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DISCHARGES IN MAMMALIAN SYMPATHETIC NERVES.

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RECORDS of sympathetic impulses in the cutaneous nerves of the frog have been published already [Adrian, 1930; Adrian, Cattell and Hoagland, 1931], and when these were made it was found that slow impulses, presumably sympathetic, could be detected in the cutaneous nerves of the cat when the hairs were erected as a result of asphyxia. The present work deals with the persistent or "tonic" discharges which are found in mammalian sympathetic nerves and are chiefly vaso-constrictor in effect. Records have been made from the cervical sympathetic and from various nerves in the abdomen such as the hypogastric and the nerves running from the cœliac ganglia. For the cervical sympathetic we have used rabbits under urethane or chloralose and for the abdominal nerves, rabbits and cats.

METHODS.

The usual technique for recording nerve impulses was employed, but as the arrangement at present in use for mammalian nerves has not been described, a brief account may be given here.

The animal is placed in a large, double-walled, metal container which is earthed to the water pipes of the laboratory and acts as a screen against electric disturbances and also as an incubator. The space between the walls is filled with water and heated to 45° C. The floor of the chamber is covered with water and the front is closed by a glass panel hinged at the top to allow access to the preparation. The atmosphere in the chamber is warm and moist enough to keep an exposed nerve in good condition without frequent irrigation, but there is little or no trouble from deposition of moisture on the electrode leads which are fixed in the roof of the chamber. As the body of the animal must be insulated, it is placed on a wooden stand coated with hard paraffin wax, and this rests in a wooden framework which keeps it above the level of the water on the floor of the chamber. The electrodes are small glass tubes containing Ringer's fluid and plugged at the lower end with kaolin or

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gelatine. A spiral of silver wire coated with silver chloride dips into the Ringer, and contact with the nerve is made by a moist thread running from the kaolin plug or by a small paint brush filled with gelatine. As a rule, the nerve is cut distally, the input electrode is near the distal end and the earthed electrode proximal to it, but when it is desired to record the impulses without cutting the nerve three electrodes are used, the middle leading to the amplifier input and the two on either side leading to earth. With this tripolar arrangement potential changes in the body of the animal (*e.g.* from the heart) do not affect the electrode system, though it is impossible to tell whether the impulses are ascending or descending. Movements of the nerve (from pulsating vessels, etc.) are prevented by looping it over a small glass hook.

The amplifier used in the present work has five valves, resistance-capacity coupled, leading to the four pentode output valves of the Matthews oscillograph. The coupling condensers and grid leaks were chosen so that a steady potential difference would be reproduced as a deflection falling to half its initial value in 0·5 or 0·05 sec. In most of the records shown in the figures the amplifier is working at ¼ or ⅛ of its maximum sensitivity. With ¼ sensitivity an input potential of 10 microvolts gives a deflection of 5 mm. on the recording surface.

The potential changes are viewed with a revolving mirror and converted into sound with a large cone loud speaker driven by a separate amplifier and giving adequate reproduction of bass notes. As the sympathetic impulses give very slow potential changes, they may be inaudible if the loud speaker has a poor response in the bass.

A few experiments have been made on cats previously decerebrated under chloroform and ether, otherwise the animals have been under full anæsthesia throughout.

GENERAL CHARACTER OF SYMPATHETIC IMPULSES.

When a sympathetic nerve is dissected out, cut distally and placed on the electrodes, it is usually found that a succession of slow potential waves passes down the nerve as long as the animal is in reasonably good condition. Typical records from the rabbits' cervical sympathetic and from various abdominal nerves are given in Fig. 1. The discharge consists of diphasic potential waves travelling centrifugally (as indicated by the direction of the first phase). The waves vary in size, but as a rule the majority of them do not vary much in contour or duration. The usual controls (killing the nerve, substituting a moist thread, etc.) show that the waves are due to nerve impulses and are not artefacts caused by movement or by potential changes in some other part of the animal.

Before discussing the grouping of the impulses and the frequency of the discharge under different conditions, we have to deal with the form of the individual waves and the nature of the fibres which produce them. Do they represent the activity of single fibres or of groups working more or less synchronously, and are they due to pre- or to post-ganglionic fibres or to both? Since the sympathetic fibres are too small to be examined individually, it is impossible to decide the number of fibres contributing to any given wave, but the potential changes are certainly larger than we might expect from single fibres of the sympathetic system. Many of them are at least three or four times as large as those produced in a nerve of the same size by single motor or sensory fibres of the somatic system. This may be shown by placing a small motor nerve (*e.g.* the top root of the phrenic) side by side with the cervical sympathetic on the electrodes and recording both somatic and sympathetic discharges simultaneously. The short circuiting by inactive tissue will be the same for both nerves, and it is found that the slow sympathetic waves are much larger than the rapid waves in the phrenic. As the sympathetic nerves do not give a greater potential change than the somatic when they are injured or stimulated electrically it is unlikely

