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THE ACTIONS OF ANTIDROMIC IMPULSES ON GANGLION CELLS

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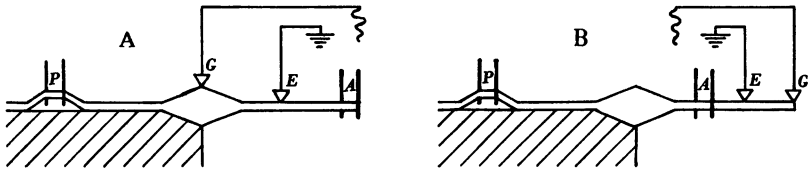
Antidromic impulses backfired into motoneurones have been employed in many recent investigations on motoneurones [Denny Brown, 1928, 1929; Eccles, 1931; Eccles & Sherrington, 1931*b*, *c*; Eccles & Hoff, 1932; Gasser & Graham, 1933; Umrath, 1933; Hughes & Gasser, 1934*a*; Lorente de Nó, 1935*b*], but complications introduced by the uncertain extent to which motoneurones are played upon by internuncial neurones have always presented difficulties in the interpretation of the experiments. On account of the absence of these internuncial neurones the superior cervical ganglion [cf. Brown, 1934] is particularly suitable for this attempt to reinvestigate the action of an antidromic impulse on a nerve cell, a subject on which there is much conflict of opinion [cf. Lorente de Nó, 1935*b*]. A preliminary account of this work has already been published [Eccles, 1935*d*].

The method of experiment is similar to that previously described [Eccles, 1935*a*], but, on account of the frequent shortness of the postganglionic trunk in cats, Belgian hares have been employed in five out of the thirty experiments. With the exception of the non-medullated S_1 postganglionic fibres [Bishop & Heinbecker, 1932], the S_1 and S_2 groups of ganglion cells correspond with those in cats, so no special reference need be made to the experiments on Belgian hares. In all experiments antidromic volleys in the postganglionic trunk have been set up by induction shocks applied through electrodes placed on this trunk well clear of the ganglion, and the responses of the ganglion cells have been recorded by electrodes G and E placed in either of the positions of Text-fig. 1. In position A the electrical responses of the ganglion cells to preganglionic or antidromic volleys are recorded directly, while in position B these responses are only indirectly observed, appearing as changes in the

impulses discharged by the ganglion cells in response to a preganglionic volley set up at electrodes *P*. This latter method of recording was only used in some of the experiments of section D. Stimulus artefacts are diminished by carefully stripping the sheath off the postganglionic trunk, by keeping the nerve free of excess moisture between the stimulating electrodes and the earthed lead, and by employing an earthed lead as large as possible. An earthed bridge balancing device has not been used.



Text-fig. 1. Diagrams showing the positions of the recording electrodes, *G* (grid) and *E* (earth), and the stimulating electrodes, *P* (preganglionic) and *A* (antidromic). The shaded region shows the extent of the contact of the preganglionic trunk and the ganglion with the body of the cat.

Results

A. *The ganglionic action potential set up by an antidromic volley*

Pl. I, fig. 1, shows typical spike potentials set up by single stimuli applied either to the postganglionic trunk (observations 1 and 3) or to the preganglionic trunk (obervation 2), the arrangement of the stimulating and recording leads being as shown in Text-fig. 1A. Shortly after the stimulus artefact in observation 1, a diphasic action potential begins with a negativity of the lead nearer the stimulating electrodes on the postganglionic trunk. This potential change is obviously due to the volley of impulses propagated antidromically, and from the latent period the approximate conduction velocity may be calculated—in this case about 2 metres a second. There is also a considerably faster volley (at least 4 metres a second), which in observation 1 is largely submerged by the stimulus artefact, for it appears in observation 3 when this artefact is shortened by diminishing the stimulus strength. This volley is transmitted by postganglionic fibres whose threshold and conduction velocity show that they form the S_1 group [Eccles, 1935*a*], the larger and slower volley being mainly in the S_2 group of fibres, though presumably the S_3 and S_4 groups are also included. The absence of this distinct S_1 response with Belgian hares may be correlated with the uniform character of their postganglionic fibres, all groups being non-medullated.

With the upward deflection in observation 1 (Pl. I, fig. 1) the lead on the ganglion becomes negative to the postganglionic lead, thus signalling the arrival of the antidromic volley at the ganglion. The area (potential × time) of this upward deflection is always much larger than the initial downward deflection, suggesting that an antidromic impulse is not blocked at the origin of the axon, but traverses the ganglion cell and possibly the dendrites, setting up there a larger spike response than in the axon. Now a preganglionic volley evokes a response in which with identical leads the initial upward deflection is much larger than the later downward deflection (observation 2), *i.e.* the spike potential evoked from the ganglion is again larger than that from the postganglionic trunk; hence it also appears probable that the impulse discharged from a ganglion cell down its axon traverses in addition that cell and possibly its dendrites [cf. Eccles, 1935*a*, section E]. A comparison of the action potentials shows that the ganglion cell responses evoked by a maximal preganglionic volley are always more asynchronous than those set up by a maximal antidromic volley, and this probably is sufficient to account for the upward deflection in observation 2 being smaller than in observation 1 without assuming that the maximal preganglionic volley fails to set up a discharge from some ganglion cells. This greater asynchronism of the preganglionic response is of course due to the dispersion in the durations of the individual synaptic delays.

In addition to the diphasic spike response an antidromic volley always sets up a slow potential change in which the ganglionic lead is positive to the postganglionic lead (Pl. I, fig. 2, observations 2 and 4). This slow positive wave resembles that set up by a preganglionic volley, being practically confined to the ganglion [cf. Eccles, 1935*c*, section A], and having a similar time course (cf. Pl. I, fig. 2, observations 1 and 3 with 2 and 4), but it always reaches a maximum sooner than the preganglionic slow positivity, and, when both volleys are maximal, it often is considerably smaller in potential. In about half the experiments, however, the maximum positivity is little if any less than that set up by a maximal preganglionic volley, but even then the rate of decay is always quicker for the antidromic response (cf. Text-fig. 3).

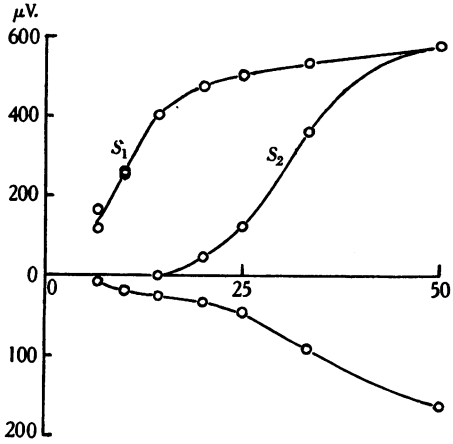
In making this comparison every precaution has been taken to ensure that the antidromic volley is fully maximal. Thus maximality is not assumed until a considerable further increase in the strength of the antidromic stimulus fails to increase either the spike or the slow positivity of the antidromic response. But such strong stimuli may give such large

artefacts that the base-line of the amplifier is displaced throughout the whole duration of the slow positivity. These displacements of the base-line may be detected by a shift of the S_2 diphasic spike relative to the initial base-line, but their later course can only be controlled by two methods to be described later, one depending on the removal of the slow positive wave by nicotine (Pl. I, fig. 4, observation 5), and the other on the occlusion of the positive wave by a P wave set up by a preganglionic volley at various intervals later (Text-figs. 13, 17B). When the stimulus artefact is thus controlled, an antidromic volley still sets up a slow positive wave smaller than that of a preganglionic volley. As the slow positivity is largely if not entirely produced by the ganglion cells, any injury blocking conduction in postganglionic fibres central to the cathode of the antidromic electrodes would necessarily result in a submaximal antidromic response regardless of the strength of the antidromic stimulus. Doubtless in some experiments such injury has played a part in diminishing the antidromic response, but by careful dissection of the postganglionic trunk this has been avoided as far as possible, and in any case submaximality of the antidromic response would not explain the faster decay of the slow positivity. It may, therefore, be provisionally concluded that a maximal antidromic volley sets up in the ganglion a slow positive wave which occasionally may be almost as large as that set up by a maximal preganglionic volley, but which is often much smaller and always decays more quickly.

