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THE NERVOUS MECHANISM OF CARDIOVASCULAR CONTROL[1]

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THE coördinated control of the heart and blood vessels is one of the most important and remarkable reflexes in the organism. Because the circulation supplies the essential and varying needs of the complex body, it can best fulfill its functions under the integrated regulation of the nervous system. The way in which this is accomplished is a striking example of precise and efficient nervous action.

In speaking before your Society, which honors William Harvey, I would choose one of his observations as an appropriate introduction to my remarks. But I find in his writings little mention of possible nervous influences on the circulation. The capacity of the heart for independent action he recognized, as in his admonition: "Nor must we disagree from Aristotle concerning the principality of the heart, that it does not receive motion and sense from the brain" (1). The control of the heart's independent contractility by the nervous system was not discovered until more than two hundred years later.

In 1845 the brothers Weber (2) described the regulation of the heart as being due to the balanced action of vagus and sympathetic nerve fibers. They showed that impulses coming to the heart over the vagal fibers have primarily an inhibitory function, slowing the rate and decreasing the strength of the beat. For sympathetic fibers they postulated an accelerator and augmentor action. The proof of this suggestion was given by many succeeding investigators and finally completed by Schmiedeberg and Ludwig (3) in 1871. Such a nervous control of the heart makes possible an adjustment of the circulation to the varying demands of the body.

[1] Lecture delivered May 17, 1934.

This adjustment is likewise dependent on the caliber of the vessels, variations in their size altering the distribution of blood to the various parts and organs in accordance with their several needs. As early as 1733 the notion that the small arteries change their caliber was put forward by Stephen Hales. From that time on the conception gradually developed that these changes were somehow due to a nervous influence, until in 1831 E. H. Weber (4) proposed for the first time, I believe: "that pallor and blushing could be explained if it were taken for granted that the caliber of the peripheral arteries could under nervous influence become smaller or larger." The means by which this is accomplished were soon discovered. It was found that arteries are supplied by nerves, and about the same time Henle (5) demonstrated involuntary muscle cells in the middle coat of the small arteries.

Thus was the stage set for the famous discovery by Claude Bernard (6) which definitely proved the existence of a vasomotor mechanism. It is so familiar that it needs little recounting. The vessels in a rabbit's ear were seen to dilate when the cervical sympathetic was cut, and it was therefore reasonable to assume that certain of the blood vessels were under the influence of vasoconstrictor nerves. This conclusion was soon substantiated by Brown-Sequard (7), Bernard (8) and Waller (9), who showed that electrical stimulation of the peripheral stump of the cut nerve causes the vessels to constrict again. And then finally Schiff (10) and more especially Bernard (11) established the existence of a second type of vasomotor nerve with a dilator function. By this dual mechanism the distribution of blood in the body is effectively controlled.

A feature of great importance in this controlling and regulating mechanism was subsequently discovered by Ludwig and Cyon (12). Stimulation of the central ends of a certain pair of nerves which end in the aortic arch caused a decreased heart rate and a marked depression of blood pressure. These so called depressor—or aortic—nerves were soon found to play an important part in the reflex regulation of the circulation. More recently Hering (13), following Pagano and Siciliano (14), has discovered a nerve with similar functions coming from each carotid sinus—or bulbous

enlargement at the bifurcation of the common carotid artery. Stimulation of the central ends of these carotid sinus nerves likewise gives a reflex slowing of the heart and lowering of the blood pressure. There is a further similarity. The fibers of both these nerves end in receptors located in the walls of the vessels and normally they are stimulated by a distention of the vessel wall. Eyster and Hooker (15), for instance, have shown that stretching the aorta causes a reflex inhibition of the heart and a fall in blood pressure, and the many beautifully executed experiments of Heymans and his collaborators (16) have given abundant evidence of such reflex effects when the carotid sinus is distended.

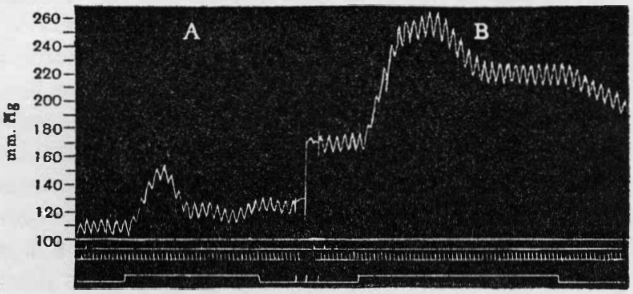

FIG. 1. Left splanchnic nerve cut and peripheral end stimulated at *A* and *B*. Between *A* and *B* both common carotids closed. (Izquerido (17).)

These effects have their origin in the receptors which, lying in the walls of the vessels, are sensitive to variations in pressure. It is their function to signal changes in blood pressure, and it is the function of their afferent fibers to provide a means for communication between these receptors and the central nervous system. Thus the centers are kept informed regarding the pressure within the blood vessels.