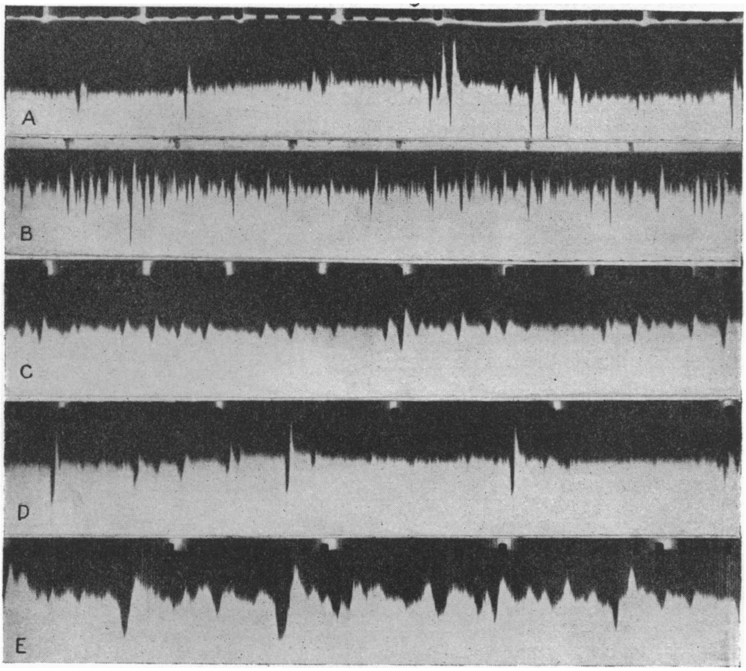

Fig. 1. Typical records of the persistent discharge in various sympathetic nerves. A. Exp. 13. Rabbit, urethane. Nerve from the cœliac ganglion to the inferior vena cava. B. Exp. 23. Rabbit, urethane. Left cervical sympathetic. C. Exp. 19. Cat, decerebrate. Left hypogastric nerve. D. Exp. 2. Cat, urethane. Left pre-sacral nerve (from lumbar chain to inferior mesenteric ganglion). E. Exp. 3. Cat, decerebrate. Nerve from the inferior mesenteric ganglion to the gut. Time marker (at the top of each strip) in these and all low speed records gives intervals of 0·25 sec.

that the potentials developed by each fibre are greater, but the general arrangement of the sympathetic system makes it quite likely that groups of fibres would be found working in very close connection, and a grouping of this kind would account for the large size of the waves.

It is probable, then, that the larger waves are due to groups of nerve fibres acting synchronously, but, if so, the different fibres in the group are often so well synchronized that they may be regarded as a single unit. This follows from the identical time relations of many of the waves: Fig. 1 shows that the interval between the two phases is fairly constant in any given record, and the uniform contour can be seen more clearly in Fig. 2 which gives several records made from the cat's hypogastric nerve with a high speed camera. It should be added, however, that besides the waves of constant form there are often some of more complex shape and longer time relations. One showing a double crest is given in Fig. 2 D. In two abdominal nerves all the waves have been very long and obviously complex, although the diphasic character is still retained (Fig. 1 E). Such waves are evidently due to volleys in a number of fibres discharging not quite simultaneously.

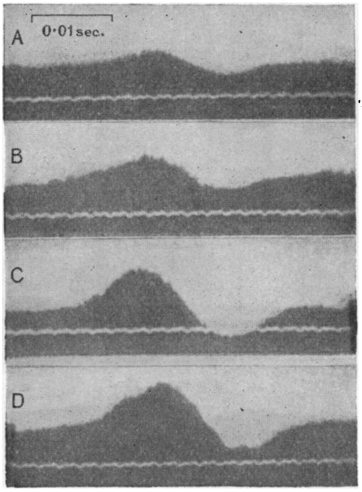

Fig. 2. Records of individual waves in hypogastric nerve discharge. A, B and C are examples of simple waves of different size. D is complex. Exp. 19. Cat, decerebrate. Left hypogastric nerve. 9 mm. between electrodes. Temp. 32° C. Time marker gives intervals of 0·0025 sec.

RATE OF CONDUCTION.

When the discharge consists mainly of simple waves of constant form we may fairly assume that the potential change in each fibre has the same form, whatever may be the number contributing to the wave. As Bishop, Erlanger and Gasser [1926] have shown, it is difficult to secure monophasic recording by damaging the nerve when its time relations are very slow, but we can gain some idea of the rate of conduction by varying the distance between the electrodes. Fig. 3*a* gives three diphasic waves from the cat's hypogastric made with electrode separations of 5, 9 or 15 mm. Waves of approximately the same size have been chosen, but in each case the wave has the same time relations as the others in the same record. By assuming that the potential change under each electrode has the form shown in Fig. 3*b* it is possible to reconstruct the three diphasic waves with fair accuracy. The rate of conduction then works out at 0·8 metre a sec. and this agrees very well with the rate of conduction of the potential wave produced by electric stimulation, for Fischer [1911] gives 0·7 metre a sec. for the splenic nerve of the ox and pig, and Erlanger and Gasser [1930] give 0·7 to 1·0 metre a sec. for the slow fibres in the white and grey rami (dog and cat). It agrees also with Dennig's measurements [1929] in which the latency of the end effect was recorded with stimuli at different points on the nerve, his figures being 0·8 metre a sec. for the nerve fibres to the sweat glands of the cat's foot and 0·71 metre for those to the nictitating membrane. The experiment shown in Fig. 3 was the only one in which we measured the rate of conduction, but the time relations of the diphasic waves in other experiments were always of the same order for a given electrode separation.

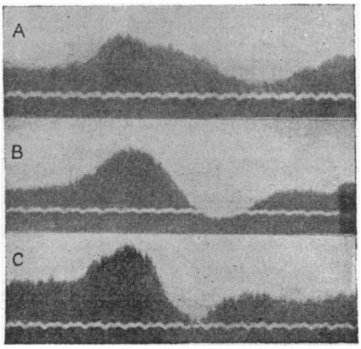

Fig. 3*a*.