Pl. I, fig 3, shows a typical series of antidromic responses elicited by stimuli of different strengths, the absence of an S_2 spike showing that the weakest stimuli (observations 1, 2 and 3) only set up antidromic impulses in S_1 fibres. The small, slow, positive wave set up in these observations must be produced by S_1 ganglion cells. The much larger positive wave in observation 5 must be mostly due to the large S_2 response which is evoked by the stronger stimulus, for the S_1 spike is but little larger than in observation 3. The time course of the S_1 positive wave is slightly quicker than that of the combined response, and hence must be a little quicker than the S_2 positive wave. The relative sizes of the slow positive waves set up by S_1 and S_2 antidromic volleys may be deduced from Text-fig. 2, in which the potentials of the S_1 and S_2 spikes and the slow positive waves are plotted against the respective strengths of the antidromic stimuli. The rapid increase in the P wave is clearly due to the increasing S_2 response. Text-fig. 2 shows that for the same spike potential the slow positive wave of the S_2 ganglion cells is about three times that of

the S_1 ganglion cells. There can be little doubt that this ratio, which is typical of other experiments, is too great to be explained by greater asynchronism of the S_2 response giving rise to a relatively greater reduction in the S_2 spike; hence it seems likely that an antidromic impulse evokes a slow positive wave whose potential relative to the spike potential is greater for an S_2 than for an S_1 ganglion cell.

Analysis by varying the strength of the preganglionic stimulus, by the action of nicotine in various concentrations, and by interaction of successive preganglionic volleys, has shown that the slow potential wave

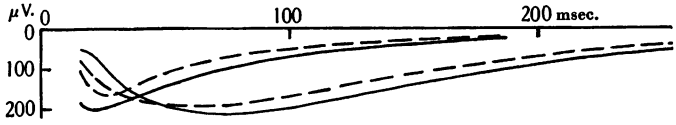


Text-fig. 2. The potentials of the S_1 and S_2 antidromic spikes are plotted as ordinates against as abscissæ the respective strengths of the stimuli in arbitrary units. The potentials of the corresponding slow positive waves are plotted downwards.

set up in the ganglion by a preganglionic volley is composed of a negative wave N overlapping a slower positive wave P [Eccles, 1935*c*], both waves reaching their maximum at about 20 msec., but N decaying at more than twice the rate of P. The more rapid decay of N results in the phase of increasing positivity for 100–150 msec., and beyond this point of maximum positivity the absolute rate of decay of N is less than that of P. Pl. I, figs. 2, 3 and 4, show that the slow potential wave set up by an antidromic volley also has a phase of increasing positivity, though it usually does not last for more than 100 msec., and this suggests that this slow positive wave is also compounded of a short negative wave N running concurrently with a positive wave P. Moreover, painting the ganglion with dilute nicotine always removes simultaneously the phases of increasing positivity with both preganglionic and antidromic responses

(Pl. I, fig. 4, observations 3, 4). The provisional conclusion that an antidromic volley sets up an N wave similar to that set up by a preganglionic volley is confirmed by experiments on the interaction of antidromic and preganglionic volleys in section C.

After the removal of the N wave by nicotine the slow positive wave is seen to be maximal right at the end of the ganglionic spike, hence it may be concluded that normally the P wave is maximal not later than this point, i.e. within 20 msec. of the setting up of the antidromic volley. The N wave also must normally reach the maximum within 20 msec., and so both the N and P waves set up by an antidromic volley have time courses similar to the N and P waves set up by a preganglionic volley [cf. Eccles, 1935*c*, Text-fig. 9]. However, the N wave set up by a maximal antidromic volley is always smaller than that set up by a preganglionic volley and sometimes it is much smaller (Pl. I, fig. 2), for with an



Text-fig. 3. Superimposed curves of the slow potential waves shown in Pl. I, fig. 4, the preganglionic responses being shown by the continuous lines and the antidromic by the broken lines. The two lower curves are obtained before, the two upper after painting the ganglion with 0·005 p.c. nicotine.

antidromic volley the N wave is always smaller relative to the P wave than it is with a preganglionic volley. In some experiments this relationship is obscured, for the early part of the antidromic N wave always suffers an apparent increment on account of the overlapping latter part of the antidromic spike response of the ganglion, which is of course in the same direction; while, conversely, the early part of the preganglionic N wave always appears diminished on account of the diphasic artefact of the spike response. The smaller antidromic N wave accounts for the earlier point of maximum positivity after an antidromic volley, and the allowance for the larger preganglionic N wave would also result in the preganglionic P wave being larger relative to the antidromic P wave than at first appeared from comparison of the slow positive waves.

Pl. I, fig. 4, observations 3 and 4, shows that, in addition to removing the N wave, nicotine also shortens and diminishes the P waves set up both antidromically and preganglionically [cf. Eccles, 1935*c*, section C]. However, it will be seen in Text-fig. 3 that the preganglionic P wave is

still larger. This identical sensitivity to nicotine suggests that an antidromic volley sets up *N* and *P* waves exactly like those set up preganglionically.

In Pl. I, fig. 4, observation 5, a still larger dose of nicotine has almost abolished all the slow positive wave after the spike. It is possible that the small remaining positive wave is due to displacement of the base-line by the stimulus artefact. In this way the action of nicotine provides a control demonstrating that the stimulus artefact is certainly reduced to negligible proportions within 50 msec. This dose of nicotine, while hardly affecting the antidromic spike response, almost completely abolishes the spike set up by a preganglionic volley (observation 6). It may, therefore, be concluded that nicotine prevents a preganglionic volley from setting up a discharge of an impulse from a ganglion cell by a block central to the point to which an antidromic impulse can penetrate.

When both amplifier leads are on the preganglionic trunk, an antidromic volley does not give rise to any action potential, thus confirming the irreversibility of transmission through the ganglion observed by Bishop & Heinbecker [1932] and Brown [1934]. Moreover, when one amplifier lead is on the ganglion and one on the preganglionc trunk, only a very small action potential is produced by an antidromic volley, the preganglionic trunk acting as a non-specific lead from the ganglion cells and the postganglionic fibres [cf. Eccles, 1935*a*]. With concentric needle electrodes in the ganglion an antidromic volley gives rise to a diphasic spike potential, the first phase being as usual of opposite sign to that set up by a preganglionic volley. The slow potential waves produced by the antidromic volley were not originally detected with these leads [Eccles, 1934], for they were obscured by the large slow stimulus artefact.

Discussion. When an antidromic volley is backfired into motoneurones of the frog's spinal cord, Umrath [1933] recorded a series of potential changes very similar to those described here for ganglion cells—an initial spike followed by slow negative and positive waves—but he suggested that the slow negative wave was the action potential produced by the antidromic impulses traversing the motoneurones. Stimulation of the dorsal roots produced the same sequence of waves, both being larger and the positive wave longer, but these waves presumably would be partly produced by internuncial neurones. Application of 1 p.c. phenol to the spinal cord removed the negative wave set up by a dorsal root volley, thus resembling dilute nicotine action on the ganglion, but contrary to the ganglion observations an antidromic volley still produced its full *N* wave.

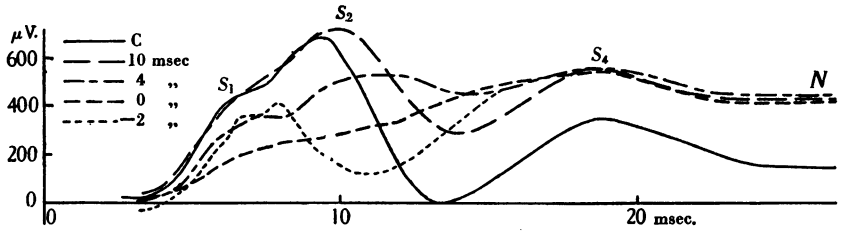
In apparent contradiction to Umrath, Gasser & Graham [1933] and Hughes & Gasser [1934*a*] found that an antidromic volley set up a spike action potential but no slow waves in the cat's spinal cord. However, the leads employed by Gasser and his co-workers are unsuitable for detecting potential waves developed by the motoneurones, and, on account of Umrath's observations on the frog, it seems likely that such waves would be recorded with suitable leads, for as shown by Gasser and his co-workers and Barron & Matthews [1936] nerve cells in the spinal cord certainly develop slow *N* and *P* waves, and one would expect frog's motoneurones to resemble a cat's motoneurones at least as closely as a cat's ganglion cells. The spike action potential followed by *N* and *P* waves might, therefore, well be the characteristic response evoked in any nerve cell by an antidromic impulse.

