THE ACTIVITY OF THE CARDIAC SYMPATHETIC CENTERS

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The development of methods for recording the nerve impulses going to and from the centers provides an effective means for studying the activity of the sympathetic nervous system (Adrian, Bronk and Phillips, 1932). Such a direct analysis of the behavior of the sympathetic nerve cells is especially valuable because it is difficult to determine their functional characteristics from the response of the organs which they supply. The inertia of these effectors is so great that the activity produced by the individual nerve impulses is masked or obscured, a situation which is quite different from that in the somatic system where a study of the contraction in striated muscle has given much information regarding the properties of the individual motor nerve cells.

In the present investigation we have undertaken to determine the character of the sympathetic nerve discharge to the heart. The purpose of the experiments has been to add to our knowledge concerning the activity of the sympathetic nervous system and to give a clearer understanding of the nature of cardiac control.

METHODS AND PROCEDURES. Most of the experiments were performed on cats under light nembutal anesthesia but in a few cases decerebrate animals were employed without significantly different results. In every case the animal was kept in a humid chamber at a temperature of about 34°C. The chest wall was removed from the first to the sixth ribs, after which respiration was maintained by means of a pump. It was then possible to reach the long cardiac-sympathetic nerves which run from the stellate ganglia to the inferior cardiac plexus and contain both chronotropic and inotropic fibers. One of these nerves was dissected free from the surrounding tissues and transected some distance from the heart. The proximal portion was then slung onto silver-silver-chloride brush electrodes leading to a direct-coupled or resistance-capacity-coupled amplifier and

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Matthews oscillograph. In this way the efferent sympathetic impulses in the cardiac nerves were recorded.

RESULTS. The tonic discharge. Records of the sympathetic discharge to the heart are shown in figure 1. In all our experiments on 46 animals we have found such continuous activity in the cardiac sympathetic nerves, provided the animal was in reasonably good condition. This statement is not to be construed, however, as meaning that the degree of that activity is constant. It is indeed increased by asphyxia, decreased by overventilation or a rise in blood pressure, and largely modified by numerous other factors. But in general, under the conditions of our experiments in which the blood pressure and depth of respiration were permitted to vary within wide limits, there was a persistent discharge of impulses. This is positive evidence, then, in support of the view held by Hunt (1899) and others that the heart is under a continual influence of sympathetic impulses.

Fig. 1. Records showing ungrouped “tonic” discharge of impulses in a sympathetic cardiac nerve from the stellate ganglion. A, in relatively few fibers; B, in the whole nerve. Time marker in this and subsequent records gives ½ second intervals.

The fiber pathways. The impulses shown in figure 1 and elsewhere in this paper have been recorded in postganglionic fibers for they are abolished by painting the stellate ganglion with nicotine. The pathways of the pre-ganglionic impulses by which they are initiated have been determined by cutting successively the first to the fifth thoracic rami. When the first or second thoracic ramus is severed there is little decrease in the magnitude of the postganglionic discharge. Section of either the third or fourth ramus, on the other hand, produces a very considerable decrease, and when they are both cut practically all the impulses are eliminated. Our experiments show therefore that most of the sympathetic impulses going to the heart from the stellate ganglion enter by way of the third and fourth thoracic rami.

The course of many of the postganglionic fibers is in one or more nerves running from each ganglion to the cardiac plexus. A considerable number
of the fibers, however, go directly from the ganglia to the vagi and run with those nerves toward the heart so that it is always possible to observe a discharge of sympathetic impulses in the vagus nerves.

It is of course not possible in our experiments to restrict the fibers under observation to those concerned with the control of the rate and force of the cardiac beat. But anatomical evidence indicates that the great majority of the efferent fibers in these nerves going to the cardiac plexus from the stellate ganglia have that function. It is fair to assume therefore that our results give typical evidence concerning the activity of the sympathetic nerve cells regulating the heart.

The source of the potentials. The type of action potential with which we are dealing is illustrated in figure 2A. A maximum electric stimulus was applied to a postganglionic nerve from the stellate ganglion and the response recorded after an interval which indicates that the impulses are transmitted with a velocity which varies from 0.6 to 1.5 m. per second in different fibers. They are characterized by large positive after potentials which become especially apparent at the end of a period of sustained stimulation or whenever the normal efferent discharge is suddenly inhibited reflexly as in figure 2B.

