T interval changes in most experiments were of sufficient magnitude to exceed such errors satisfactorily. Experiments numbered 1 to 12 in figure 3 represent twelve different animals in which the right stellate ganglia were removed. In these animals there was always a prolongation in Q-T interval ranging from 20 to 70 msec. Experiments 13 to 18 illustrate the results from animals in which the left stellate ganglia were removed. In these experiments changes in Q-T duration were slight.

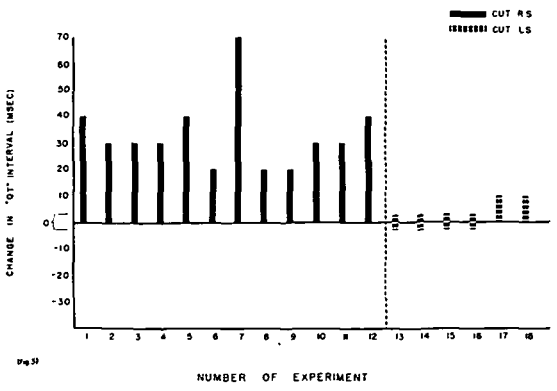

FIGURE 3

Q-T interval prolongations on anterior ventricular surface following stellate ganglionectomy. Experiments labeled 1-12 on the abscissa illustrate the change in Q-T intervals (solid bars) following right stellate ganglionectomy in 12 animals. Experiments labeled 13-18 illustrate the change in Q-T intervals (hatched bars) following left stellate ganglionectomy. Ordinates are changes in Q-T intervals in milliseconds; + values represent increase over control.

II. ELECTROCARDIOGRAPHIC CHANGES FOLLOWING STELLATE STIMULATION

Since the data presented above demonstrate that the ST-T wave form changes differed for right and left stellate ganglionectomies, the electrocardiographic form changes following unilateral stellate stimulation were studied. Figure 4 illustrates these changes after stellate stimulation, as described under Methods. Although changes in electrocardiographic wave form occurred during stimulation, particularly when continued beyond a ten-second period, the presence of shock artifact frequently made analysis of wave form difficult. Therefore, the induced changes which persisted consistently after the period of stimulation were studied during the poststimulation period. In 46 animals left stellate stimulation produced changes like those demonstrated in examples A-C. Left stellate stimulation often caused a brief period of A-V nodal tachycardia followed by a period of slowing, possibly of reflex origin. In order to maintain constant rate in these experiments, the hearts were driven at a fixed rate from the atrium. Following LS stimulation there was usually an increase in the positivity of the terminal phase on the T wave resulting in a marked increase in the area under the T wave. In most experiments RS-T segment depression occurred with LS stimulation. Q-T interval prolongations were also observed. Q-T interval prolongation varied from 10 to 90 milliseconds in different experiments with a mean change of 46 milliseconds in fifteen experiments in which this interval was measured. In 10% of the animals a brief period of T-wave inversion preceded the increased positivity of the T wave, as illustrated by example C in figure 4. The tracings returned to their control configuration one to five minutes following termination of the stimulation. These changes induced by LS stimulation were similar to the results following RS ganglionectomy.

Right stellate stimulation always resulted in a marked sinus tachycardia. For this reason it was often difficult to demonstrate T-wave changes. Thirty-seven animals were studied, and clearly demonstrable form changes appeared in 16 animals (45%). Examples of these changes are illustrated in figure 4 D-F. In these animals RS stimulation depressed the terminal portions of the T waves resulting either in T-wave inversion (D, E) or in flatten-