B. *The refractory period set up by an antidromic volley*

Pl. II, fig. 5, shows a typical series of ganglionic spike potentials set up when single maximal antidromic and preganglionic volleys are fired into the ganglion at various short intervals apart, the control observations 1 and 6 being respectively the isolated preganglionic and antidromic responses. In observation 5 a preganglionic volley clearly gives rise to a spike potential resembling the control but a little smaller than it, showing that at this interval (11·4 msec.) the ganglion is but little affected by the preceding antidromic volley; while in observation 4 an antidromic stimulus applied 11·9 msec. after the preganglionic produces almost no change in the subsequent course of the preganglionic action potential, indicating that at the time of the antidromic stimulus most of the postganglionic fibres are refractory—presumably on account of the volley just previously discharged along them in response to the preganglionic volley.

The other observations of Pl. II, fig. 5, require analysis. Now if the antidromic volley is not too late relative to the preganglionic volley, it will excite all the ganglion cells before any impulses have been set up in them by the preganglionic volley. Under such conditions it may be assumed that the spike potential of the antidromic volley is unaffected by the preganglionic volley; hence the action potential set up by the latter volley can be determined by subtracting the antidromic action potential from the combined action potential. The subtracted action potentials of Text-fig. 4 show, however, a complication that is always introduced by the slow potential waves. Thus a preganglionic volley 10 msec. after an antidromic volley sets up an S_2 spike which in the subtracted curve is actually

higher than the control, but it declines much less, for there is apparently a much larger slow negative wave. It will be seen later (section C(3)) that this is really due to the occlusion by the antidromic *P* wave of most of the *P* wave set up by the preganglionic volley. The *N* wave of the subtracted curve therefore resembles the preganglionic *N* wave as it would appear in the presence of a much smaller *P* wave. If allowance be made for the *P* wave occlusion, the potential of the S_2 spike of the subtracted curve is less than that of the control response, and the summit is about 0·6 msec. later. When the preganglionic volley follows the antidromic at a shorter interval (4 msec., Text-fig. 4), the S_2 spike is still smaller and later, and the S_1 spike is also smaller and perhaps a little delayed. Finally, when the preganglionic and antidromic stimuli are



Text-fig. 4. The continuous curve shows the ganglionic potential set up by a maxima preganglionic volley, the other curves being the subtracted action potentials for this volley when it is set up at the indicated intervals later than a maximal antidromic volley. At the interval indicated as −2 msec. the preganglionic volley preceded the antidromic volley by 2 msec.

simultaneous, there is no sign of either an S_1 or an S_2 spike in the subtracted curve, which ascends gradually for about 20 msec., being probably an *N* wave [cf. Eccles, 1935*c*, Text-figs. 6*c*, 9] complicated only by the unoccluded part of the *P* wave and the late S_4 spike indicated in the figure. If allowance be made for synaptic delays and the pre- and post-ganglionic conduction times, this curve shows that firing an antidromic volley into the ganglion prevents a preganglionic volley from setting up a discharge of the S_1 and S_2 ganglion cells for at least 2·5 and 5 msec. respectively. The curve at a stimulus interval of 4 msec. shows that recovery of S_1 and S_2 ganglion cells is well advanced 6·5 and 9 msec. respectively after an antidromic volley, while the curve at 10 msec. interval shows that 12·5 msec. after an antidromic volley the S_1 recovery is almost complete, though the S_2 response is still considerably diminished and delayed. It will be seen in section D that especially with S_2 ganglion cells the refractory period overlaps with a later period of depression.

Text-fig. 4 (interval −2 msec.) illustrates a change in the subtracted curve that always arises if the preganglionic volley is placed very early relative to the antidromic volley. The subtracted curve shows an early spike and it is followed by a trough, i.e. it resembles a diphasic spike. This apparent diphasic response is even more obvious when the preganglionic volley is moved yet farther forward. It clearly cannot be a preganglionic response subsequent to the antidromic volley, for even when earlier, e.g. at 0 interval, this volley blocks all response to a preganglionic volley. Now the subtraction method for determining the preganglionic response is no longer applicable when the antidromic volley fails to excite some ganglion cells before impulses have been set up in them by the preganglionic volley; for, as no spike potential would be produced in these cells by the antidromic volley, the control antidromic spike potential (which is subtracted) would be too large. The trough so produced in the subtracted curve is compensated by the earlier spike potential of the forestalling preganglionic response, hence the apparent diphasic action potential of the subtracted curves at such intervals.

Altogether thirteen other experiments have been performed, but in ten the antidromic volley failed to prevent an S_1 and S_2 preganglionic response, though this response was always greatly diminished at intervals such as at 0 and 4 msec. of Text-fig. 4. Presumably in such experiments the antidromic volley was not maximal, and this may be attributed either to the stimulus being too weak or to damage to the postganglionic trunk.

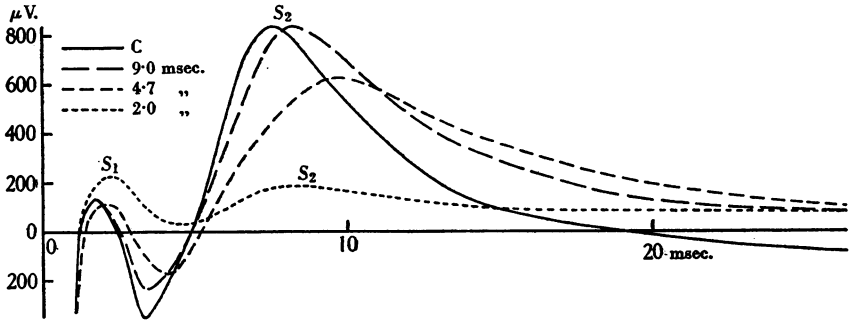
Brown [1934] similarly found that, in some experiments on S_1 ganglion cells in the superior cervical ganglion, an antidromic volley (presumably maximal) failed at all intervals to interfere completely with the discharge of impulses set up from the ganglion cells by a preganglionic volley. Rejecting as unlikely a repetitive ganglion cell discharge in response to a single preganglionic volley, he suggested that an asynchronism of more than 2 msec. in this discharge would be sufficient to account for the incomplete interference; but, as will be seen in a later paper, his observations show that an asynchronism of at least 5 msec. is necessary. Usually, however, there was an absolute and later a relative interference (as in Text-fig. 4) between the antidromic volley and the discharge set up by the preganglionic volley, and the experiments where this cannot be demonstrated presumably are explicable without being exceptions to the general statement that an antidromic impulse sets up in the ganglion cell a short period of depression during which a preganglionic volley cannot excite it to discharge an

impulse. No precise measurement of this period is possible in our experiments, and, as Brown's experiments give no indication of the time of the earliest discharge set up after an antidromic volley, no figures are deducible from them; however, the above experiments provide no reason for supposing that this period differs in duration from the period of similar inexcitability determined by two preganglionic volleys, for which a value of 3 msec. is probably the best estimate for S_1 ganglion cells [Eccles, 1935*a*, section I]. This period may be termed a functional refractory period [cf. Derbyshire & Davis, 1935]. It must be longer than the true absolutely refractory period, for the testing preganglionic volley provides a stimulus to the ganglion cells of only a limited strength.