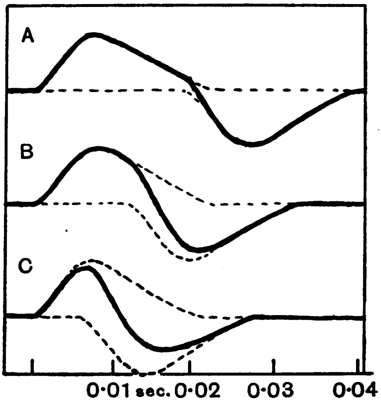

Fig. 3*b*.

Fig. 3*a*. Form of diphasic response with different electrode separations. Exp. 19. Cat, decerebrate. Left hypogastric nerve. Temp. 32° C. In A the distance between the electrodes was 15 mm., in B 9 mm. and in C 5 mm.

Fig. 3*b*. Reconstruction of potential change assuming a monophasic wave form as shown and a rate of conduction of 0·8 metre a sec.

In their investigation of the potential waves produced by electric stimulation Erlanger and Gasser [1930] found that the grey ramus contains some fibres which conduct at 10–20 metres a sec. in addition to those conducting at 0·7–1 metre. The faster fibres, which form the B group in their classification, arise, or develop their characteristic rate, in the sympathetic ganglia, since they are not found in the white rami or in the dorsal or ventral roots of the cord. We have not yet detected any potential waves which could be clearly ascribed to such fibres. Small and rapid fluctuations of potential have appeared occasionally, but we have not been able to decide whether they were true action potentials or merely interference effects caused by the overlapping of the slower waves. In some preparations of the cervical sympathetic there have been rapid ascending waves recurring in groups with the frequency of the heart beat, but further dissection has shown them to be due to fibres of the cardiac depressor running with the sympathetic trunk. It is usually possible to separate the strand giving the discharge of rapid impulses; it agrees in every way with the discharge of the cardiac depressor, and this is so characteristic that it can safely be used to identify the origin of the fibres.

PRE- AND POST-GANGLIONIC FIBRES.

According to Dennig and to Erlanger and Gasser the pre-ganglionic fibres conduct no faster than the post-ganglionic, but there might well be characteristic differences in the size of the individual waves or in their general arrangement. At present the only difference which we can be sure of is that the waves in a post-ganglionic discharge are on the whole larger than those in a pre-ganglionic. The origin of a given discharge can be decided by Langley's nicotine method, *i.e.* by painting ganglia with 0·5 p.c. nicotine solution or by injecting 10–30 mg. of nicotine into a vein. Painting the ganglion will break the connections in it between pre- and post-ganglionic fibres and injecting nicotine will break them throughout the body. By these methods we have found, as might be expected, that many of the potential waves appearing in the upper part of the cervical sympathetic are due to pre-ganglionic fibres, since they persist after a nicotine injection, and that those in the hypogastric nerve and other branches form the inferior mesenteric and cœliac ganglia are mostly post-ganglionic. The waves in the cervical sympathetic are fairly large and there is little to distinguish them from those in the other nerves, but in several experiments on the abdominal nerves where a ganglion has been painted, all the larger waves have dropped out leaving a succession of small waves of more uniform size. These may well be due to impulses in single pre-ganglionic fibres, the larger waves in the cervical sympathetic being due to a group of fibres acting in unison. It is, of course, to be expected that a post-ganglionic volley in a number of fibres acting as a unit would give a greater potential change than a single pre-ganglionic impulse, for the bulk of the nerve fibres concerned must be much greater.

In two experiments on the cervical sympathetic, cut below the superior cervical ganglion, it was possible to detect waves passing both up and down the nerve. The ascending waves were smaller, and as they remained after a nicotine injection they were evidently pre-ganglionic. The descending waves, some of them very large, were abolished by nicotine, and presumably arose from a group of nerve cells embedded in the nerve trunk and sending post-ganglionic fibres down it. In one of the experiments the presence of the nerve cells was verified histologically. A record showing both ascending and descending waves is given in Fig. 4. Owing to the close spacing of the waves it is not possible to make out any definite relation between pre- and post-ganglionic impulses, but it is evident that a preparation of this kind might be made to yield valuable information about the transference of activity from one neurone to another.

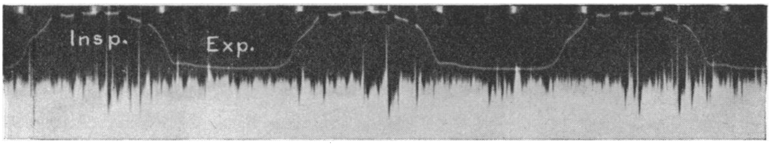

Fig. 4. Record from the cervical sympathetic showing ascending waves (first phase downward) and descending waves (first phase upward). The latter are post-ganglionic. The record also shows the respiratory grouping of the waves (cf. Fig 6). Exp. 20. Rabbit, urethane.

THE FUNCTION OF THE PERSISTENT DISCHARGE.