The reflex action of the afferent and efferent nerves we have been describing is admirably illustrated by a simple experiment of Izquerido (17). In figure 1 at *A* the peripheral end of the left splanchnic nerve was stimulated with the usual rise in blood pressure due to constriction of the vascular bed in this area. Sub-

sequently both carotid arteries were clamped so that the receptors in the carotid sinuses were non-functional. This produced a rise in blood pressure which may be explained on the assumption that this afferent mechanism had been reflexly holding down the pressure until it was taken out of action, whereupon the blood pressure rose. Stimulation of the splanchnic nerve, as at *B*, now produced a much greater rise in pressure due to the fact that the rise was not held in check by the carotid sinuses.

Such then is the mere outline of a system which provides for the nervous regulation of the heart and blood vessels. It is of profound importance in controlling the blood pressure and holding it within certain limits against factors which would otherwise produce too great fluctuations. It effects a balance and distribution of blood among the various parts and organs in accordance with their several needs. It is of great significance in many pathological conditions. Without stopping longer to discuss the vast literature pertaining to the subject I wish to go on to a consideration of the nervous mechanism whereby this regulation is achieved.

The most direct method of attacking the problem is to intercept and record the nerve messages which accomplish the control. Thus shall we see how the receptors in the vessel walls signal arterial pressure, what is the character of the nervous discharge from the centers which govern the heart and regulate the caliber of the vessels and how the activity of these cardio-vascular centers is reflexly modified by impulses coming over the afferent pathways.

It is possible to record these messages going to and from the central nervous system because the impulses of which they are composed are accompanied by electrical pulses in the nerve. This physical evidence of nervous activity is very small and very brief but it can be accurately measured and recorded with the aid of vacuum tube amplifiers and rapid electrical recording devices. The method is as follows. An afferent or efferent nerve is freed from the surrounding tissues, and electrical connection is made between two points on the nerve and the input of an amplifier. The exceedingly small potential changes in the nerve appear in the output stage greatly amplified. These potential fluctuations, or amplified nerve action potentials, are applied to an oscillograph

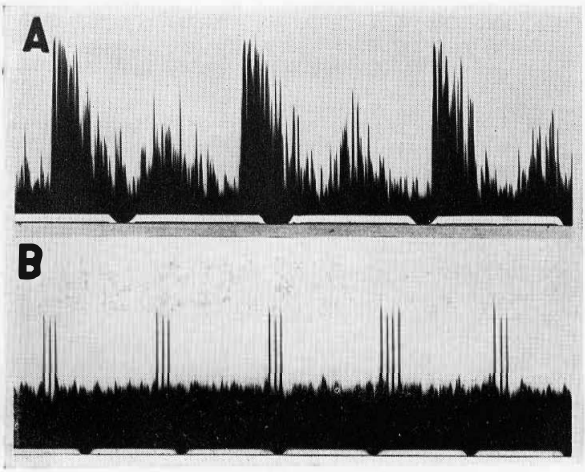

FIG. 2. *A*. Action-potential record of carotid sinus nerve, all fibers intact. *B*. Same after cutting the fibers from all but one end organ. Time marker gives $\frac{1}{5}$-second intervals. (Bronk and Stella (19).)

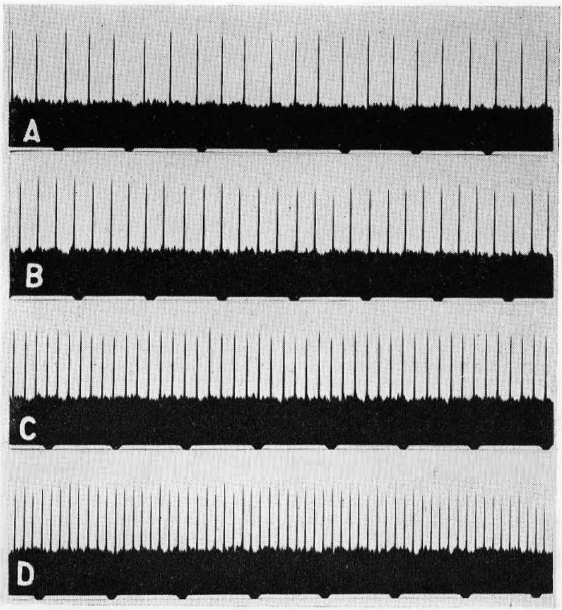

FIG. 3. Afferent impulses from a single end organ in the carotid sinus stimulated by constant pressures within the sinus. In *A* 40 mm. Hg.; *B*, 80 mm. Hg.; *C*, 140 mm. Hg.; *D*, 200 mm. Hg. Time marker gives $\frac{1}{5}$-second intervals. (Bronk and Stella (23).)

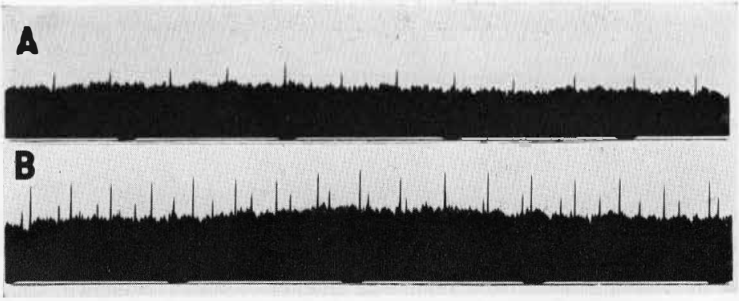

FIG. 4. Discharge of impulses from two end organs in carotid sinus, *A*, when stimulated by a pressure of 70 mm. Hg. and *B*, 100 mm. Hg. The second end organ comes into action in *B*. Time marker gives $\frac{1}{5}$-second intervals. (Bronk and Stella (23).)