Brown [1934] gives a value of 15 msec. for the duration of the period of gradual recovery from this period of inexcitability, and this is in good agreement with out experiments, e.g. the recovery of S_1 ganglion cells is nearly complete in 12·5 msec. in Text-fig. 4. It is most improbable that this depression is caused by an absolutely refractory period of some ganglion cells, i.e. an absolute block set up by the antidromic volley in some part of the postganglionic-ganglionic pathway, for within a similar group of ganglion cells there would not be the wide range of absolutely refractory periods from 3 msec. to more than 15 msec. The depression must, therefore, be due to the relatively refractory period following the antidromic volley [cf. Eccles, 1931, p. 565]. The preganglionic volley excites some ganglion cells so strongly that they discharge impulses very early in this relatively refractory period, e.g. after 3 msec., others are excited only just above their normal threshold and so can only discharge impulses at the very end of the relatively refractory period, e.g. after 15 msec., and all transitions exist. Since, therefore, this relatively refractory period set up by an antidromic volley raises the threshold at which a ganglion cell responds to excitation by preganglionic impulses, the antidromic volley must penetrate at least as far as the locus at which the ganglion cell discharge is set up; hence distal to this locus conduction is reversible.

A closer approximation to the true absolutely refractory period of the ganglion cells may be determined by analysing by the subtraction method the ganglionic action potentials produced by two antidromic volleys at various intervals apart. Text-fig. 5, which is typical of such experiments, shows that, when the stimulus interval is as short as 2 msec., the second volley produces both an S_1 and a small S_2 spike response, but after a delay longer than the normal control response by about 0·5 msec. for S_1 and 1·0 msec. for S_2 ganglion cells. At a stimulus interval of 4·7 msec. the

S_2 spike begins earlier, but its summit is further delayed, presumably on account of the slower postganglionic fibres and their ganglion cells which were not stimulated at 2 msec. interval. Finally at 9 msec. interval the S_1 spike and the beginning of the S_2 spike are almost normal, but the summit of the S_2 spike is delayed by about 0·7 msec., and its potential is lower if allowance be made for the occlusion of the P wave (cf. section C (1)), which is indicated by the subtracted curves declining less than the control curve (cf. Text-fig. 7). It may therefore be concluded that, as far as the antidromic impulse penetrates, there is almost complete recovery from the relatively refractory period of the S_1 ganglion cells at 9 msec., and recovery of the S_2 ganglion cells is then far advanced.



Text-fig. 5. The continuous curve shows the ganglionic action potential evoked by a maximal antidromic stimulus, the other curves being the subtracted action potentials produced by it when it is preceded at the indicated intervals by an antidromic volley set up by a similar maximal antidromic stimulus.

Now even at stimulus intervals as short as 4·7 and 2 msec. the subtracted S_2 spike appears to have its normal diphasic character, indicating that at such intervals, if the second stimulus sets up an antidromic impulse in a postganglionic fibre, that impulse penetrates as far as normally into the ganglion cell; hence it may be concluded that the absolutely refractory period of a ganglion cell is little if any longer than that of its axon, a conclusion similar to that of Lorente de Nó [1935*b*] for the motoneurones of the internal rectus muscle. The increased delay of the ganglionic spikes set up by the antidromic stimuli in Text-fig. 5 is presumably due to the slower conduction of the antidromic volley during the relatively refractory period of the postganglionic fibres. The absolutely refractory period of the ganglion cells is determined by adding this extra delay to the shortest stimulus interval at which a response was evoked, 2 and 3 msec. being the upper

limiting values so determined for the refractory periods of the fastest S_1 and S_2 ganglion cells.

The delay of the S_2 spike summit and diphasic artefact in Text-fig. 4 has been characteristic of all our experiments, and though in many it has been greater than in Text-fig. 4, a delay of more than 2·5 msec. has never been observed. A selective blocking of the discharge from those ganglion cells which normally have the shortest synaptic delays would perhaps be an adequate explanation of the small delay of the S_2 spike in some experiments, but delays as long as or longer than those of Text-fig. 4 certainly indicate that there is a lengthening of the synaptic delay associated with the relatively refractory period set up by the antidromic volley. Slowed conduction in the postganglionic pathway cannot of course be invoked as an explanation, for the delayed spike is recorded directly from the ganglion cells. As the preganglionic volley is set up progressively earlier relative to the antidromic volley, the synaptic delay appears in each experiment to reach a limiting value beyond which it cannot be lengthened, for any further displacement of the preganglionic volley diminishes the S_2 discharge to extinction without further altering its synaptic delay. The conditions obtaining for S_1 discharge appear to be similar, but the lengthenings are smaller, and cannot be so easily demonstrated in records of action potentials on account of the overlapping S_2 wave. This question will be further considered in a later paper.

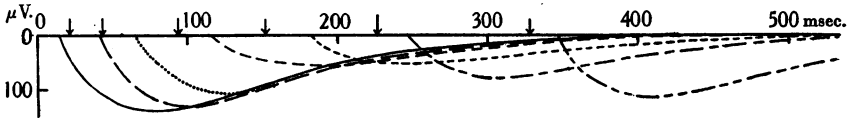
When a refractory period of ganglion cells was set up by a preganglionic volley, the synaptic delay of S_1 and S_2 ganglion cells was also found to be increased at very short intervals [Eccles, 1935*a*, section I], but the simultaneous facilitating influence of the initial preganglionic volley rapidly overcame this effect of the refractory period. A lengthening of the synaptic delay of the spinal flexor reflex is also produced by the refractory period set up in motoneurones by an antidromic volley [Eccles, 1931], but Lorente de Nó [1935 *b*] states that an antidromic volley produces if anything a shortening of the synaptic delay of the internal rectus motoneurones. However, in some at least of the records which are referred to in support of this statement, antidromic impulses would be prevented from reaching some motoneurones by impulses discharged from these motoneurones. Moreover, his conclusions depend on the interpretation of muscle action potentials, i.e. of responses beyond the neuromuscular junction, and so will be complicated by the increased neuromuscular delay of the second response during the relatively refractory period, a curve of Lucas' type C actually being obtained for the nerve muscle preparation [Lorente de Nó, 1935 *a*]. The effect of anti-

dromic impulses on motoneurones of the third nerve may not therefore be different from their effect either on motoneurones of the spinal cord or on ganglion cells.

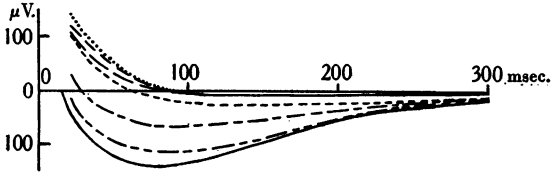
C. *Interaction of the slow potential waves set up in the ganglion by two successive volleys*

(1) *Two antidromic volleys.*

If, during the phase of slow positivity produced in the ganglion by an antidromic volley, a second antidromic volley be set up, there is always a brief diminution of this positivity [cf. Eccles, 1935 *c*, section F,



Text-fig. 6. The continuous line shows the slow potential wave set up by a single maximal antidromic volley (the initial spike not being drawn in this and all subsequent figures), and the other curves (cf. Pl. II, fig. 6) show the course of the slow potential waves after a second maximal antidromic volley for the stimulus intervals indicated by the arrows (the corresponding curves beginning about 20 msec. later). The latter part of the curve at a stimulus interval of 43 msec. (dotted line) is not drawn as it practically coincides with that at 21·5 msec.



Text-fig. 7. The subtracted slow potential waves set up by the second antidromic volley for each of the corresponding combined responses shown in Text-fig. 6, the same conventions of line being used. The latter parts of the curves for the three shortest stimulus intervals coincide in the continuous line just below the zero line.

interaction of preganglionic volleys], followed by its redevelopment (Pl. II, fig. 6). If, however, the observations at the various intervals are superimposed with the first volleys synchronized (Text-fig. 6), the slow positivity following the second antidromic volley is found, for stimulus intervals less than 100 msec., to be very little greater than that set up by the first volley alone, i.e. the second volley has produced very little change in the course of the slow positivity. As the stimulus interval is lengthened beyond 100 msec., the second antidromic volley gradually recovers its power to produce its normal full-sized slow positivity, but

there is with stimulus intervals of about 150 msec. a well-developed minimum for the combined slow positivity, Text-fig. 6 being typical of all such experiments (six in all).