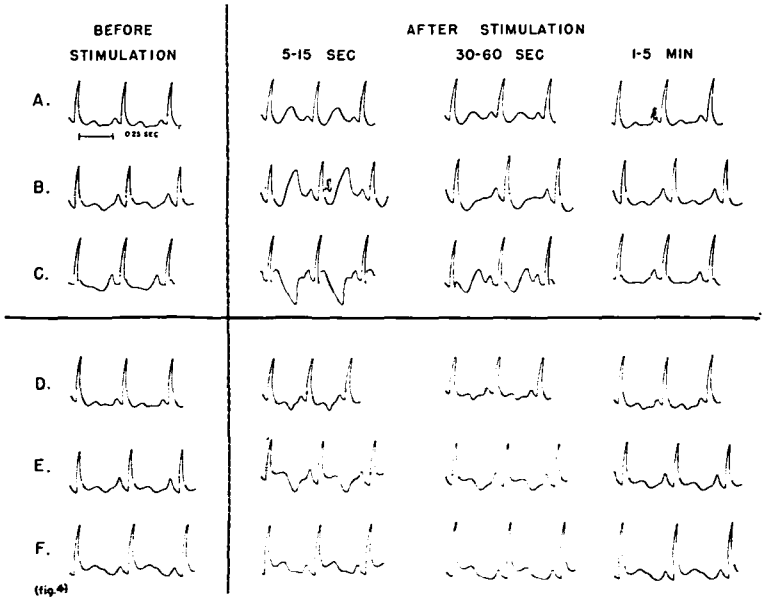

FIGURE 4

Electrocardiographic changes following stellate stimulation. Records labeled A-C illustrate the ECG changes 5 to 15 sec, 30 to 60 sec, and 1 to 5 min after left stellate stimulation. Records labeled D-F illustrate these changes following right stellate stimulation. Time line is 0.25 second.

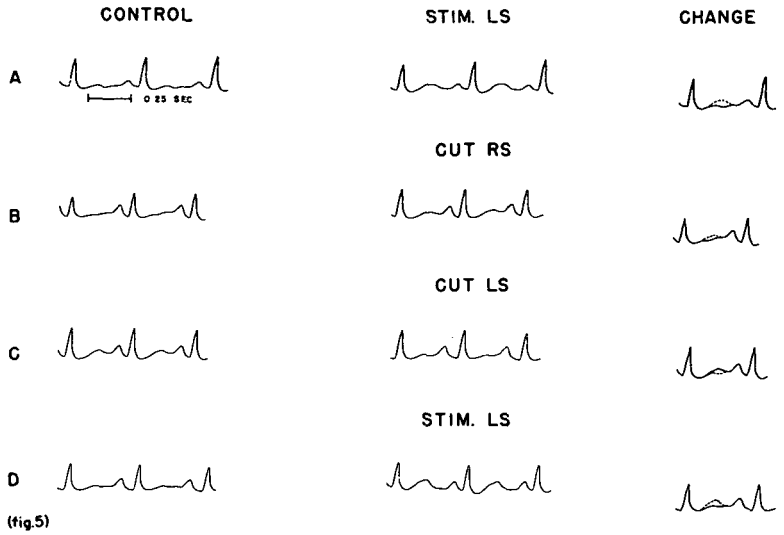

FIGURE 5

Electrocardiographic changes following stellate stimulation and stellate ganglionectomy in one animal. In A, both ganglia are intact and the left ganglion is stimulated. In B, right stellate ganglion is sectioned. In C, left stellate ganglion is sectioned. In D, the peripheral end on the cut left stellate is stimulated. The column on the right illustrates the ECG change superimposed upon the control tracing, taken prior to each procedure. See text. Time line is 0.25 second.

ing of the terminal T wave (F). RS-T segment elevation accompanied these changes. Increasing the driving frequency, in the absence of stellate stimulation, had no effect on the form of the T wave, thus eliminating rate as a factor in these changes.

A comparison of the electrocardiographic form changes produced following stellate stimulation and following stellate ganglionectomy in the same animal is shown in figure 5. Left stellate stimulation with intact ganglia produced an increase in the positivity of the T wave with Q-T prolongation, as illustrated in A. In B, right stellate ganglionectomy resulted in a similar change in the form of the T wave, with Q-T interval prolongation. Following RS ganglionectomy, LS ganglionectomy decreased T-wave area, which approached that of the control ST-T wave form, as illustrated in figure 5 C. Finally, as shown in D, stimulation of the distal end of the cut left stellate again produced an increase in the positivity of the T wave with Q-T interval prolongation. The column on the right in figure 5 indicates the various changes in the T wave superimposed upon their control tracings.

III. REFRACTORY PERIOD CHANGES FOLLOWING STELLATE GANGLIONECTOMY

The preceding data demonstrate that electrocardiographic changes consisting of Q-T interval prolongation and widely elevated T waves can result either from RS ganglionectomy with an intact left stellate, or from LS stimulation with or without an intact right stellate. That these form changes do not involve ventricular depolarization is supported by the observation that the QRS complex does not change significantly following stellate ganglionectomy or stimulation. Since the T wave is the electrocardiographic counterpart of ventricular repolarization, it was desirable to investigate the relationship between changes in sympathetic tone and changes in the duration of ventricular repolarization. To accomplish this, changes of refactory period were studied in the ventricular myocardium after stellate ganglionectomy.