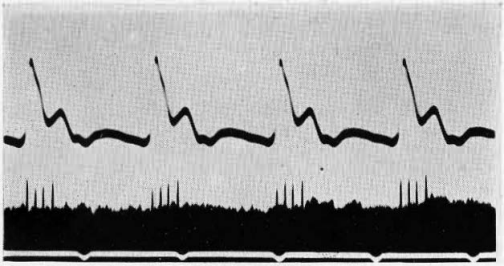

FIG. 5. Nerve impulses from a single end organ photographed simultaneously with optical record of arterial blood pressure. (Bronk and Stella (19).)

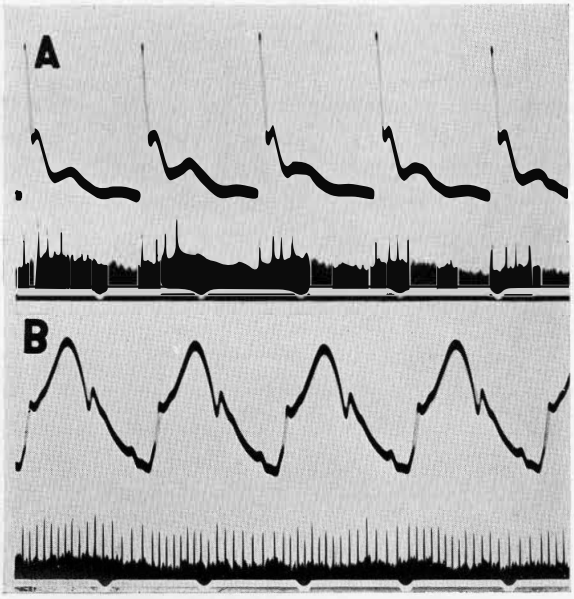

FIG. 6. The effect of increased mean blood pressure on the discharge from a single receptor in the carotid sinus. *A*. Mean blood pressure, 55 mm. Hg. *B*. Mean blood pressure, 135 mm. Hg. (Bronk and Stella (19).)

which transforms them into movements of a beam of light. Thus we obtain a photographic record of the activity in the nerve. Precise physical methods of analysis have in the past played a major rôle in the study of the circulation—through the use of the electrocardiograph, the measurement of blood pressure, the determination of blood flow. Here again the use of a new physical tool serves well in the investigation of an important circulatory mechanism.

A typical message (18, 19) from a group of vascular sense organs is given in figure 2A. It consists of periodic bursts of impulses and a less active continuous discharge. The analysis cannot be carried much further because of a difficulty which is common in physiological investigation in general and neurological investigation in particular. It is frequently responsible for the variability of biological data and the impediment one meets in their analysis. I refer to the fact that when we study the activity of a large number of cellular units we gain little information regarding the behavior of any one unit and often as little about the behavior of the aggregate. This is because the activity of the individuals is so varied that the integrated result is a jumbled confusion. If, by analogy, we wished to investigate the social activity of a community we would not intercept and record the simultaneous conversations of a thousand citizens by connecting a receiver to a telephone trunk cable. On the contrary we would eliminate all but one or a few of the circuits at a time. Only then could we understand any one of the messages. And only then could we attempt an integrated picture of the activity of the community as a whole out of the information gained from the several individuals. Similarly, in order to understand the nerve messages which keep the central nervous system informed as to the level of arterial pressure we must put all but one or a few of the nerve fibers or receptors out of action. Means for doing this are available in a well-known method for recording impulses from single sensory and motor nerve cells. (Adrian and Zotterman (20), Adrian and Bronk (21) and Bronk (22).)

It is readily possible, for instance, to cut all but one of the active fibers in the carotid sinus nerve and thus make physiological con-

nection with a single pressure receptor in the walls of the sinus (19). The record, figure 2B, of the impulses from the single receptor represents a much simpler message. It consists of short bursts of impulses, the impulses in each burst following one another with remarkable regularity. The simplification is striking, and the individual receptors apparently behave in a very orderly fashion. It should now be possible to consider how they signal differences in vascular pressure.

In order to do this Stella and I (23) have investigated certain of their properties under carefully controlled conditions. The sinus was isolated and all of the associated arteries ligated excepting the common and external carotids. Into these two, cannulae were inserted through which the sinus could be perfused at any desired, constant pressure. The distention of the vessel wall by such a steady pressure stimulates the receptors, and from each of them goes out a continuous train of impulses. Such a series of impulses, regularly spaced and of a definite frequency, is the characteristic form of all sensory nerve messages. And indeed the properties of nerve fibers are such that we could expect nothing else.