The discharges which we have recorded must be chiefly concerned in maintaining the tone of the blood vessels. It is known, for instance, that the cervical sympathetic exercises a persistent action on the blood vessels and on the plain muscle of the eye [Langley, 1900], but that its action on other structures (hairs and glands) is only occasional. The sympathetic nerves in the abdomen may exert a persistent inhibitory effect on the gut as well as a persistent vaso-constrictor effect on the blood vessels, but we have not succeeded in producing any clear modification of the discharge by stimulating the viscera, *e.g.* distending the bladder or pinching the gut. Indeed the only clear modifications have been produced by procedures which would be likely to affect the centres directly, such as the induction of asphyxia or the injection of nicotine, and by drugs which would affect the blood vessels and so give rise to reflex changes in vaso-motor tone.

In the rabbit or cat an injection of adrenaline (0·5 to 1 mg.) into a vein is followed at once by a complete cessation of activity in the sympathetic nerves. The pause lasts as long as 5–10 minutes and there is then a gradual return of the discharge, beginning with occasional isolated waves at long intervals (Fig. 5). The injection of histamine (1–2 mg.) in the cat has been followed by a great increase in the discharge, and we have occasionally seen a definite increase after inhalation of amyl nitrite. These effects may be due in part to a direct action of the drugs on the sympathetic centres or on the blood vessels supplying them, but the rise and fall of blood-pressure caused by the peripheral action of the drugs would be naturally followed by a reflex decrease or increase in the vaso-motor discharge. Moreover, adrenaline produces only a slight and evanescent change if the cardiac depressor nerves have been cut and the carotids tied above and below the sinus caroticus (two experiments). It is therefore a reasonable assumption that the discharge is influenced reflexly by the state of the vascular system, and that its function is mainly that of vaso-constriction. This conclusion lends an added interest to the fact discussed in the following section—namely, that the waves commonly occur in groups with the frequency of the heart beat or of respiration.

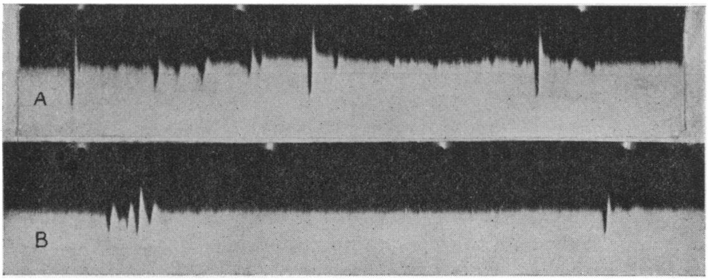

Fig. 5. Effect of adrenaline. Exp. 2. Cat, urethane. Pre-sacral nerve. A. Normal discharge. B. Return of the discharge after temporary abolition by an injection of 0·5 mg. adrenaline.

THE GROUPING OF THE WAVES.

The respiratory grouping.

In the rabbit one of the most remarkable features of the persistent discharge is that the frequency of the waves often rises and falls in time with the movements of respiration. The respiratory grouping was first noticed in the cervical sympathetic and we thought that it might be confined to this nerve, but it was then found that a rhythm just as well marked was usually present in the discharge of the abdominal nerves, *e.g.* those from the cœliac ganglion to the inferior vena cava. The respiratory rhythm has been definitely present in eight rabbits with vagi intact (three under chloralose and five under urethane) and absent initially in three (all under urethane). It has always been very well marked after section of the vagi (four experiments). Most of the experiments on cats were made before we had realized the importance of recording the respiration, but in the discharge of the abdominal nerves in decerebrate animals it has only once been possible to detect a respiratory grouping. The much slower rate of breathing may account for the difference, for in one cat under urethane with a respiratory rate of 30 a min. there is a well-marked grouping in the discharge of a nerve from the cœliac ganglion, and in another under chloroform the grouping is present in the hypogastric.

The effect is best shown in records made on a slowly moving surface. The characteristic appearance of such a record may be seen in Fig. 4, and others are given in Fig. 6. The tracing of respiration is made by a tambour leading from a 3-litre bottle which is connected to one branch of the tracheal cannula. The lever gives a downward movement on the record at the beginning of expiration; as the range of movement was very small when the other branch of the tracheal cannula was open to the air the records were usually made just after this was closed. The rate and depth of breathing were not affected for the first half-minute, and the use of the closed system gave a convenient means of testing the effect of increased CO_2, etc.

In the rabbit when the rhythm is present the discharge is at its maximum at the end of inspiration and the beginning of expiration. In animals with the vagi cut there is usually a definite pause during the latter part of expiration, but with the vagi intact there may be occasional waves throughout this period. When the respiration increases in depth and frequency as the animal breathes into the closed system the sympathetic discharge increases and the pauses may be obliterated, but the greatest activity always occurs in the same part of the respiratory cycle. When the tracheal tubes are clamped the same relation persists, the sympathetic discharge occurring at the height of each inspiratory spasm. In one decerebrate cat the discharge occurred in the hypogastric at the beginning of inspiration; in two other cats (anæsthetized) it persisted throughout inspiration.