In the first series of experiments the functional refractory periods (FRP) were measured only on the anterior epicardial surface of the ventricles. In these experiments 16 test electrodes were secured on the epicardial sur-

face; 8 on the right ventricle, and 8 on the left ventricle. Functional refractory periods were measured during a control period, and following right and left stellate ganglionectomy at each of the 16 test points, as described in the Methods section. The changes in functional refractory periods following the respective RS or LS ganglionectomy were plotted with respect to the location of the test electrodes on the surface of the heart.

An example of the distribution of FRP prolongations following RS ganglionectomy in one animal is illustrated in figure 6. The locations of the 16 epicardial test points are also shown. In this preparation the left stellate ganglion was still intact. The test points yielding the greatest change occurred predominantly in the left ventricle, indicating the primary area of right stellate influence on the anterior surface. In 14 similar experiments recovery from refractoriness was always most

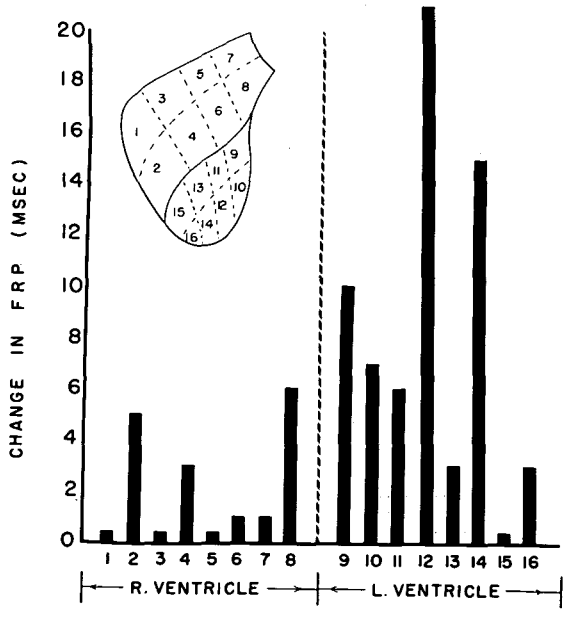

FIGURE 6

Functional refractory period (FRP) prolongations following right stellate ganglionectomy in one animal. Functional refractory period changes are plotted in msec on the ordinate for each of sixteen test sites on the abscissa. The locations of the sixteen test sites on the anterior surface of the ventricles are illustrated.

prolonged in the same general area of the myocardium. The additional changes in functional refractory period due to the subsequent LS ganglionectomy were always small on the anterior epicardial surface, indicating only slight left stellate influence on this surface of the ventricles.

A statistical analysis was done on the results of the 14 experiments, in which RS ganglionectomy was performed, using the Kendall "coefficient of concordance." The FRP prolongations following RS ganglionectomy at each of the 16 test points were ranked from 1 to 16 according to the magnitude of change. The Kendall "W" for these experiments was calculated to be 0.3, indicating the correlation, of the ranks of the 14 animals. This correlation, moreover, was found to be very significant with a probability of less than 0.001 that it occurred by chance. Since this low correlation was most likely the result of the variability in the rankings within areas of large FRP change, as well as within areas of small FRP change, three large areas were ranked from 1 to 3 according to the magnitude of the average change in each area. These areas were: (1) contiguous test points 9-13, in figure 6, representing an area of large FRP change; (2) test points 1, 7, 8, 14, representing sites of intermediate FRP change; and (3) test points 2-6, 15, 16, representing an area of small FRP change. The Kendall "W" for the new rankings in 14 experiments was calculated to be 0.8, indicating a high correlation between animals. These results suggest that the area on the anterior surface of the ventricles under the greatest right stellate influence is consistent from animal to animal and is represented by test points 9 through 13 in figure 6.

A similar series of experiments was performed on the anterior surface of the ventricles in which the left stellate ganglion was removed first, leaving the right stellate intact. Following LS ganglionectomy, in seven animals, there were only small changes in functional refractory periods on the anterior surface.