This is because when a receptor system has discharged an impulse it must go through a refractory period before it can again come into action. How soon it again discharges depends on the strength of the stimulus: the stronger the stimulus, the more rapidly do the impulses follow one another. In this way the sensory message from the arterial wall is modified by variations in vascular pressure. This is well illustrated by figure 3 where four records represent the discharge from a pressure receptor in the carotid sinus in response to pressures in the sinus ranging from 40 to 200 mm. Hg. It is obvious that the frequency of impulses in the afferent train varies with the pressure.

There is another important effect of pressure variations on the afferent discharge. Every sense cell requires a certain intensity of stimulus in order that it may respond; some have low, others higher thresholds. And so, as the pressure within the carotid sinus or aorta is raised, more and more receptors should come into action. In order to observe this it is necessary to deal with several receptors instead of just one. This is the situation in

figure 4 where, with a pressure of 70 mm. Hg, there is a discharge of impulses from one receptor at a frequency of 15 a second. When the pressure was increased to 100 mm. Hg the frequency of response from that receptor went up to 25 a second, and a second receptor came into action. By means of these two mechanisms—by variations in the frequency of impulses from the individual unit and by variations in the number of active units—these receptors should be capable of keeping the central nervous system informed of the pressure in the vessels.

We may now consider how they do so under normal conditions of arterial stimulation. In a lightly anesthetized cat or rabbit, one of the carotid sinus or aortic nerves is freed from the surrounding tissues, and electrical connection made between a single nerve fiber and an amplifier-recording system. In this way we find that the characteristic discharge from a receptor (fig. 5) consists of a volley of impulses synchronous with each systolic rise in pressure, the impulses dropping off in frequency and finally stopping completely during diastole. Because it is the function of the receptors to signal variations in blood pressure, the character of the discharge will presumably be different at different pressures. How it varies is shown by altering the mean blood pressure with injections of adrenalin, by occlusion of the descending aorta, by inhalation of amyl nitrite, etc. Typical results are shown in figure 6. With a rise in mean blood pressure the average frequency of impulses increases, as would be expected on the basis of the preceding paragraph. And furthermore the duration of the discharge increases from a short burst during systole to a train of impulses which lasts into diastole and, at still higher pressures, throughout the cardiac cycle. If several or more end organs are under observation we also find that the number in action increases with the rise in blood pressure.

The variable then in the sensory message which indicates the level of pressure in the vascular system is the total number of afferent impulses going to the centers in a given time. This depends on (*a*) the frequency of discharge from any one end organ, (*b*) the number of end organs that are active, and (*c*) the portion of each cardiac cycle they are in action. Such a triple mechanism greatly

increases the range of the signalling system. Of the three, the variation in frequency is presumably most useful for giving sensitive indications of the finer fluctuations in pressure, as illustrated in figure 7. The frequency speeds up with the systolic pressure rise, the small drop in pressure at the incisura is definitely reflected in the decreased impulse frequency, which again increases and falls with the pressure during diastole. The parallelism is remarkably faithful.

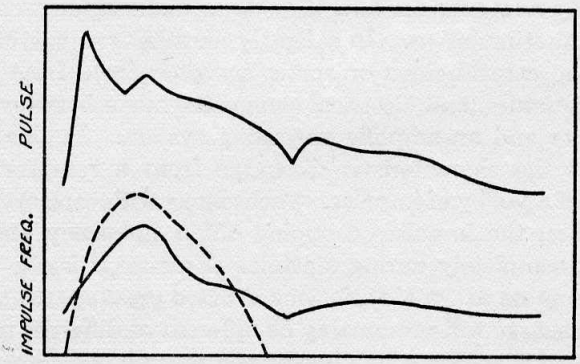

FIG. 7. Above: Tracing of arterial pressure pulse. Below: Frequency of impulses from two end organs in carotid sinus throughout the cycle, plotted as reciprocals of the intervals between successive impulses. (Bronk and Stella (19).)

This fidelity would be lost if the receptors were extremely sensitive to variations in the chemical composition of their environment as is true of certain other sense organs. This consideration and the findings of Heymans (24) and of Schmidt (25) that the carotid sinus has an important rôle in the chemical regulation of respiration led us to inquire whether the response of the pressure receptors in the carotid sinus is modified by variations in the chemical composition of the blood. If this were so, their report of blood pressure would be false because it would be modified by other variables than variations in pressure. And so we have perfused the sinus with normal arterial blood and recorded the frequency of impulses elicited by various steady pressures. The

blood was then flowed back into the general circulation and the animal was asphyxiated or caused to rebreathe a mixture low in oxygen until the blood was highly venous, when it was again perfused into the sinus. The pressure level was now varied as before. In the case of every individual receptor studied, the frequencies at each pressure in the two series (fig. 8) were practically identical. From such experiments we conclude that the pressure receptors are insensitive to variations in the composition of the blood. This is a property which increases their capacity