The closeness with which at short stimulus intervals the combined slow positivity follows the control slow positivity suggests that the slow positivity set up by the first antidromic volley continues its course unaffected by the second volley, which, however, itself produces little additional slow positivity. This provides a method for determining the course of the slow potential set up by the second volley, the slow potential of the first volley being subtracted from the combined slow potential [cf. Hughes & Gasser, 1934 *b*; Eccles, 1935 *c*, section E]. Subsequent evidence justifies this procedure, but a conclusive proof of its correctness is not at present possible. The subtracted curves so determined (Text-fig. 7) show that the second antidromic volley produces an increased slow negativity at the same time as the decreased slow positivity.

On the basis of the analysis of the slow potentials into *N* and *P* waves (section A) the decreased slow positivity is clearly due to a diminished *P* wave, i.e. there seems to be an occlusion of the second *P* wave by the pre-existent *P* wave, which, however, must be a delayed action, for Text-fig. 6 shows that the occlusion does not diminish until the pre-existent *P* wave is considerably reduced; hence the well-developed minimum of slow positivity in the combined response. Likewise the increased slow negativity appears to be largely due to a diminution of *P*, and not to a great increase in *N*. However, the occurrence of a small change in *N*, which would bring it into line with the observations on preganglionic volleys [Eccles, 1935 *c*, section F], is typically shown by the observations of Text-fig. 7 at the short intervals. While the stimulus interval lengthens from 21·5 to 94 msec., and the slow positivity (and hence the *P* wave) remains unaltered, the slow negativity (and hence the *N* wave) first increases and then diminishes. The initial increase is much more obvious if still shorter intervals are chosen, and it shows that, when set up during the *N* wave of the first antidromic volley, the second antidromic volley produces a diminished *N* wave, i.e. there is an occlusion of this *N* wave. Further, the increase of the *N* wave to a maximum, which occurs when the second antidromic volley is set up during the phase of the greatest positivity following the first antidromic response, indicates that the *N* wave is increased when it is set up during a background *P* wave.

If the increase in the slow negativity of the second response be plotted against the stimulus interval, a curve is obtained closely resembling an inversion of the slow potential wave of the first response (cf. Text-figs. 13

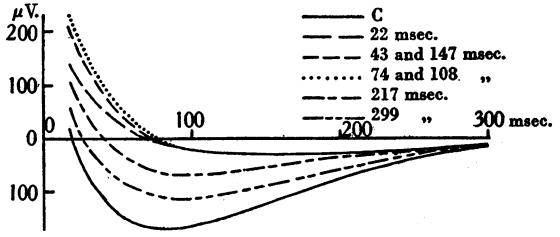
and 14 for a second preganglionic volley). This agreement suggests that the pre-existent N and P waves are directly responsible for the changes in the N and P waves set up by the later antidromic volley (cf. section C(3)). Thus qualitatively the interaction of the N and P waves set up by two antidromic volleys is similar to that observed for the interaction of two preganglionic volleys, the only differences being the much larger occlusion of the antidromic P waves, and the smaller increase of the antidromic N wave when set up in a background P wave.

(2) *Interaction of a preganglionic with a later antidromic volley.*

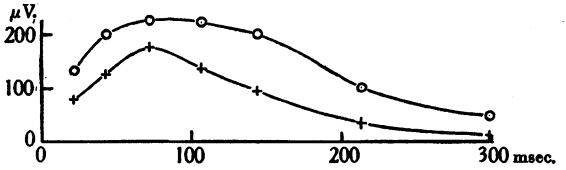
When an antidromic volley is set up during the slow potential wave following a preganglionic volley, the effect on its slow potential wave resembles that produced by a preceding antidromic volley (Pl. II, fig. 7). However, when the observations at various intervals are plotted with the initial preganglionic volleys superimposed, the antidromic volley usually produces a greater augmentation of the slow positivity than in Text-fig. 6 (the two exceptional experiments are not reliable, as they are complicated by a large artefact produced by the antidromic stimulus). The subtracted curves in Text-fig. 8 differ from those of Text-fig. 7 only in the larger P wave with short stimulus intervals, and the same conclusions as in the previous section may be drawn with regard to N and P wave interaction, thus further supporting the evidence of section A in proving the identity of the N and P waves set up antidromically and preganglionically.

If the heights of the S_2 ganglionic spikes of the second antidromic responses be measured from the base-lines provided by the previous responses (cf. Pl. II, figs. 6 and 7), these heights are found to be increased relative to the normal control whether the preceding volley be antidromic or preganglionic. When plotted against the stimulus interval, the increase of the spike height always runs approximately parallel to, but at a lower level than, the increase in the slow negativity measured immediately after the spike (Text-fig. 9). It, therefore, seems probable that the increased spike height is an indicator of the partial completion of the increased negativity produced by the occlusion of the P wave and, presumably, the increase of the N wave, these effects being thus shown to be more than half completed at the time of the S_2 ganglionic spike, which in Text-fig. 9 was only 6·7 msec. after the antidromic stimulus. Since probably 3 msec. would be occupied in the conduction time of the S_2 antidromic impulses, the N and P waves must normally be set up almost immediately these impulses reach the ganglion cells, and the waves must

quickly reach a maximum, for this was certainly attained in the upper curve of Text-fig. 9 only 18 msec. after the antidromic stimulus. Such a rapid increase of the *N* and *P* waves is also indicated by the experiments in which nicotine removed the *N* wave, for the *P* wave appeared to be maximal at least as soon as the end of the antidromic spike (Pl. I, fig. 4), and it is in agreement with the rapid increase also found for the *N* and *P* waves set up by a preganglionic volley (section B) [cf. Eccles, 1935 *c*, sections C and F].



Text-fig. 8. Subtracted slow potential waves as in Text-fig. 7, but for a maximal antidromic volley preceded at the indicated intervals by a maximal preganglionic volley (observations shown in Pl. II, fig. 7). The continuous line is the response to the antidromic volley alone. The curves for stimulus intervals of 43 and 147 msec. practically coincide throughout their course, as also do those at 74 and 108 msec.

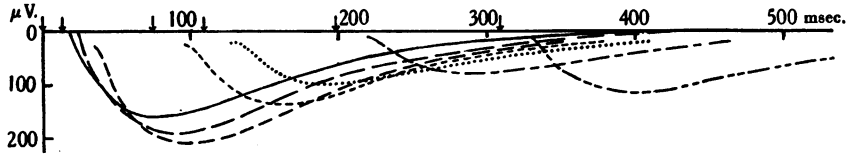


Text-fig. 9. For the crosses the increase in the antidromic S_2 spike is plotted against the stimulus interval, and for the circles the increase in the slow negativity immediately after the spike is similarly plotted, the observations being partly shown in Pl. II, fig. 7.

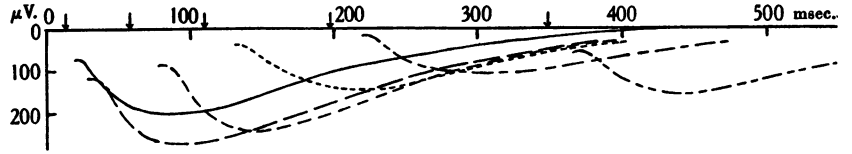
(3) *Interaction of an antidromic with a later preganglionic volley.*

Pl. III, fig. 8, shows that a maximal preganglionic volley always adds considerably to the slow positivity set up by a maximal antidromic volley, the interaction thus differing from that occurring between two antidromic volleys. When the curves are plotted with the antidromic volleys synchronized (Text-fig. 10), this addition to the slow positivity is well seen, and the close similarity to the interaction between two preganglionic volleys is revealed by Text-fig. 11, where such observations from the same experiment are similarly plotted. Despite the considerable addition to the slow positivity, this in Text-figs. 10 and 11 passes through well-

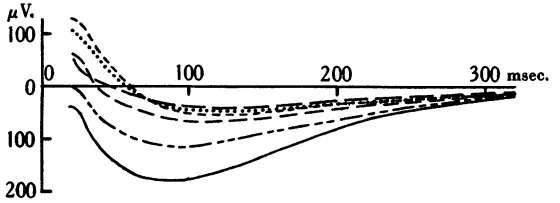
developed minima with stimulus intervals of about 200 msec. (cf. Text-fig. 6). The smaller positivity with simultaneous stimuli in Text-fig. 10 is observed in all experiments when the stimulus intervals are so short that the refractory period of the antidromic volley prevents the preganglionic volley from setting up a discharge from some or all of the ganglion cells (cf. section B).