To investigate further the changes of refractory period after stellate ganglionectomy, the posterior surface of the ventricles was

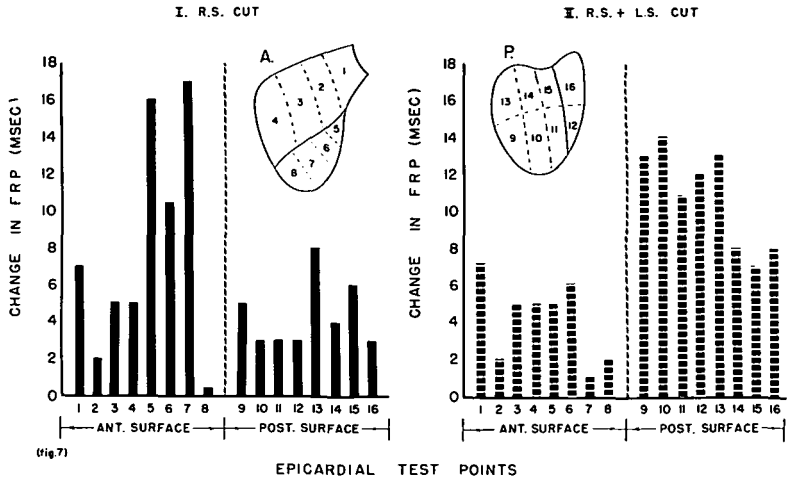

FIGURE 7

Functional refractory period (FRP) prolongations following bilateral stellate ganglionectomy. Panel I (left) illustrates FRP changes plotted on the ordinate for each of sixteen test sites on the abscissa following right stellate ganglionectomy with the left stellate intact. Panel II illustrates the additional FRP changes after the subsequent removal of the left stellate. The locations of the test sites on the anterior (A) and posterior (P) surfaces of the ventricles are shown.

studied and compared with the anterior surface. Sixteen test electrodes were secured on the surface of the epicardium, 8 on the anterior surface and 8 on the posterior surface. Functional refractory periods were measured as in the above experiments.

Figure 7 illustrates one experiment in which the anterior and posterior surfaces of the ventricles were studied. The locations of the sixteen test electrodes are also shown. In this animal the right stellate ganglion was removed first, leaving the left stellate intact. The distribution of FRP prolongations following RS ganglionectomy is illustrated in panel I. Test points 5-7 on the anterior surface of the left ventricle represent the area of greatest change, which confirms the results illustrated in figure 6. The changes on the posterior surface were small by comparison. Panel II illustrates the *additional* changes of refractory period following subsequent LS ganglionectomy. Only small changes were found on the anterior surface, as was expected. The posterior surface, however, showed a greater change, indicating that the posterior ventricular surface received the major left stellate innervation.

Figure 8 illustrates the changes of functional refractory period that followed LS ganglionectomy in another experiment in which the anterior and posterior surfaces of the ventricles were studied. In this animal the left stellate was removed leaving the right stellate intact. The area of greatest change was located again on the posterior surface with only slight changes on the anterior surface. This experimental result demonstrates that prolongation of refractory period on the posterior surface of the ventricles can result from left stellate removal alone and is not dependent upon prior excision of the right stellate ganglion as could be inferred from figure 7.

Ten animals were studied comparing anterior and posterior ventricular surfaces following LS ganglionectomy. The FRP prolongations following LS ganglionectomy at each of the 16 test points were ranked from 1 to 16 according to the magnitude of change. Using the Kendall "coefficient of concordance" the test points were grouped into three large areas as follows: (1) contiguous test points 9-11 and 13-15, in figure 8, representing an area of large FRP change; (2) test points 1, 4-6, 12, 16, representing sites of intermediate FRP change; and (3) test points 2, 3, 7, 8, repre-