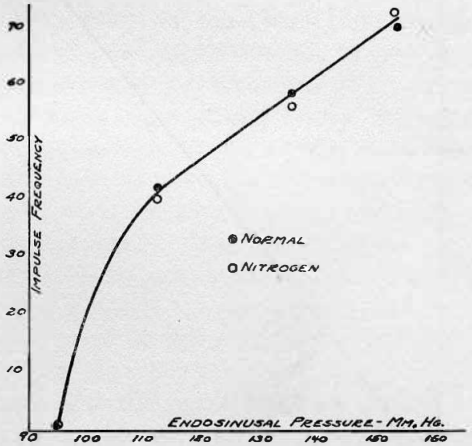

FIG. 8. The response of a pressure receptor at various pressures, *a* (full circles), with the sinus perfused with normal arterial blood and, *b* (open circles), with blood from the animal after a prolonged period of rebreathing N_2. (Bronk and Stella (23).)

for signalling without ambiguity the level of pressure at every instant.

There are obvious teleological considerations which make the aorta and the carotid sinuses ideal regions for the location of pressure receptors. There are equally important considerations, however, which indicate that there would be advantages to the organism in having such receptors in other parts of the vascular system as well. At present little is known about additional zones of vascular sensibility, but the method of recording nerve messages

which I have been describing should readily reveal their location and functional character—if they exist.

Thus Gammon and I (26) have found that there are periodic volleys of afferent impulses synchronous with the pulse in the splanchnic nerve which, of course, come from an area of great importance in circulatory adjustment and regulation. We traced the impulses down the mesenteric nerves, out their terminal twigs

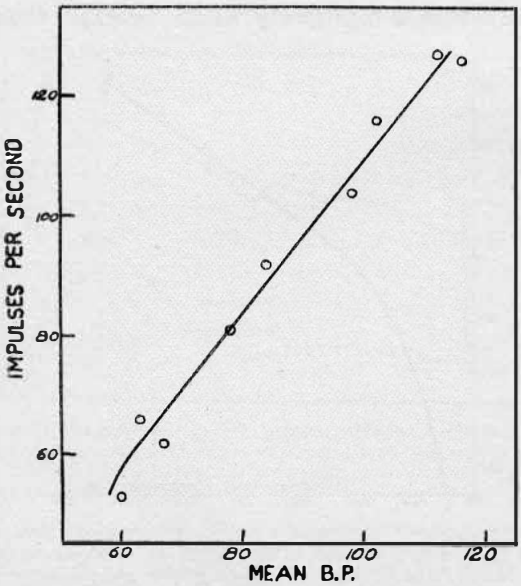

FIG. 9. Number of afferent impulses per second at different blood pressures. Several end organs. (Bronk and Stella (19).)

and so to Pacinian corpuscles in the mesentery. Here large numbers of these sense organs are massed about the vessels where they would be readily susceptible to mechanical deformation resulting from arterial distention. It had already been shown by Adrian and Umrath (27) that similar end organs located in the joints are readily stimulated by mechanical pressure. That they are here under the influence of the vascular system we have shown by isolating a portion of the mesentery, perfusing the vessels and

recording the impulses in a nerve twig coming from one or a few Pacinian corpuscles. Under such conditions there is a continuous discharge of impulses, the frequency of which increases as the pressure in the vessels is increased. Here is a rôle for these structures whose function has been so long debated.

Let us consider how they respond to varying circulatory conditions. For instance, the impulse discharge has been recorded, and the blood volume then reduced by bleeding the animal. As a result the frequency of impulses from the single end organs has invariably fallen, and the number of end organs in action has decreased. Reinjection of the blood promptly increased again the number of impulses from the region. This then is a mechanism for signalling the degree of distention of the splanchnic vessels.

Thus far we have not established with any certainty its reflex rôle. Certain preliminary experiments, however, indicate that as the vessels dilate and the Pacinians are stimulated they discharge afferent impulses which, acting upon the centers, cause reflex vasoconstriction of these same vessels. It would be the function of the reflex to check too great distention of the splanchnic vessels and thus prevent the pooling of too much blood in that area. But the proof of this suggestion must wait upon further experiments. On the other hand, the afferent mechanism is clear-cut and, inasmuch as this region plays an important part in determining the distribution of blood in the organism and the general blood pressure, the mechanism may have great functional importance. I believe it is reasonable to assume that there are still other portions of the vascular system which give rise to afferent impulses signalling blood pressure and the degree of distention of the vessels.

The number of these impulses playing upon the cardio-vascular centers in a given interval of time varies with the pressure and the degree of arterial distention. (See fig. 9.) It has been pointed out that this variation in number of impulses is due to three factors. The reflex effect on the blood pressure of those three variables in the afferent discharge has been determined by introducing these same variables into the electrical stimulus applied to the central ends of either the carotid sinus or aortic nerves.