Text-fig. 10. A series of observations drawn as in Text-fig. 6, but for a maximal preganglionic volley preceded at various intervals by a maximal antidromic volley (cf. Pl. III, fig. 8). The continuous curve shows the slow potential wave set up by the preganglionic volley alone, and the longest broken line the potential when the preganglionic and antidromic volleys are simultaneous.



Text-fig. 11. As in Text-fig. 10, but for two maximal preganglionic volleys.



Text-fig. 12. Subtracted curves as in Text-figs. 7 and 8, but for the series of observations shown in Text-fig. 10, the line conventions again corresponding. The curve for the interval of 199 msec. was not plotted as it was practically superimposed on that at 19 msec.

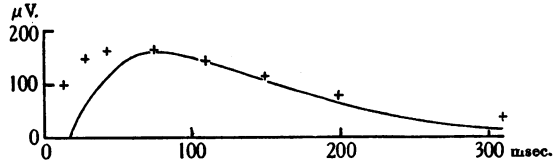
Besides this minimum at simultaneity the subtracted preganglionic potentials, i.e. the ganglionic potentials set up by the preganglionic volley, also usually show a minimum slow positivity with intervals of about 100–150 msec. (cf. dotted curve, Text-fig. 12), which has never been observed with subtracted antidromic potentials (cf. Text-figs. 7 and 8). This minimum is sometimes also present with the interaction of two preganglionic volleys (cf. curve at 109 msec. interval, Text-fig. 11), but

has not been detected when the inhibition of the second preganglionic volley is small (cf. Eccles, 1935 *c*, Text-fig. 12). Moreover, this minimum occurs over just that range of intervals at which the inhibition is maximal, hence it is concluded that it results from the diminution of the second preganglionic discharge by the inhibitory effect of the first volley. The diminution of the spike response to a preganglionic volley, which is also produced by a preceding antidromic volley (see section D and Pl. III, figs. 8 and 10), similarly would account for the minimum of Text-fig. 12. This diminution of the spike response by the inhibition or depression set up by a preceding volley does not occur for a second antidromic volley (cf. Pl. II, figs. 6 and 7), hence the absence of a minimum in Text-figs. 7 and 8. Thus the minimum slow positivity of the subtracted action potentials at stimulus intervals of 100–150 msec. appears to be related to that at very short stimulus intervals, both being due to the failure of the preganglionic volley to set up a discharge from some ganglion cells.

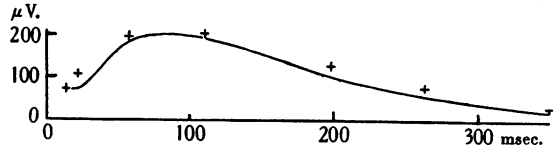
When the preganglionic volley is simultaneous with the antidromic volley, the subtracted curve in Text-fig. 12 shows that it produces a large *N* wave even though a discharge of impulses has been set up from very few ganglion cells. Such a relatively unchanged *N* wave has also been produced by a preganglionic volley in all series of observations in which the discharge of impulses has been prevented by the refractory period following an antidromic volley (cf. the observation of Text-fig. 4 with simultaneous stimuli). The production of the *N* wave by a preganglionic volley is therefore but little affected by a refractoriness of the ganglion cells which prevents the discharge of impulses, thus differing from the production of the *P* wave which is considerably diminished though apparently not abolished under such conditions.

In Text-fig. 13, for the series of observations of Text-fig. 12, the maximum increase of the preganglionic slow negativity has been plotted against the stimulus interval. Except for the shortest stimulus intervals the plotted points lie very close to the curve in Text-fig. 13, which shows the inverted course of the slow potential set up by the initial antidromic volley. There is a similar good agreement in all such series of observations when the artefact produced by the antidromic stimulus is small, and also, as shown in Text-fig. 14, in series obtained by the interaction of two preganglionic volleys. This agreement provides additional evidence supporting the conclusion that the pre-existent *N* and *P* waves are directly responsible for the modifications in the *N* and *P* waves set up by a preganglionic volley [cf. Eccles, 1935 *c*, section F; and section C(1) where the *N* and *P* waves set up by an antidromic volley are similarly

affected]. The maximum increase in the slow negativity set up by a preganglionic volley at various times after an antidromic or preganglionic volley may therefore be used to construct the approximate course of the slow potential set up by these volleys, a construction which is useful in comparing the slow potentials set up by antidromic and preganglionic volleys when the antidromic potential is distorted by stimulus artefact (cf. Text-fig. 17 B).



Text-fig. 13. The points show the stimulus intervals plotted against the corresponding maximum increases of the slow negativity set up by a preganglionic volley (series partly shown in Text-figs. 10 and 12). The curve shows the inverted course of the slow potential wave set up by the antidromic volley (cf. continuous line in Text-fig. 10).



Text-fig. 14. As in Text-fig. 13, but for the two maximum preganglionic volleys of Text-fig. 11. The curve shows the inverted course of the slow potential wave set up by the preganglionic volley.

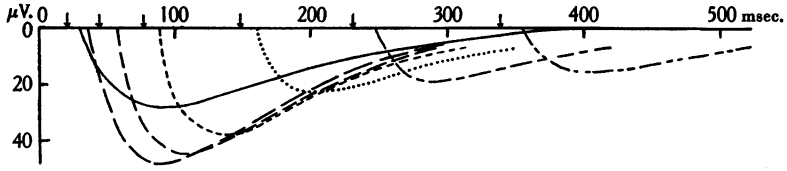
The minimum of the subtracted slow positivity at intervals of about 120 msec., and the larger fraction of its slow positivity which is added by a preganglionic volley, provide the only points in which the interaction of an antidromic with a preganglionic volley differs from the interactions considered in the preceding sections. It may therefore be concluded that in all the possible interactions between antidromic and preganglionic volleys a pre-existent *P* wave in excess of *N* diminishes the *P* wave and increases the *N* wave set up by a later volley, while a pre-existent *N* wave similarly diminishes the *N* wave set up [cf. Eccles, 1935 *c*].

(4) *Interaction of submaximal volleys.*

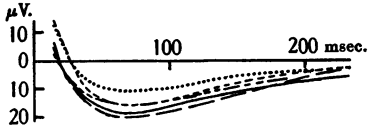
When testing the interaction between a submaximal preganglionic and a submaximal antidromic volley, it must be recognized that there will only be a partial overlap of the fields of ganglion cells acted on by

these respective volleys. However, when testing interaction between two preganglionic volleys or between two antidromic volleys which are set up by identical stimuli applied through the same electrodes, the incompleteness of the overlap probably does not reach significant proportions, for the spontaneous changes of excitability [Blair & Erlanger, 1933, 1936] are probably very small.

The interaction of two submaximal antidromic volleys exhibits a behaviour identical with that described for maximal volleys, and this is observed even when both volleys are restricted to S_1 fibres; hence it may be concluded that with antidromic volleys the interaction of N and P waves is similar for S_1 and S_2 ganglion cells.



Text-fig. 15. A series of observations plotted as in Text-fig. 6, but for a submaximal preganglionic volley followed by a submaximal antidromic volley (cf. Pl. III, fig. 9).



Text-fig. 16. Subtracted potentials as in Text-fig. 8, but for the submaximal responses of Text-fig. 16, a similar line convention being used, but in order to avoid confusion only some observations are plotted.

In investigating the interaction between submaximal antidromic and preganglionic volleys a relatively large overlap may be ensured by employing stimuli which are almost maximal for the respective preganglionic and postganglionic S_1 fibres, for such stimuli are then almost below threshold for the S_2 fibres, and there is an almost complete overlap on the S_1 ganglion cells.