The individual potential pulses in such efferent discharges as are shown in figure 1 are of considerable magnitude and may be as great as 50 microvolts. They are therefore too large to be the action potentials in single postganglionic fibers. In discussing similar large potential pulses in the hypogastric and cervical sympathetic nerves Adrian, Bronk and Phillips (1932) suggested that they are produced by many postganglionic fibers functioning as a unit and in fairly close synchronism. This is because one preganglionic fiber activates many postganglionic fibers (Billingsley and Ranson, 1918). Thus the ganglion functions as a natural amplifier.
The random and irregular character of the discharge in figure 1 indicates that we are dealing with more than one such group of postganglionic fibers innervated by a single preganglionic fiber. We have frequently tried to observe the impulses in a single unit by cutting and splitting the trunk but the small size of the fibers and the fragile character of the nerve make this a difficult task. One can more readily record the impulses in a single preganglionic fiber, and that is just as useful in analyzing the activity of the individual sympathetic motor nerve cell. In such single preganglionic fibers we have observed impulse frequencies as low as one or two per second and seldom higher than ten or twenty a second. This is in marked contrast with the activity of somatic motor nerve cells from which the rate of impulse discharge may be five or ten times as great (Adrian and Bronk, 1928). Such differences are interesting in view of the slower characteristics and greater inertia of the organs supplied by the sympathetic nervous system. Mammalian skeletal muscle fibers require 30 to 350 impulses a second in order that they may develop their maximum tension (Cooper and Eccles, 1930), whereas sympathetic stimulation of 10 to 15 a second produces maximum cardiac acceleration (Bronk and Pumphrey, 1935). Bozler (1936) has also found that low frequencies of sympathetic stimulation (2–3 a second for the frog) are sufficient to maintain the blood vessels in a state of maximal constriction, and only when the frequency of sympathetic stimulation is low are dorsal root impulses effective in modifying the degree of contraction.

Grouped impulses. One of the most striking characteristics of the nervous discharge in the cardiac sympathetic fibers is the frequent grouping of impulses to form waves which may be several hundred microvolts in amplitude. Because of their size and their form they almost certainly represent the activity in many more postganglionic fibers than are supplied by a single preganglionic fiber. These waves are therefore not due to the type of ganglionic grouping referred to above. It might still be argued, however, that they are the result of some property of the ganglion whereby the activity of the various units is synchronized. Such a possibility is indeed suggested by Tower's (1933) interesting observation of wave-like groups of impulses in sympathetic fibers from the isolated viscera of a frog. She tentatively proposes that "it is not beyond possibility that the cellular plexi of the viscera or ganglia contain something analogous to a synchronizing mechanism."

It is more probable however that these volleys of impulses which we are considering may be due to a more or less synchronous rise and fall in the level of excitation of large numbers of sympathetic motor cells in the cardiac centers. That this is the correct explanation is shown by the fact that similarly grouped impulses are observed in the preganglionic nerves. Such synchronized firing of the cells in the sympathetic centers is further
illustrated by an experiment which was designed to observe the relation between the activity on the two sides of the body. A nerve from the right stellate ganglion was placed on electrodes leading to one amplifier and oscillograph; a nerve from the left stellate ganglion was placed on electrodes leading to a second amplifier and oscillograph. In this way simultaneous records were made of the impulses from the ganglia on the two sides. A

Fig. 3. Grouped impulses in right and left sympathetic cardiac nerves recorded simultaneously with two recording systems, to show synchronization of activity on the two sides.

Fig. 4. Efferent sympathetic cardiac impulses grouped into regularly recurring waves. A. Record from relatively few fibers. Frequency of waves, 6 per second. B. More fibers in action, lower amplification. Frequency 7 per second. C. Frequency 20 per second.

typical record is shown in figure 3, where it will be seen that the groups of impulses from the two ganglia are synchronous. Because this rhythmic activity is bilaterally synchronous we must conclude that the groups of motor cells on the two sides are closely connected, so that they readily interact and modify each other's activity, or are subject to a common driving influence which causes their rhythmic excitation. This is reminiscent of the findings of Gasser and Newcomer (1921) on the discharge of
motor impulses in the phrenic nerves. Recording simultaneously the impulses in the nerves on both sides they found rapidly recurring waves of activity within each respiratory cycle which occurred simultaneously in the two nerves. From such experiments they decided that “the intervals at which impulses are discharged from the cord into the nerve from the two sides are controlled by the same common point.”