The frequency of stimulation was varied, corresponding to a variation in the frequency of discharge from the individual receptors; the strength of stimulus was varied, and that is the equivalent of a variation in the number of end organs in action; the stimulus was altered from a series of short bursts interspersed with periods of no stimulation to continuous excitation, which

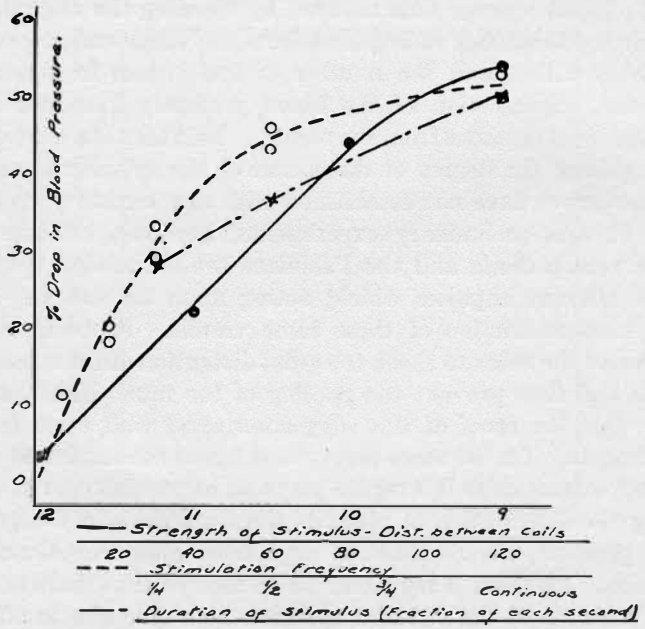

FIG. 10. Drop in blood pressure resulting from variations in the character of carotid sinus nerve stimulation.

simulates the change from the volley type of discharge to a continuous train of impulses. Each one of these variations accomplished a reflex modification of the blood pressure as shown in figure 10. The three variations in the normal sensory message are therefore effective in regulating the activity of the cardio-vascular centers and constitute the quantitative basis for the afferent side of this reflex.

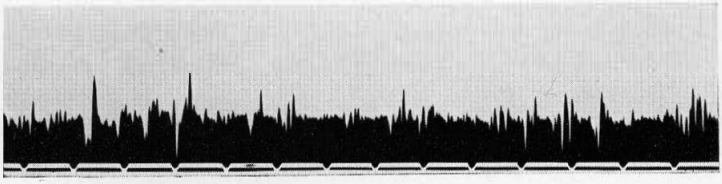

FIG. 11. Vaso-constrictor impulses in a sympathetic nerve. Time marker gives $\frac{1}{5}$-second intervals.

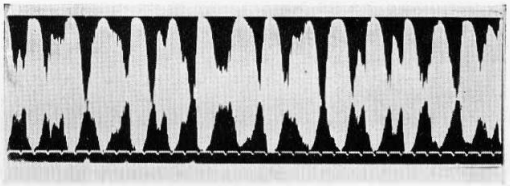

FIG. 12. Above: Volleys of accelerator impulses in right cardiac sympathetic nerve. Below: Simultaneous record of impulses in left cardiac sympathetic nerve. (Bronk, Ferguson and Margaria (29).)

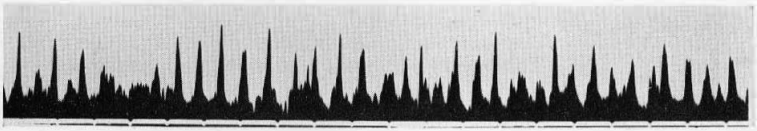

FIG. 13. Rhythmic groups of sympathetic impulses in a few fibers of a cardiac nerve. (Bronk, Ferguson and Margaria (29).)

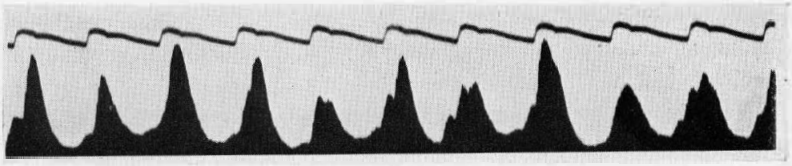

FIG. 14. Volleys of cardiac-accelerator impulses synchronous with pulse. (Bronk, Ferguson and Margaria (29).)

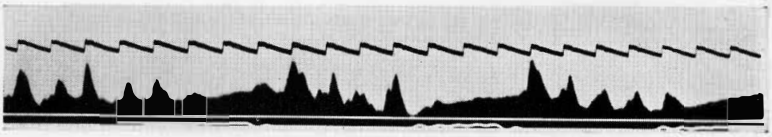

FIG. 15. Cardiac-accelerator impulses inhibited with each inflation of the lungs. Upward movement of lowest line indicates inflation. (Bronk, Ferguson and Margaria (29).)

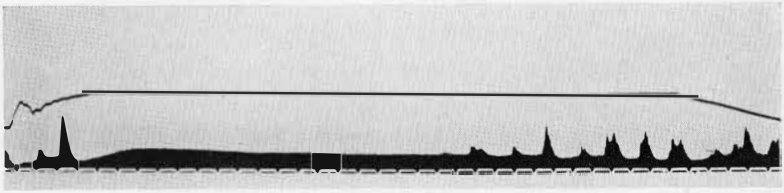

FIG. 16. Inhibition of efferent sympathetic impulses to the heart by distention of the carotid sinus. Upper record: Pressure in the sinus. Lower record: Sympathetic impulses. (Bronk, Solandt and Ferguson (30).)