The interaction of two such volleys is illustrated in Pl. III, fig. 9, and in Text-fig. 15 the initial preganglionic volleys are synchronized for the various responses. With short stimulus intervals, e.g. observations 4 and 7, the large additional slow positive wave distinguishes these observations from those with maximal stimuli (Text-fig. 8). The subtracted curves (Text-fig. 16) show that the added positive wave may even be larger

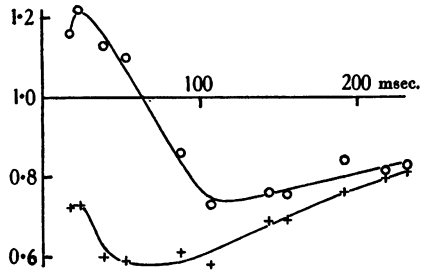
(interval 21 msec.) than the positive wave set up by the antidromic volley alone. As the stimulus interval lengthens, the positive wave of the subtracted curve decreases to a minimum of about half the maximum value (interval 148 msec.), increasing again with very long intervals. This decrease to a minimum proves that with short stimulus intervals the large positivity of the subtracted curves is not due to an absence of overlap between the fields of ganglion cells acted on by the preganglionic and antidromic volleys. The unlikely explanation of the minimum by an inhibition or depression of ganglion cells blocking the entrance of antidromic impulses (cf. for maximum preganglionic volley, section C (2)) is contraindicated by the ganglion spike potentials (cf. Pl. III, fig. 9, observation 3), which show on the contrary a small increase running parallel with the increased slow negativity of the subtracted curves, and presumably corresponding to that of Text-fig. 9. Hence it must be concluded that antidromic impulses at short intervals after a preganglionic volley set up a larger additional slow positivity, and hence P wave, than at longer intervals.

This increased P wave at short intervals is always present when two weak preganglionic volleys interact [Eccles, 1935 *c*, section H], the experimental evidence suggesting that the production of P wave by preganglionic impulses is increased by a pre-existent slow negativity, i.e. when the N wave is larger than the P wave. A similar explanation seems likely for the increased P wave in Text-fig. 16, for the N wave is there initially in excess of the P wave, such a condition always obtaining when the preganglionic stimuli are so weak that practically only the S_1 ganglion cells are excited; hence it may be concluded that a pre-existent N wave in excess of P increases the production of P wave by an antidromic as well as by a preganglionic volley. With a maximal preganglionic volley the large P wave of the S_2 ganglion cells is usually greater than the N wave, there being no phase of slow negativity, hence even at short intervals there is a large occlusion of the antidromic P wave (Text-fig. 8). Presumably the antidromic volley would still set up the facilitated P wave in the S_1 ganglion cells, but this would form a hardly detectable fraction of the combined S_1 and S_2 responses to maximal volleys.

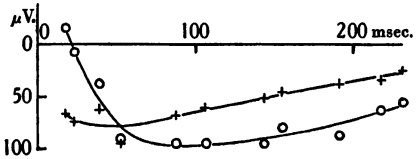
D. *Actions of an antidromic volley on the excitability of ganglion cells*

Pl. III, fig. 10, shows part of a series of observations in which the excitability of S_2 ganglion cells is tested by their response to a submaximal preganglionic volley at various intervals after either a maximal

antidromic volley or a maximal preganglionic volley, and in Text-fig. 17 A the potential of the testing preganglionic spike response is plotted against the stimulus interval for the whole series of observations. The curve thus obtained after an initial preganglionic volley is of course the inhibitory curve of Text-figs. 11, 12 and 15 in a previous paper [Eccles, 1935 *b*], resembling the two former in having a preponderating facilitatory effect at short intervals. On the other hand, an antidromic volley is followed by a large depression of the excitability of the S_2 ganglion cells even at the shortest interval, this depression overlapping with the brief



Text-fig. 17 A.



Text-fig. 17 B.

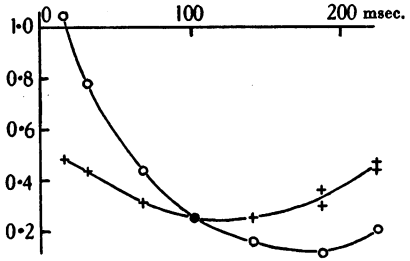
Text-fig. 17 A. The potentials of the S_2 spike responses evoked by the testing preganglionic volley (measured from the summit to the diphasic artefact and expressed as a fraction of the normal control responses similarly measured) are plotted against the stimulus intervals after either a maximal antidromic volley (crosses) or a maximal preganglionic volley (circles), part of the series being shown in Pl. III, fig. 10.

Text-fig. 17 B. The maximum increase in the slow negativity of the testing preganglionic response is plotted downwards against the stimulus interval after a maximal antidromic volley (crosses) or a maximal preganglionic volley (circles). The same series of observations as in Text-fig. 17 A.

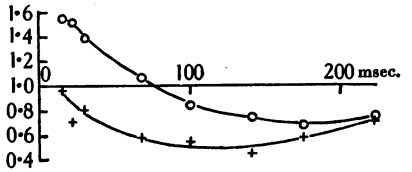
depression regarded as characteristic of the relatively refractory period (section B). After a brief initial increase the depression soon diminishes and at the longest intervals is very little more than after a preganglionic volley. This relationship between the two curves is characteristic of nine of our experiments. The other six experiments have differed only in the larger depression produced by the preganglionic volley at long intervals (cf. Text-fig. 18 A).

An antidromic volley sets up a depression of excitability of S_1 ganglion cells which even at long intervals is never less than any depression following a preganglionic volley (Text-fig. 18 B). However, as shown in Text-fig. 19 a preganglionic volley producing a large facilitatory effect may not give rise to any late depression of excitability, though an

antidromic volley produces its normal depression. At short intervals after an antidromic volley there may actually be a period of facilitation of S_1 ganglion cells separating the brief depression of the relatively refractory period (section B) from the later prolonged depression. In the experiment illustrated by Text-fig. 18 B there would be no continuity between these



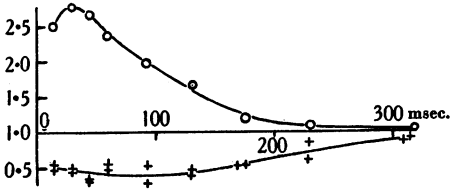
Text-fig. 18 A.



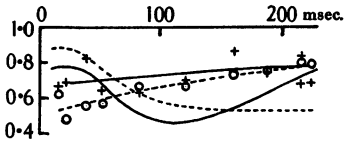
Text-fig. 18 B.

Text-fig. 18 A. For S_2 responses as in Text-fig. 17 A, but in another experiment.

Text-fig. 18 B. Same experiment as Text-fig. 18 A, but for S responses.



Text-fig. 19.



Text-fig. 20.

Text-fig. 19. For S_1 responses as in Text-fig. 18 B, but in another experiment.

Text-fig. 20. The circles and the crosses show the testing preganglionic S_2 responses at the corresponding intervals after a maximal preganglionic and a maximal antidromic volley respectively, the ganglion having been painted with a 0·01 p.c. solution of nicotine about 25 min. previously. In addition to the curves through these points, the corresponding curves before the action of nicotine are also shown, the continuous lines showing the antidromic curves and the broken lines the preganglionic curves (cf. Text-figs. 17 A and 18 A).

two depressions. This transient facilitation suggests that an antidromic impulse sets up c.e.s. in the ganglion cells and that the initial period of increasing depression is really due to the more rapid decay of the facilitatory effect that opposes the more long-lasting depression, which itself actually reaches a maximum much earlier than is indicated by the composite curves of Text-figs. 17 A, 18 and 19.

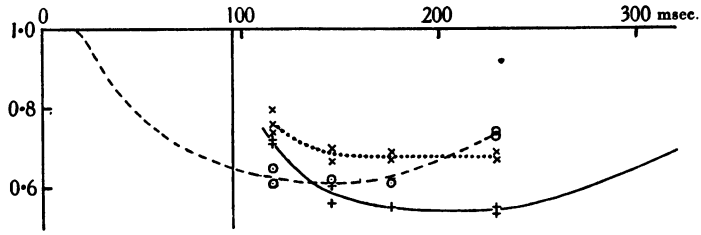
The action of small doses of nicotine in removing the phase of increasing S_2 inhibition at the same time as the S_1 facilitation indicated

such a solution for the S_2 inhibition set up by a preganglionic volley [Eccles, 1935 *b*, section L]. Similarly the period of increasing depression set up by an antidromic volley is removed by small doses of nicotine (Text-fig. 20), the latter parts of the curves simultaneously obtained after preganglionic and antidromic volleys being much less affected. This confirms the suggestion that the short period of increasing depression after an antidromic volley is also due to the more rapid decay of a small facilitatory effect set up by the antidromic volley. Further confirmatory evidence is provided below by a study of the interaction of preganglionic and antidromic volleys.