The groups of impulses in the cardiac nerves are sometimes discharged at irregular intervals, or at other times with marked regularity as shown by figure 4. In A the frequency of the waves is about 6, in B about 7 and in C they occur 20 times a second. These are three rhythms commonly observed in the sympathetic system; the form of the waves indicates that there is a periodic increase and then decrease in the number of motor nerve cells in action. This cyclical fluctuation in the activity of a large group of cells in the central nervous system, occasionally at a rate corresponding to that of the Berger rhythm, is of especial interest at the present time when considerable attention is being paid to rhythmic processes in the brain.

Such regularly recurring waves as are described in the previous paragraph do not often persist continuously for more than a few seconds at a time. A rhythm appears for a short interval, then disappears or becomes obscured by a more irregular activity, and reappears again. Two other types of rhythmically grouped discharges of lower frequency are more persistent, and the mechanism of their production is more susceptible to analysis. They are discussed in the next section.
Cardiac and respiratory groupings. Although the rhythmic volleys of impulses we have been considering are related to no other obvious rhythm of the organism we have often observed groups of impulses in phase with the heart beat or respiration. This periodic activity synchronous with the cardiac or respiratory cycles has already been found in sympathetic nerves supplying constrictor impulses to blood vessels (Adrian, Bronk and Phillips, 1932).

An instance in which the impulses are grouped into large waves, occurring with the frequency of the heart, is shown in figure 5 where synchronous with each cardiac cycle there is a large volley of efferent sympathetic impulses. The activity of the motor nerve cells is in some way inhibited or stimulated synchronous with the pulse, so that there is a rhythmic beating of the centers. The mechanism will be discussed later.

Less frequently we have observed a grouping of the impulses with respiration as shown in figure 6, the discharge occurring during expiration.

In many animals both the cardiac and respiratory groupings are present at the same time, as in the figure presented.

It is apparent that those groups of motor nerve cells which control the rate and force of the cardiac contraction possess no one characteristic rhythm. The cells show a marked tendency to work in synchronism with a resulting grouped discharge; but the rhythm with which these volleys occur is highly variable for the sympathetic centers appear to be extremely labile and subject to various influences. Certain of these can be described.

Afferent control of sympathetic rhythms. There are two fairly obvious explanations of the bursts of sympathetic impulses which occur with the frequency of the pulse. A. The periodic pulsation of blood pressure within the central nervous system might act as a mechanical stimulus to the motor nerve cells causing their periodic excitation. B. Bronk and Kaltreider (1931), and Bronk and Stella (1932), have shown that there is a volley of afferent impulses discharged from the receptors in the arch of the aorta and the carotid sinus with each systolic rise in pressure. These rhythmically
recurring groups of impulses, playing upon the sympathetic centers, may cause them to function with a corresponding rhythm.

Our experiments show the latter to be the most important, if not the sole cause, of the cardiac grouping for section of the carotid sinus and aortic nerves usually abolishes such synchronized activity in the sympathetic nerves. A frequent observation which gives further support to this view is illustrated in figure 7. Previous to the beginning of the record the blood pressure in the upper part of the animal had been elevated by clamping the descending aorta; it will be observed that as the record begins the sympathetic cells discharge a volley of impulses with each cardiac cycle. When the pressure falls there is more continuous activity and no simple grouping of the impulses synchronous with the pulse. The lower pressure is a less effective stimulus of the receptors in the carotid sinus and aorta, and the consequent reduction in number of afferent impulses makes less effective their influence on the sympathetic centers. It seems probable, therefore, that when the excitation of the cells in the cardiac sympathetic centers rises and falls with the frequency of the heart the variation in activity is somehow due to the pulsatile volleys of afferent impulses from the walls of the blood vessels.

In rare cases there is a suggestion of a cardiac rhythm in the sympathetic discharge after both carotid sinus and aortic nerves are cut. In such cases there is the possibility that impulses from blood vessels which travel over other afferent pathways may be the responsible agents. Thus Gammon and Bronk (1935) have reported impulses from Pacinian corpuscles in the mesentery which are sometimes in volleys synchronous with the pulse, and recently such grouped afferent impulses have been observed in fibers passing through the stellate ganglion (Bronk and Larrabee, 1935).

The cessation of sympathetic impulses during inspiration has been described earlier in the paper. Such rhythmic activity appears to be due to periodic inhibition of the centers by afferent impulses from stretch receptors in the lungs, for the rhythm disappears after section of the vagi. This control of the cardiac sympathetic centers is further illustrated by experiments in which the lungs are distended to varying degrees and so maintained. On distention there is a complete inhibition of the sympathetic discharge for a period of time which depends upon the degree of inflation, and subsequently there is a gradual escape from the inhibition. Similar results are obtained by electrical stimulation of the central ends of the cut vagi.