Before going on to a discussion of how the reflex effects are accomplished it will be profitable to consider the nature of the efferent nerve messages transmitted from the central nervous system to the heart and blood vessels. For it is these messages that are modified by the afferent impulses in effecting the regulation of the cardio-vascular system.

The character of the vasomotor discharge has been determined (Adrian, Bronk and Phillips (28)) by recording the impulses in sympathetic nerve twigs going to blood vessels. Under fairly normal conditions of blood pressure there is a succession of potential waves passing down the nerves, and the function of the impulses which they represent is presumably to maintain the tone of the vessels. In any event, conditions which reflexly or centrally induce vasodilatation cause a cessation of these impulses.

Similar persistent discharges are found (Bronk, Ferguson and Margaria (29)) in the cardiac sympathetic nerves from the stellate ganglia which confirms previous evidence that the heart is normally under a tonic accelerator influence. Thus far we have not investigated very thoroughly the nature of the efferent discharge over the vagi but many experiments have shown that these nerves also conduct to the heart a steady succession of impulses. The normal activity of the heart is carried out under the balanced control of vagal and sympathetic influences.

The activity in the vasomotor and cardiac sympathetic nerves is characterized by two types of impulse groupings. The first results because each pre-ganglionic fiber synapses with a considerable number of post-ganglionic fibers, and consequently a whole group of the latter act synchronously and as a unit. By thus synchronizing the activity of a considerable number of these small post-ganglionic fibers, the ganglion functions as a natural amplifier and makes readily possible the determination of the activity of the individual units. This unitary activity is characteristically less regular than the sequence of impulses from a sense organ or a somatic motor nerve cell. It is quite true that rhythmic activity is frequently observed for short periods, but the rhythm is soon interrupted and lost, due presumably to the suceptibility of the sympathetic centers to many influences. The degree to which

their activity is modified by various factors is shown in the consideration of a second type of impulse grouping.

This second grouping is a more or less synchronized volley of impulses in a much larger number of fibers and is revealed by large potential waves in the nerve. That this is due to a fairly well synchronized beating of the cells in the centers has been shown by recording simultaneously the activity in a cardiac sympathetic nerve from the right stellate ganglion and in one from the left. It will be seen in figure 12 that the general time relations of the waves in the nerves on the two sides are the same. This certainly can not be due to coincidence and must be interpreted as the result of a synchronized rise and fall in the activity of the cells in the centers.

Often, as in figure 13, these bursts of impulses have a fairly regular rhythm which is related to no other obvious rhythm of the organism. We can only say that they represent groups of impulses which, when they arrive at the heart, produce increased cardiac activity. At other times, however, the waves are very definitely related to the pulse rhythm, sometimes to the respiratory rhythm and often to both. It will probably have occurred to the reader that certain of these periodic variations in sympathetic activity play some rôle in periodically modifying the frequency of the heart beat. They might for instance provide an explanation of certain of the arhythmias. In general, however, the inertia of the effector mechanism in both the heart and the blood vessels is sufficiently great to smooth out such variations in the frequency of efferent impulses, so that the results of sympathetic activity are due to the total number of impulses arriving in a fairly long period of time.

In connection with these centrally determined rhythms I would like to call attention to the extremely labile character of the cells in the sympathetic centers and the extent to which their activity is modified by variations in their environment. The inhibition of sympathetic impulses, synchronous with respiration for instance, is due to some influence exerted by the respiratory center directly, for the effect persists after all afferent pathways are interrupted. Asphyxia invariably and promptly produces a marked increase in the discharge of impulses to the heart and blood vessels. Drugs

such as acetyl-chlorine, which acting peripherally produce vaso-dilatation, aid that dilatation when acting centrally by inhibiting the activity of the sympathetic cells with a consequent decrease in the discharge of constrictor impulses. Veratrine not only has its well-known stimulating action on the vagal centers but also inhibits the discharge of accelerator and constrictor impulses from the sympathetic centers, thus giving a remarkable picture of direct reciprocal action on two groups of nerve cells.

But we are primarily concerned with the nervous mechanism of cardio-vascular control as determined by normal reflex influences. How, to be specific, are the efferent messages to the heart and blood vessels modified by the afferent messages coming in from the outlying pressure receptors in the carotid sinus or aorta? To answer this question we have arranged to vary the pressure in the carotid sinus by means of a perfusion system while recording the discharge of sympathetic impulses (30). The effect is dramatic and striking. As the pressure is increased the number of efferent impulses decreases, and if the pressure be raised to 120 to 140 mm. Hg the impulses stop completely. Thus the accelerator and constrictor impulses are checked by the arrival at the centers of afferent messages signalling a rise in blood pressure.