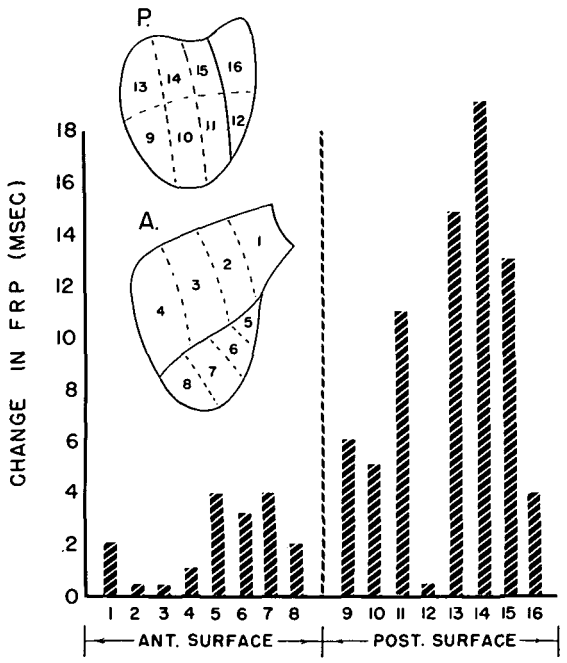

FIGURE 8

Functional refractory period (FRP) prolongations following left stellate ganglionectomy in an animal with an intact right stellate. FRP changes are plotted on the ordinate for each of the sixteen test sites on the abscissa. The locations of the test sites on the anterior (A) and posterior (P) surfaces of the ventricles are shown.

senting sites of small FRP change. When these three areas were ranked from 1 to 3, according to the average magnitude of change, a large and significant trend was observed between animals ($W = 0.8$, $P = 0.001$). These results demonstrate that the left stellate ganglion exerts its major influence on the posterior surface of the left ventricle.

A similar analysis of the anterior and posterior ventricular surface was performed following RS ganglionectomy in five animals. Again, as noted previously, a significant trend of FRP prolongations was found from animal to animal, indicating that the anterior surface of the left ventricle and perhaps the right base were innervated primarily by the right stellate ganglion.

A comparison of results from epicardial test points with those from endocardial test points was made in five animals. In each test area where an endocardial test electrode was used, another test electrode was placed on the overlying epicardial surface. Figure 9 illustrates two of the experiments in which the endocardium was studied. Experiment A shows the FRP prolongations following RS ganglionectomy with an intact left stellate. The areas of greatest prolongation are located on the anterior surface, with changes on the endocardial surface paralleling those on the overlying epicardium. Experiment B represents an animal in which the left stellate was removed with the right stellate intact. Again, changes on the endocardium were similar to those on the overlying epicardium, with the areas of greatest FRP prolongation occurring in the posterior myocardium. These results suggest that the refractory period changes following stellate ganglionectomy are not purely a surface phenomenon, but that the entire myocardium is probably involved.

Discussion

The exact distribution of the cardiac nerves in the heart has not been adequately defined anatomically. The studies of Nonidez[18] and Woollard[19] suggest that the ventricles are free from parasympathetic innervation. Histologic evidence for autonomic postganglionic fibers within the ventricular myocardium has been reported by a number of investigators,[18–22] although such studies have not differentiated the patterns of right and left sympathetic innervation. A functional distinction of these patterns has been shown by Randall and Rohse[23] who found that left stellate stimulation produced mainly inotropic changes, while right stellate stimulation produced both inotropic and chronotropic changes.

Changes in the form of electrocardiograms from a longitudinal lead following sympathetic stimulation were first described by Rothberger and Winterberg in 1910.[24] They reported ST segment elevation and T-wave inversion following right sympathetic stimulation. Two types of changes were observed on left sympathetic stimulation. Depression of the ST segment and increased amplitude of the T wave were seen in most preparations, and in others