An interaction between the respiratory and vaso-motor centres is known to occur under certain conditions, for the heart rate is often increased during inspiration by inhibition of vagal tone, and after curare the blood-pressure may continue to show waves with a respiratory rhythm although the chest is motionless[1]. It seemed worth considering, however, whether the grouping of the sympathetic discharge in the present experiments might not be due to some reflex or mechanical effect arising from the movements of the chest wall. Sensory impulses from

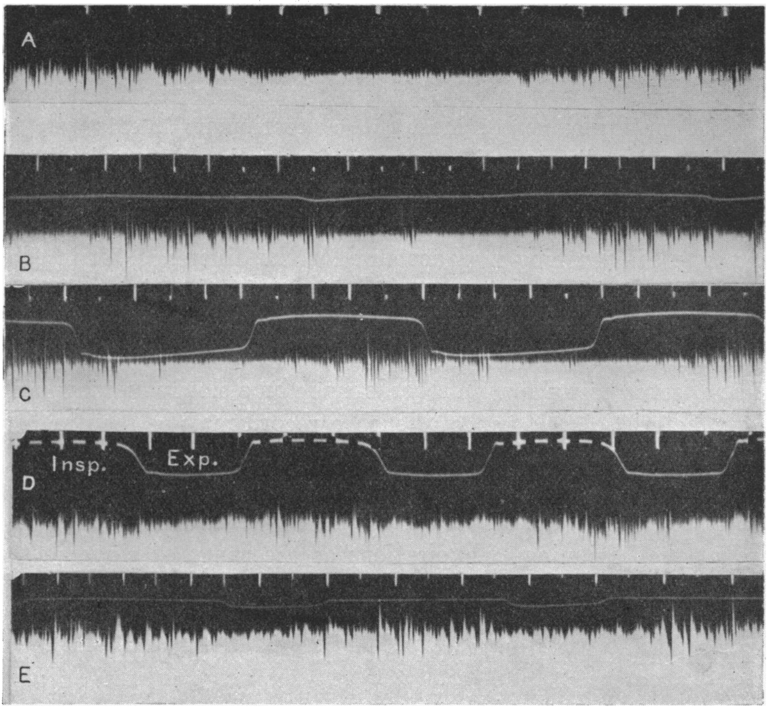

Fig. 6. Records from different nerves showing the grouping of the sympathetic discharge in phase with respiration. A. Exp. 11. Rabbit, chloralose. Right cervical sympathetic. B. Exp. 13. Rabbit, urethane. Vagi cut. Nerve from cœliac ganglion. Normal breathing. C. Exp. 13. Rabbit, urethane. Dyspnœa from breathing into closed system. D. Exp. 14. Rabbit, urethane. Left cervical sympathetic. E. Exp. 27. Cat, chloroform and ether. Left hypogastric. In the record of the breathing a downward movement denotes expiration.

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[1] Daly [1930] has repeated Fredericq's experiment in which the blood-pressure was recorded after the thorax and abdomen had been opened and the phrenic nerves cut. The pressure then falls during inspiration and rises during expiration. (Experiments on cats.)

the vagus could be ruled out, since the rhythm was most clearly marked when both vagi had been cut. To eliminate the effect of the lung movements one experiment was made in which the thorax was opened and the lungs were inflated by a pump. During the artificial respiration the discharge in the cervical sympathetic was irregular, but when the pump was stopped a definite rhythm appeared in time with the movements of the ribs. In this animal the vagi were intact, and the absence of the rhythm during artificial ventilation may have been due to the sensory impulses reaching the respiratory centre at each inflation of the lungs and interfering with the proper rhythm of the centre. In three more experiments the preparation was made so as to allow a more complete isolation of the brain stem from sensory impulses. The vagi and cardiac depressors were cut and the carotids were tied, in one case both above and below the sinus caroticus. Enough curare was injected to stop all movement and the respiration was continued artificially. In all three experiments the sympathetic discharge occurred in well-marked groups

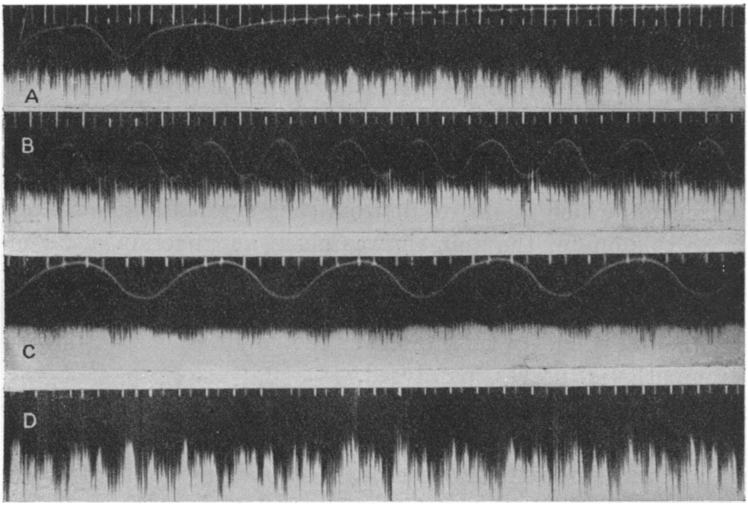

Fig. 7. Grouped discharges in the cervical sympathetic persisting after active respiratory movements have been paralysed by curare. Exp. 23. Rabbit, urethane. Vagi cut and carotids tied. Artificial ventilation. A. The rhythm is absent during over-ventilation, but returns as soon as the pump is stopped. B and C. The rhythm is independent of the frequency of the passive chest movements. In both records the groups occur at the rate of 71 a min. D. Asphyxia. The discharge is increased, but there is still some evidence of grouping. In the record of artificial respiration a downward movement denotes inflation of the chest.

at intervals of 1–2 sec., *i.e.* at intervals corresponding to the respiratory rate before curare. Records are given in Fig. 7, and it will be seen that the rhythm of the discharge is independent of that of the artificial respiration. In fact an increase in the rate of ventilation causes a decrease in the rhythm and *vice versa*, though the change in rhythm does not often amount to more than 10 p.c. When ventilation is stopped the number of waves in each group increases and the rhythm quickens, though again the change is not very great. At a later stage, as the blood-pressure begins to rise, the intervals between the groups become filled up, but the rhythm can still be detected by ear, although in the records the waves are often too closely crowded to show it.