Such a relation between the respiratory cycle and the activity of the cardiac sympathetic centers has been observed in fourteen animals; in only one have we found a discharge of impulses during inspiration and in that instance the rhythm persisted after section of the vagi. This latter observation recalls the experiments of Adrian, Bronk and Phillips (1932).
in which there was occasionally a respiratory grouping in the cervical sympathetic and hypogastric nerves, the discharge occurring during inspiration. Because the influence of respiration on sympathetic activity was greater after section of the vagi and because in the curari-immobilized animal there were bursts of sympathetic impulses synchronous with the motor discharges in the phrenic nerves it was concluded that the respiratory grouping “was due to the direct action of the respiratory center on the vaso-motor center.” Our present experiments indicate that the cardiac sympathetic center may likewise be directly excited by the respiratory center but is more often under the inhibitory influence of afferent impulses from the lungs or, more often still, is free from any apparent nervous connection with respiratory activity.

Rhythmic driving of the centers. The preceding experiments indicate the importance of afferent impulses from the viscera in regulating the rhythmic

![Fig. 8. Rhythmic waves of activity (grouped impulses), recorded in sympathetic cardiac nerve and reflexly driven by stimulating central end of aortic nerve at times indicated by arrows. Each wave is associated with the previous stimulus (interval between stimulus and the associated wave 0.3 sec.).](http://ajplegacy.physiology.org/)

tivity of the cardiac sympathetic centers. Such afferent determination of the efferent rhythm is well illustrated by the following observations.

During the course of an experiment in which we were stimulating electrically the central end of an aortic nerve we found at high stimulus frequencies inhibition of the centers and subsequent escape. But as the rate of stimulation was lowered the centers began to discharge rhythmically and with the frequency of the stimulus. This is shown in figure 8. When the frequency of afferent excitation was lower than a certain critical level the centers failed to follow, and the discharge again became random and irregular. We have repeated this on many different animals, stimulating either the aortic or carotid sinus nerves, and we frequently find that the cells comprising the cardiac sympathetic centers can be driven rhythmically at rates varying from about 2 to 15 per second. Apparently the time constants of the cells are such that they are unable to respond with synchronous and grouped discharges above and below these frequencies.

It is not improbable that the genesis of such artificially induced rhythms is similar to that of the grouped discharges synchronous with the pulse.
In both cases the mechanism would appear to be an inhibition of the sympathetic activity by the volley of afferent impulses, followed by release, and again inhibition by the next afferent volley. Thus a systolic rise in pressure initiates in the carotid sinuses and aorta bursts of afferent impulses which, arriving at the centers inhibit their activity. The discharge begins again during the latter part of diastole as in figure 5, reaches its maximum during the next systole and is again inhibited by the afferent impulses accompanying that systole. The phase of the cardiac cycle during which the impulses are observed in the sympathetic nerve will of course depend upon the conduction times for the afferent and efferent impulses and the latent period of the centers.

The sequence of events in figure 8 is probably to be accounted for in a similar manner but certain observations indicate that the complete explanation of the phenomenon may involve additional considerations. For instance, in two experiments the volleys of sympathetic impulses persisted for several seconds after the cessation of the stimuli and at the same regular frequency, a persistence which was much longer than could be accounted for by a lag or latency of the centers (only 0.3 sec. at the beginning of the stimulus). Only gradually did the centers lose the rhythm which had previously been imposed upon them by the volleys of afferent impulses. We must conclude that there are some obscure factors in the mechanism whereby the activity of the sympathetic motor cells is set into resonance with the afferent impulses.

Discussion. The importance of the sympathetic nerve supply to the heart has been debated frequently and some authors have doubted whether the accelerator and augmentor fibers are normally in action. The present experiments give definite evidence as to the actual state of activity in those fibers and show that they conduct a fairly continuous series of impulses to the heart. They thus support the view of Hunt (1899) and others that the heart is under a continual sympathetic influence. It is the opinion of such writers that the efficacy of vagal impulses is largely determined by the accelerator background existing at any moment; the greater the sympathetic activity, the greater the effect produced by a given variation in vagal discharge. If such be the rôle of the cardiac sympathetic impulses, effective control of the heart would depend in considerable measure upon a ready modification of the sympathetic discharge by impulses reporting the condition of the viscera. Such a lability of the cardiac sympathetic centers under the influence of afferent impulses has been amply revealed by our experiments and is in agreement with the original observations of Hering (1894) and of Hooker (1907) which established the reflex control of the cardiac accelerator nerves.