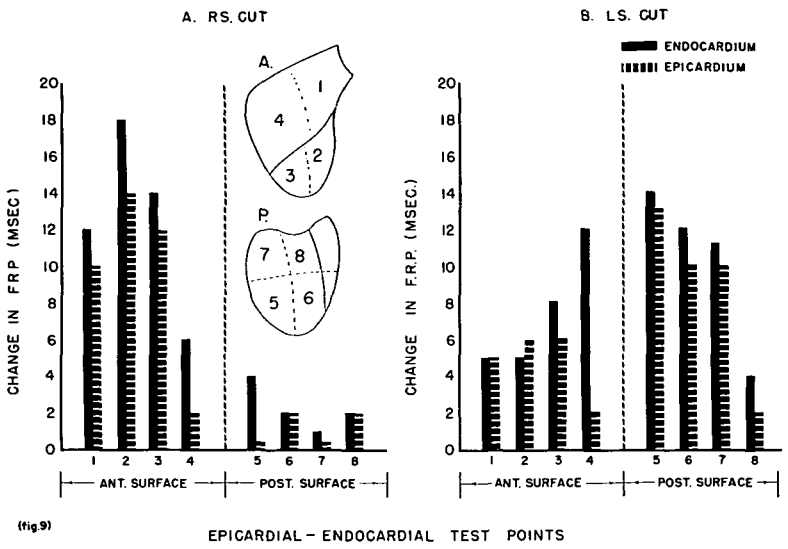

FIGURE 9

Functional refractory period (FRP) prolongations following stellate ganglionectomy comparing endocardial (solid bars) and epicardial (hatched bars) test electrodes. In each test area where an endocardial test electrode was used, an epicardial electrode was secured on the overlying epicardial surface. Panel A illustrates the FRP changes plotted on the ordinate for each of the eight test areas listed on the abscissa following right stellate (RS) ganglionectomy in an animal whose left stellate (LS) was intact. Panel B illustrates the changes following LS ganglionectomy in an aniaml whose right stellate was intact. The locations of the test areas are shown on the anterior (A) and posterior (P) surfaces of the ventricles.

there was a transient period of T-wave inversion followed by increased amplitude of the T wave. More recently Ueda et al.[25] demonstrated vector cardiographic changes with stellate ganglion stimulation. In the sagittal plane, right stellate stimulation produced superior displacement of the T loop, while left stellate stimulation displaced the T loop inferiorly with an occasional transient superior displacement. In the present study, electrocardiographic changes similar to those already reported have been observed following right and left stellate stimulation. In addition, unilateral stellate ganglionectomy in these experiments also produced significant and predictable electrocardiographic changes. These results suggest that there are important differences in the distribution of the right and left cardiac sympathetic nerves within the ventricular myocardium.

Consideration of the physiologic origin of the T wave is essential in attempting to elucidate the mechanism for the neurogenic electrocardiographic changes observed in these experiments and in patients with central nervous system lesions. Since the T wave represents the electrical forces resulting from recovery of activated ventricular muscle fibers to their resting states, a major factor influencing T wave configuration is the temporal and spatial pattern of excitation. Altered patterns of excitation will alter secondarily the patterns of recovery and thus, the form of the T wave. This is unlikely to be the mechanism for the observed T-wave changes in the foregoing experiments, for the QRS complex did not change significantly following alterations in sympathetic tone. Visually observable changes, although slight, were seen in less than 10% of our animals. The other major factor influencing T-wave configuration is independent of the pattern of excitation and is due to the nonhomogeneous nature of the recovery process, i.e., variations in the shape and the duration of individual action potentials of the myocardial cell population. Differences in repolar-

ization of various ventricular areas result in measurable electrical forces, the temporal and spatial patterns of which determine the magnitude and form of the T wave.

The data presented in this paper demonstrate that unilateral section of sympathetic fibers to the ventricles results in localized areas of refractory period prolongation which could account for the observed changes of T wave form. Also, unilateral stellate stimulation has been shown to produce electrocardiographic form changes which can be presumed to be the result of localized areas of refractory period shortening. In an earlier study, Barger et al.[26] observed ST-T wave form changes in dogs in which catecholamines were infused into the anterior descending coronary arteries. Presumably the mechanism for the observed electrocardiographic changes was altered repolarization in the area supplied by that artery.

The electrocardiographic form changes following alterations in sympathetic tone involve not only the shape of the T wave but also its duration, as reflected by changes in the Q-T interval. In these experiments the Q-T interval was prolonged by procedures in which sympathetic tone was both decreased and increased; i.e., right stellate ganglionectomy and left stellate stimulation respectively. It is not surprising that right stellate ganglionectomy should prolong the Q-T interval, because removal of sympathetic tone from the ventricles might be expected to prolong the duration of the action potential.[27] It is less obvious how increasing sympathetic tone by left stellate stimulation, a procedure known to shorten the duration of the action potential,[27] can also prolong the Q-T interval. This apparent paradox can be explained in terms of changes in the pattern of ventricular recovery. A net change in the duration of the individual action potentials occurring in a localized area of the myocardium can be expected to alter the temporal pattern of the electrical forces associated with the recovery process. This change in the temporal pattern of ventricular recovery may unmask previously cancelled activity, thereby altering the ST-T deflection. Cancellation of electrocardiographic effects of electrical activity has been documented for ventricular excitation.[28] The longer time course of the recovery process makes it likely that the phenomenon of cancellation is a significant factor in determining the form and duration of the ST segment and T wave. Although definitive experimental results are lacking, a possible mechanism for the Q-T interval prolongation in our experiments and possibly in patients with central nervous system lesions, may be the unmasking of previously cancelled activity during repolarization by alteration of sympathetic tone to discrete areas of the ventricles.