In these experiments the rhythm of the sympathetic discharge could not have been determined reflexly by the movements of the lungs or chest wall, but there was still a possibility of reflex control from the sensory effects which might result from each sympathetic outburst. To eliminate this one of the animals was given an injection of 30 mg. of nicotine to break the connection between pre- and post-ganglionic fibres. The rhythm remained as definite as before, though it was increased in rate by the injection. In this animal as the vagi were cut and the motor and sympathetic nerves paralysed, the rhythm could only be maintained reflexly through the action of the remaining parasympathetic nerves, and the likelihood of this must be very small.

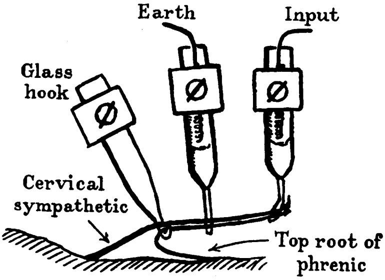

Fig. 8. Arrangement of electrodes for recording simultaneously from the cervical sympathetic and the highest root of the phrenic.

It remains to prove that in the curarized animal the rhythm of the sympathetic discharge still keeps pace with that of the respiratory centre, for although the rate is altered by asphyxia or over-ventilation it is conceivable that the sympathetic centres are now working with an automatic rhythm of their own. The point can be decided by recording the impulses in the phrenic nerve as well as those in the cervical sympathetic. The uppermost root of the phrenic is easily accessible in the rabbit, and when cut distally it can be looped back so as to lie at the side of the cervical sympathetic on the recording electrodes (Fig. 8).

The motor impulses in the phrenic give brief action potentials which make a much greater noise in the loud speaker than the slow sympathetic waves, but the magnitude of the potential changes is less and the phrenic discharge may be almost invisible in a record showing large sympathetic effects. To equalize the slow and fast waves one of the coupling condensers in the amplifier was made small enough to reduce the size of the slow waves without affecting the fast. A capacity of 0·006 mfd. was found by trial to give records in which both could be distinguished.

A record showing both the phrenic and sympathetic discharge in the curarized animal with vagi cut is given in Fig. 9, together with records of the two nerves separately, one taken immediately after the other.

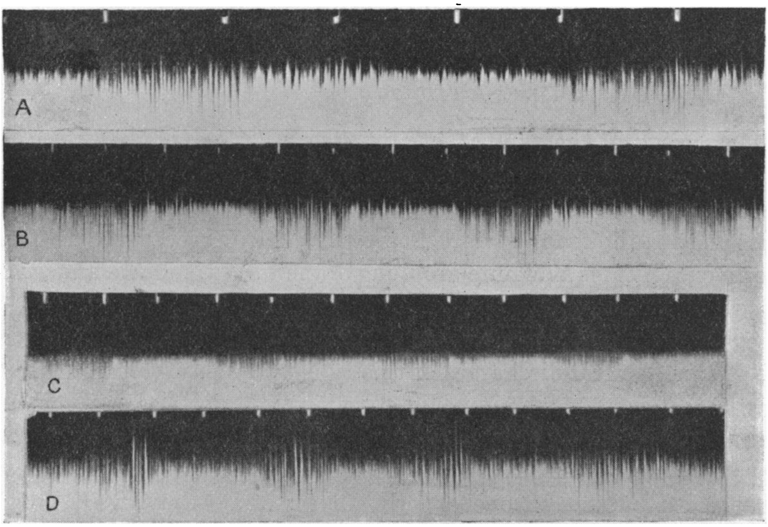

Fig. 9. Sympathetic and phrenic discharges in the curarized animal with artificial respiration. Exp. 23. Rabbit, urethane. Vagi cut and carotids tied. Sympathetic waves reduced in size by 0·006 mfd. Coupling condenser. A before and B shortly after an injection of 30 mg. of nicotine. The sympathetic discharge (slow waves) keeps in phase with the phrenic (rapid waves), though the phrenic outbursts are of shorter duration. The individual waves are scarcely visible in the record as reduced, but the pause between each combined outburst can be seen clearly. C. Record from the phrenic root alone. D. Record from the cervical sympathetic alone, taken shortly after C.

The phrenic discharge begins well before the main sympathetic outburst and ends well before the latter has begun to decline. The same relation between the two discharges was preserved throughout the experiment, though the rhythm was varied by under or over-ventilation, asphyxia, nicotine injection, etc., the only change being that in partial asphyxia the sympathetic discharge was more continuous whereas the phrenic still gave distinct outbursts with pauses between. It follows that in the absence of sensory impulses from the vagi the sympathetic centres in the rabbit are directly stimulated by each period of activity in the respiratory centre. When the vagi are intact it is possible that the sensory discharge at inspiration also affects the sympathetic centres directly, though it seems more likely that the respiratory centre is still the controlling factor. But the occasional absence of the respiratory rhythm in rabbits and its more frequent absence in cats shows that the respiratory centre is not always in control, and when it is not it is interesting to find that the sympathetic discharge may now show a grouping corresponding to that of the heart beat.

The cardiac grouping.