The pronounced grouping of the efferent impulses which results from the rhythmically synchronized discharge of the motor nerve cells appears as
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one of the most striking and characteristic properties of the sympathetic system. This is not without analogy in somatic nerves although there the frequency of the grouping is usually quite different. For instance, Dittler and Garten (1912) and Gasser and Newcomer (1921) have shown that in the electric response of the whole phrenic nerve there are oscillations at the rate of about 70 a second. Adrian and Bronk (1928) subsequently found that when the individual motor nerve cells are discharging at a low frequency there is no synchronization of the discharge from the several cells; not until the frequency of impulses rises to 60-70 a second does any appreciable synchronization develop. Thus a smooth contraction is maintained if there were synchronized groups of impulses of a low frequency they would cause a gross tremor of the muscle. Here in the sympathetic nerves, however, we find the frequency of the impulse volleys varying from one every 3 or 4 seconds to about 20 per second. It is of interest to consider their effect upon cardiac activity.

The nature of the cardiac musculature and its relation to the extrinsic nerves are such that it is probably of little significance whether the impulses in the several fibers arrive synchronously or out of phase with one another. But the relative effects of volleys of impulses recurring at frequent or infrequent intervals is less obvious. In preliminary experiments (Bronk and Pumphrey, 1935) we have imitated these efferent volleys of various frequencies by electrically stimulating the peripheral end of a sympathetic cardiac nerve. When short bursts of impulses are delivered more frequently than every five seconds no rhythmic variation in the heart rate is observed. If the groups of stimuli are applied at longer intervals than that, the heart rate shows fluctuations synchronous with the periods of stimulation. From this it would appear that the only type of efferent sympathetic rhythm which could be reflected in the cardiac rate is the respiratory grouping, and that only when the rate of respiration is fairly slow.

This raises the question as to whether the periodic inhibition of the cardiac sympathetic discharge is in part responsible for sinus arrhythmia. It is generally believed (cf. Samaan, 1935) that the arrhythmia is due to variations in vagal activity for it is said to be abolished by atropine or by section of the vagi. On the other hand, our experiments show that the sympathetic discharge to the heart does frequently vary with respiration and that these variations are capable of producing changes in the heart rate.

SUMMARY

The activity of the cardiac sympathetic centers has been investigated by recording the action potentials in the cardiac nerves from the stellate ganglia of the cat.
There is a fairly continuous discharge of impulses which exert a “tonic” augmentor and accelerator influence upon the heart. This discharge is however largely modified by changes in the chemical composition of the blood and by afferent impulses.

The principal pathways of the impulses from the cord to the stellate ganglion are the third and fourth and to a lesser extent the second and fifth thoracic rami.

The impulse frequency from the individual sympathetic motor nerve cells seldom exceeds ten or fifteen a second, and is usually considerably less. This contrasts with the much higher frequency of discharge from somatic motor nerve cells.

The potential pulses in the postganglionic nerves are of considerable magnitude because of the grouping of impulses which results from the innervation of many postganglionic fibers by a single preganglionic fiber.

There are also much larger potential waves caused by the synchronous activity in very many nerve fibers. It is shown that this is due to the co-ordinated and rhythmic discharge from large numbers of nerve cells in the centers. This activity is bilaterally synchronous.

The grouped activity is of four types. The volleys may come at irregular intervals or at other times periodically with frequencies varying from 5 to 20 a second but unrelated to any other obvious rhythm of the organism. Or, on the other hand, the bursts of impulses may be synchronous with the pulse or the respiratory cycle.

The latter two forms of rhythmic cellular activity are largely due to afferent impulses from the viscera: bursts of impulses from the blood vessels initiated by the systolic rise in pressure or the impulses from distention receptors in the lungs.

An example of the marked effect of such afferent impulses upon the activity of the sympathetic centers is found in the observation that it is possible to drive those centers by repetitive stimulation of the central ends of the carotid sinus or aortic nerves, thus causing the motor nerve cells to discharge periodically with the frequency of the afferent impulses. This can be done within a limited range of stimulus frequencies.

The characteristically grouped discharges from the cardiac sympathetic centers cause periodic variations in heart rate only if the bursts of efferent impulses are separated by some seconds. This is due to the inertia of the effector mechanism.

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