It must be emphasized, however, that the afferent control of the sympathetic centers is not quite so simple and straightforward as the preceding paragraph indicates. If, for instance, the pressure within the sinus be elevated and maintained at a given high level, there is frequently an escape from the complete inhibition after some seconds. Or, on the other hand, we have often found quite the opposite situation in which the inhibition outlasts the afferent impulses by many seconds. In the latter case the afferent impulses have developed a condition in the centers which persists long after the inflow of impulses ceases. This is a phenomenon that may be related to modern theories which explain central inhibition or excitation by assuming the formation of some humoral substance at the site of the cellular processes. In the former case the centers quickly adapt to the afferent impulses and partly escape from their influence. Such variable effects emphasize again the extreme lability of the cardio-vascular centers and the im-

possibility of quantitatively predicting the effect of a given afferent stimulus unless all of the many factors by which the centers are influenced can be controlled and maintained constant.

In any event the degree and duration of sympathetic inhibition or vagal excitation increase with an increase in the total number of impulses sent into the central nervous system over the vasomotor afferents, either as a result of increased vascular pressure or increased duration of the stimulus. Similarly the degree and duration of the inhibition increase with an increase in the total number of afferent impulses when that increase is the result of additional afferent pathways coming into action. In one case, for instance, distention of the right carotid sinus by 160 mm. Hg produced a sympathetic inhibition for 13 seconds; distention of the left carotid sinus, an inhibition for 25 seconds; while the simultaneous distention of the two gave an inhibition for 40 seconds. Distention of either sinus alone at a pressure of 120 mm. Hg did not cause a complete inhibition, but when they were distended simultaneously at this pressure they did so. Here we have definite summation of the central effects produced by the impulses from each carotid sinus. And in general the effect is determined by the total number of afferent impulses flowing into the cardio-vascular centers from the several sources.

We may now gather together our evidence into a brief, integrated summary of how the nervous system regulates the heart and blood vessels. Many details are still lacking but the essential features are clear enough. Located in the walls of the aorta, of the carotid sinuses, in the mesentery and perhaps more generally throughout the vascular system are receptors sensitive to mechanical deformation. These sense organs respond to variations in pressure within the vessels by discharging a train of nerve impulses whose frequency closely follows fluctuations of arterial pressure. The fidelity with which they do so is strikingly illustrated in figure 17 where even the smallest variation in pressure is reflected in the impulse frequency. A rise in pressure also calls more receptors into action and increases the duration of response in each cardiac cycle. Thus, as the blood pressure rises, more impulses are transmitted to the cardio-vascular centers each unit of time.

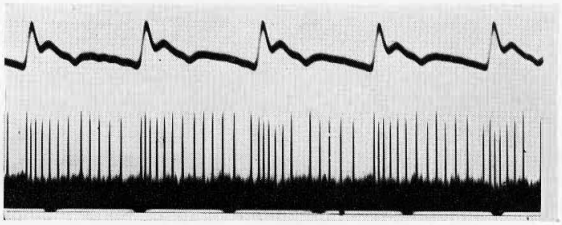

FIG. 17. Frequency of afferent impulses from a carotid sinus receptor closely following pulse pressure. (Bronk and Stella (19).)

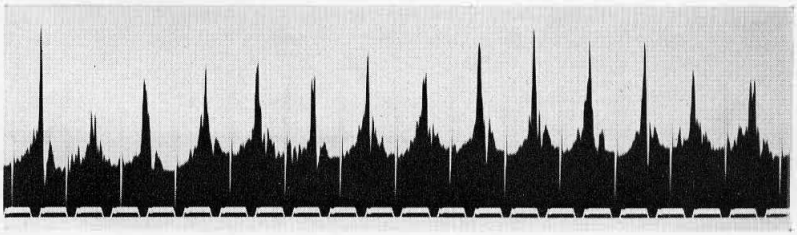

FIG. 18. Rhythmic discharge of sympathetic impulses to the heart produced by rhythmic stimulation of central end of carotid sinus nerve. Stimulus frequency shown as vertical white lines. The afferent stimulus rhythm is reflected in the efferent discharge rhythm, due, presumably to the recurring periods of sympathetic inhibition and escape. (Bronk, Solandt and Ferguson (30).)

Coming out from these centers over the sympathetic nerves is a steady stream of impulses which maintains the vessels in a state of tonic contraction and exerts a continuous accelerator influence on the heart. This is balanced by inhibitory impulses over the vagus to the heart and presumably by dilator impulses to the vessels. By such a reciprocal or balanced innervation, positive and effective control is possible.

This control is initiated by the nerve cells in the cardio-vascular centers whose activity is constantly varying in response to changes in the chemical composition of the blood, the activity of other groups of nerve cells, and especially in response to those sensory messages from the arterial walls which indicate so precisely the level of blood pressure. As these impulses signal a rise in pressure they decrease the activity of the sympathetic cells and stimulate vagus action with a resulting vasodilatation, cardiac inhibition and consequent drop in pressure. Thus the circulation is under a self-initiated control. The importance of the afferent messages in regulating the activity of the centers is shown by the last figure in which the sympathetic centers are being rhythmically driven by volleys of afferent impulses in a carotid sinus nerve.

Such are the mechanisms involved in one of the most essential regulatory systems in the body. The circulation may continue to function without it, but a delicacy of control is then lost. And such controls are characteristic of the normal organism.

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