A grouping of the sympathetic waves at a frequency equal to that of the heart beat has appeared in two rabbits and it was occasionally present in a third. A similar grouping appeared in three of the experiments on cats, though in two the heart beat was not recorded. In all these experiments there is a definite grouping of the waves, and the appearance of the cardiac rhythm is not due merely to movements of the base line caused by the pulsation of vessels transmitted mechanically to the nerve. Fig. 10 gives several discharges of this type together with records of the electrocardiogram made immediately afterwards. In the rabbits the rhythm was present initially with the animal under urethane and breathing quietly, and in all it was ultimately replaced by the usual respiratory rhythm. In one experiment section of both vagi brought about the change and in another an injection of adrenaline. In the third the cardiac grouping disappeared when the carotids were tied (the cardiac depressors having been cut previously). As it has appeared so seldom we cannot say whether it would invariably disappear when the sensory impulses from the depressors and sinus caroticus nerves are cut off, though it seems most likely that the grouping must be dependent on the rhythmic sensory outbursts reaching the brain stem from these nerves. It must be admitted that the close agreement with the cardiac rhythm might be merely a matter of chance, for the effect of varying the heart rate was not investigated; but although the regular appearance of single waves at intervals of 0·2–0·3 a sec. might have nothing to do with the heart beat, it is unlikely that all the waves in the discharge would keep so closely together unless they were controlled by some dominant rhythm.

The presence of these rhythms shows that the sympathetic centres are capable of fairly rapid fluctuations in activity, and that the conditions to which they are exposed are never likely to be steady. As long as the respiratory centre is intact its activity will presumably form a background of waxing and waning excitation, even though its effect may be too slight to appear in the discharge, and the afferent nerves from the blood vessels will also contribute a fluctuating stimulus with the rhythm of the heart beat. In view of these disturbing and competing factors it is easy to see why the sympathetic nerves never show a regular succession of waves comparable to the regular discharge of impulses from an end-organ or a motor neurone exposed to a steady stimulus. When neither cardiac nor respiratory rhythm can be detected the discharge is usually intermittent with pauses as long as half a second between some of the waves (cf. Fig. 1), though in asphyxia it becomes continuous.

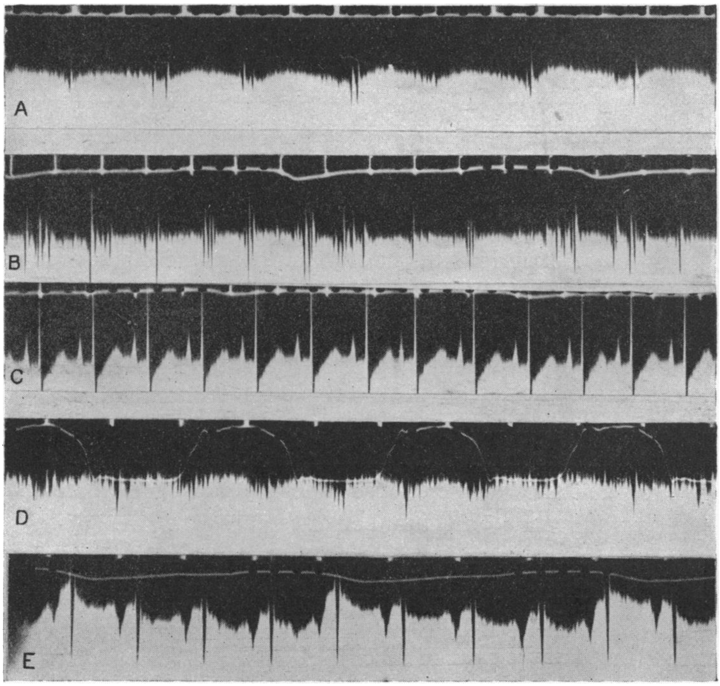

Fig. 10. Records showing the cardiac grouping of the sympathetic discharge. A. Exp. 16. Cat, urethane. Hypogastric nerve. B. Exp. 13. Rabbit, urethane. Nerve from cœliac ganglion. C. Exp. 13. Electrocardiogram made immediately afterwards. In this animal the respiratory grouping appeared after section of the vagi; it is shown in Fig. 6 B and C. D. Exp. 18. Rabbit, urethane. Cervical sympathetic. Dyspnœa from rebreathing. E. Exp. 18. Electrocardiogram made soon after. In this animal the respiratory grouping appeared after the discharge had been temporarily abolished by an adrenaline injection.

DISCUSSION.

The connection between the vaso-motor and respiratory centres.

The persistent discharges which we have recorded must be mainly vaso-constrictor in their effects. They are increased in asphyxia as the blood-pressure begins to rise and they are modified, as we should expect vaso-constrictor discharges to be modified, by the injection of drugs. The question then arises whether the grouping of the discharge in phase with respiration is of any practical value to the animal. Since the movements of the chest produce fluctuations of the blood-pressure by their mechanical effects on the vessels, it is possible that the fluctuating sympathetic discharge might tend to counteract these effects and to equalize the pressure at inspiration and expiration. In rabbits under the conditions of our experiments the maximum fall of blood-pressure was found to occur at the end of inspiration and the maximum rise at the end of expiration. The sympathetic discharge is at its height at the end of inspiration, and if its effect on the blood vessels were immediate it would counteract the fall of pressure. But it is unlikely that the mechanical effects would always tend to produce a fall of pressure at the moment when the sympathetic discharge tends to produce a rise. As Lewis [1908] has shown, the effect of the respiratory movements on the blood-pressure depends on a number of factors, and the phase relation may vary with the rate and depth of breathing, the muscles employed, etc. The sympathetic discharge seems to reach its maximum at a fixed period in the respiratory cycle, so that under some conditions it might accentuate the pressure changes instead of smoothing them out. It is also unlikely that each group of impulses would produce an immediate vaso-constriction, for with artificial stimulation of a sympathetic nerve there is a latency of a second or more before the blood vessels begin to contract. Indeed the vessels react so sluggishly that the degree of contraction is not likely to fluctuate at all when the impulse groups recur at intervals as short as 1 sec. In the curarized rabbits when the artificial respiration was stopped the blood-pressure as recorded by a mercury manometer rose smoothly in two experiments in spite of a definite respiratory grouping in the sympathetic discharge. In the third the blood-pressure appeared to rise in a series of steps, but unfortunately the rise was too great for the range of the recording system which was used in this experiment, and we cannot say where the steps appeared in relation to the outbursts in the nerve.