The observed refractory period changes following stellate ganglionectomy demonstrate that right and left stellate ganglia send fibers to different areas of the ventricles. The data show that right stellate ganglionectomy is associated with refractory period prolongation in areas on the anterior ventricular surface, while left stellate ganglionectomy is associated with refractory period prolongation on the posterior ventricular surface. It may be concluded from these results that the anterior ventricular myocardium is innervated predominantly by fibers arising in the right stellate ganglion, while the posterior ventricular surface is innervated principally by fibers arising in the left stellate ganglion. Therefore, unilateral alterations in sympathetic tone will affect discrete ventricular areas, and this type of differential change could lead to an unmasking of previously cancelled activity which is manifested by changes in electrocardiographic wave form.

The electrocardiographic form changes following unilateral right stellate ganglionectomy parallel those following left stellate stimulation; i.e., prolonged Q-T intervals and increased T-wave amplitude. These two procedures are similar in that both produce a predominating left stellate influence on the ventricular myocardium. Since our data indicate that left stellate ganglion fibers innervate primarily the posterior ventricular surface, predominance of left stellate tone results in a relatively shorter recovery process on the posterior as compared to the anterior surface. This same relationship

is created when sympathetic tone is removed from the anterior surface following unilateral right stellate ganglionectomy. Therefore, the probable basis for the electrocardiographic form changes we have observed is a change in the relative durations of repolarization on the anterior and posterior surfaces of the ventricles.

A similar mechanism can be used to explain the increased T-wave negativity following both unilateral left stellate ganglionectomy and right stellate stimulation. These two procedures produce a predominating right stellate influence on the ventricles, resulting in a relatively shorter recovery process on the anterior ventricular surface as compared to the posterior surface. This phase shift in the relative durations of repolarization would alter also the pattern of ventricular recovery, thus producing the observed electrocardiographic form changes.

The characteristic electrocardiogram disturbance observed in some patients with cerebral vascular disease and other central nervous system lesions consists of prolonged Q-T intervals and large amplitude T waves. These electrocardiographic form changes resemble those following unilateral right stellate ganglionectomy or following left stellate stimulation in our open chest dog preparations. Our data suggest that the mechanism for these form changes in the electrocardiogram of the dog involves a shift in the relative durations of repolarization such that the posterior ventricular surface recovers relatively faster than the anterior surface due to predominating left stellate tone. While there are limitations in comparing the electrocardiographic pattern of the open chest dog preparation with that in man, it is not unlikely that a similar mechanism accounts for the electrocardiogram disturbance in patients with central nervous system lesions.

Summary

Changes of the electrocardiogram and of ventricular refractory period were measured following either unilateral stellate ganglion stimulation or ablation in the open chest dog preparation.

Right stellate ganglionectomy or left stellate stimulation produces prolonged Q-T intervals and increased T-wave amplitude. Left stellate ganglionectomy or right stellate stimulation produces increased T-wave negativity without measurable change in the Q-T interval.

The differing patterns of electrocardiographic wave form resulting from changes in sympathetic tone mediated by right and left stellate innervation could be correlated with changes in ventricular refractory period. Following right stellate ganglionectomy, refractory period prolongations were most marked over the anterior ventricular surface; left stellate ganglionectomy produced the greatest prolongation on the posterior surface.

Although the right and left stellate innervations of the ventricles overlap, the left stellate influence is predominant over the posterior wall of the ventricles, while right stellate influence dominates the anterior ventricular walls.

The electrocardiographic form changes observed following unilateral alteration of sympathetic tone paralleled those electrocardiographic abnormalities seen in patients with lesions of the central nervous system, suggesting a possible functional explanation for these clinical findings.

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