Since it seems improbable that the respiratory grouping is of much value in preventing fluctuations of blood-pressure we must regard it as the natural consequence of the close connection between the vaso-motor and respiratory centres. The respiratory centre is the region most sensitive to changes in the blood, and its connection with the vaso-motor centre will enable the latter to react promptly to changes which are too small to affect its own less sensitive cells. In the goldfish brain stem Adrian and Buytendijk found that the potential gradients accompanying each phase of activity in the respiratory centre were readily detected in any part of the medulla. It is at least conceivable that these potential changes are enough in themselves to modify the activity of the vaso-motor centre without direct nervous connection, though it must be admitted that the effect is to some extent selective, for it is probable that the vagal centre is inhibited during the period in which the sympathetic centre is excited.

Comparison of sympathetic and somatic discharge.

If we compare the tonic sympathetic discharge with the discharge in a motor nerve maintaining the contraction of a skeletal muscle, the main difference is found in the much smaller number of potential waves in the sympathetic and in their greater size. If we are right in supposing that the larger waves are due to a number of fibres acting synchronously, the difference expresses the fact that the sympathetic system is arranged for the wide distribution of an activity arising in relatively few neurones in the cord. It is well known that the number of post-ganglionic fibres greatly exceeds that of the pre-ganglionic—for a particular case Billingsley and Ransom [1918] give the ratio as 32 to 1—and that the stimulation of a few pre-ganglionic fibres may produce widespread effects. If the ganglion acts merely as a region where one path branches into many, the post-ganglionic discharge would naturally consist of synchronous impulses in large groups of fibres. The effectors supplied by the sympathetic system react so sluggishly that it can make little difference whether the impulses are discharged by synchronous volleys widely spaced or by independent fire in each nerve fibre, whereas in the somatic nerves it can make all the difference between a steady contraction or a tremor, and independent firing is the rule except at high frequencies.

We are not in a position to say whether the pre-ganglionic fibres usually act independently or in groups, or whether a single pre-ganglionic impulse or volley ever sets up a succession of post-ganglionic volleys. It is clear that this does not always happen, for a post-ganglionic discharge, when cut down almost to vanishing point by an injection of adrenaline, usually consists of isolated waves separated by intervals of a second or more; each of the waves may appear at about the same time in the respiratory cycle, and it is therefore unlikely that any of them can be due to an after-discharge from the ganglion cells. On the other hand the ganglion cell, or some part of the neurone other than the axon, can be made to give a repeated discharge at a fairly high frequency. When a ganglion is painted with 1 p.c. nicotine there are often sudden outbursts of waves in a regular series which rises in frequency to about 100 a sec. and falls more slowly. These outbursts are comparable to those produced by injury in certain mammalian nerve fibres and in the nerve ganglia of insects, though their maximum frequency is lower (judged by ear and by observation with the revolving mirror). In one experiment on the hypogastric outbursts of this kind were observed for a short time immediately after the preparation was set up. They arose from a point in the nerve between the two electrodes, and on examination afterwards the nerve was found to contain a small group of nerve cells in this region. Apart from this instance, where the nerve cell outbursts were probably due to injury in dissection, and from another where the origin of the discharge was more uncertain, we have found no evidence of spontaneous activity in ganglion cells.

Many points have been left unsettled, but so far it may be said that although some of the features of the sympathetic discharge have been unexpected, we have found nothing to conflict with what is known of the reactions of nerve cells and fibres in general or of the structure and functions of the sympathetic system.

SUMMARY.

The persistent discharges which occur in mammalian sympathetic nerves have been investigated in the cat and rabbit by amplifying the potential waves in the nerve and recording them photographically. The waves are slow diphasic potential changes conducted at a rate of about 0·8 metre a sec. (one experiment). The larger waves are mostly post-ganglionic and they are probably due to volleys of impulses occurring in groups of sympathetic fibres, since they are several times as great as the action potentials produced in a nerve of the same size by single motor or sensory fibres. Some of the waves are obviously complex and due to volleys which are not quite simultaneous.

The discharges which have been recorded are mainly concerned with

vaso-constriction. In the majority of the experiments the waves tend to occur in groups with the frequency of the heart beat or of respiration. The respiratory grouping is due to a direct action of the respiratory centre on the vaso-motor centre, for it persists in the curarized animal after artificial respiration has been stopped and the outbursts in the sympathetic are still in phase with the motor discharges in the phrenic. When the respiratory grouping occurs the maximum discharge coincides with inspiration.

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