Thus the long-lasting depression produced by an antidromic volley is indistinguishable from the so-called inhibition set up by a preganglionic volley, and, as it will appear in the discussion that such a depression is responsible for part at least of the classical inhibition of spinal reflexes, forming as it does a perfect counterpart of the facilitation produced by c.e.s., it seems justifiable to extend the term inhibition to cover the long-lasting depression set up by an antidromic volley, though of course such an application is at variance with the classical conception of the nature of reflex inhibition. It might be objected that the normally interpolated facilitation provides an entirely arbitrary separation of a continuous prolonged depression into an earlier phase which has been regarded in section B as a refractory state, and a later phase now regarded as inhibitory in nature. In fact Hughes & Gasser [1934 *b*] and Lorente de Nó [1935 *b*] prefer to call the entire period of depression a relatively refractory period. However, though it is undoubted that the refractory state overlaps the inhibition, the following evidence clearly distinguishes between them in the ganglion cell. Nicotine in suitable doses abolishes the prolonged depression, i.e. the inhibition, but leaves a short period of depression which is presumably the true refractory period. Further, the prolonged depression (inhibition) is closely associated with the *P* wave which indicates that a maximum is only reached after about 20 msec. (cf. Eccles, 1935 *c*, Text-fig. 9), while, if the depression of excitability due to a refractory period is associated with any potential, it presumably would be the negative potential of the spike as may occur in peripheral nerve [Gasser & Graham, 1932]. Thus the prolonged depression (inhibition) appears to be more closely related to the subnormal excitability and the associated positive after-potential of peripheral nerve [cf. Eccles, 1935 *c*, p. 498] than to its relatively refractory state.

The interaction of two preganglionic volleys on the excitability of the ganglion cells was tested by a third preganglionic volley at various

intervals after the second [Eccles, 1935 *b*, section K]. The interaction of a preganglionic volley with a later antidromic volley has been similarly investigated, and in Text-fig. 21 the points show the potentials evoked by the testing preganglionic volley plotted against the respective intervals after the initial preganglionic and antidromic volleys. The control curves for the inhibitory effects of these volleys alone are also drawn. The inhibitory effect of the initial preganglionic volley is diminished for as long as 100 msec. after the intercurrent antidromic volley, an effect apparently corresponding to the period of increasing inhibition set up by the antidromic volley alone. This indicates that this period of increasing inhibition is due to the rapid decay of an antagonistic process



Text-fig. 21. The perpendicular line at 96 msec. shows the time of an antidromic volley following an initial preganglionic volley, and the oblique crosses show the S_2 potentials evoked by a testing preganglionic volley (expressed as a fraction of the normal control response) at four intervals later. The circles and the upright crosses respectively show the testing preganglionic responses after the preganglionic and antidromic volleys alone, the remainders of the corresponding curves being drawn from the observations made a little previous to those giving the plotted points.

which almost certainly is identical with the c.e.s. set up by a preganglionic volley, for both processes are also similar in their time course and in their sensitivity to nicotine. At all intervals after the antidromic volley the inhibitory effect of the combined preganglionic and antidromic volleys is less than that of the antidromic volley alone. This intense occlusion of the antidromic inhibition by the pre-existent preganglionic inhibition unmasks the effect of the c.e.s. which is set up by the antidromic volley and which is usually submerged beneath the more intense inhibition.

The interactions between the effects of two antidromic volleys or of an antidromic with a later preganglionic volley on the excitabilities of the ganglion cells resemble that between a preganglionic and a later antidromic volley (typically shown in Text-fig. 21), and in addition all these three types of interaction are similar to that described in section K [Eccles, 1935 *b*] for the interaction of two preganglionic volleys; hence a

general similarity of the effects of preganglionic and antidromic volleys is indicated. From all the experimental evidence stated in this section it may therefore be concluded that an antidromic volley resembles a preganglionic volley in setting up both the excitatory and inhibitory states of ganglion cells, c.e.s. and c.i.s. The antidromic c.e.s. is always much less than that set up by a preganglionic volley, but with c.i.s. there is no such large deficiency, the antidromic c.i.s. being perhaps at times even greater than that set up by a preganglionic volley.

An attempt has been made to determine the effect of an interpolated antidromic impulse on the facilitation between two preganglionic volleys. There is no doubt that some facilitation, and hence presumably c.e.s., is not inactivated by the antidromic volley, but interpretation of results is complicated because the c.e.s. and c.i.s. produced by the antidromic volley are affected by the pre-existent c.e.s. and c.i.s. Such interactions seem adequate to explain the action of the interpolated antidromic volley without assuming that it inactivates c.e.s. Such an explanation would conform with the absence of any apparent action of an antidromic volley on the preganglionic *N* wave (section B).

Discussion

(1) *The path of an antidromic impulse*

It has been previously pointed out that the histological picture of a nerve cell suggests that an antidromic impulse traverses the surface of the cell body and the dendrites to their terminations [Eccles & Sherrington, 1931 *b*]. While this suggestion is not at present susceptible to direct proof [cf. Forbes, 1934], the following evidence proves that in some nerve cells at least the antidromic impulse penetrates as far as the locus at which impulses normally are set up by a nerve cell.

(1) When an antidromic impulse is backfired into a rhythmically discharging soleus motoneurone, it not only is followed by a cycle longer than the normal cycle, but it also permanently alters the phase of the rhythmic discharge [Eccles & Hoff, 1932].

(2) If in the flexor reflex an antidromic impulse is interpolated between two centripetal volleys, there is a diminution of any facilitation which the first may exert on the second [Eccles, 1931].

(3) An antidromic impulse backfired into a motoneurone sets up a refractory state of that motoneurone which is not simply an absolute block, for the motoneurone exhibits a raised neurone threshold during a

period corresponding to a relatively refractory state [Eccles, 1931; Lorente de Nó, 1935 *b*].

(4) Similarly in the ganglion cell an antidromic impulse sets up a relatively refractory state during which the threshold for the discharge of an impulse is raised [Brown, 1934; section B above].

(5) When allowance is made for the different temporal dispersions, the ganglionic spike potentials set up by maximal antidromic and preganglionic volleys seem similar (section A), and the spike potential set up in the ganglion by a preganglionic volley is abolished when an antidromic volley prevents the setting up of a discharge by that volley (section B), thus again showing that an antidromic volley does not prevent the discharge by setting up a block peripheral to the point of origin of that discharge.

It may, therefore, be concluded that an antidromic impulse backfired into a nerve cell traverses the same path in that cell as an impulse normally set up by that cell and discharged along its axon. Hence it seems likely that an impulse discharged from a nerve cell has exactly the same action on that cell as an antidromic impulse, for in peripheral nerve the effect of an impulse is independent of the direction of its travel. An investigation of the effects of antidromic impulses on the rhythmic discharge from soleus motoneurones [Eccles & Hoff, 1932] lends experimental support to this suggestion, which is now to be examined in the light of the observations of this paper.

(2) N *wave and facilitation*

A preganglionic volley has actions on a ganglion cell other than the setting up of an impulse and actions secondary to this impulse, for it is established that it may give rise to an excitatory state and the associated *N* wave even when no impulse is discharged (section B) [Eccles, 1935 *b*, *c*]. Such additional effects produced by a preganglionic volley provide at least a partial explanation of the differences between the actions on ganglion cells of antidromic and preganglionic volleys, even if the discharge of an impulse actually has itself the same action as an antidromic impulse, for it has been shown that a maximal preganglionic volley sets up a larger *N* wave (section A) and facilitation (section D) than a maximal antidromic volley.

(3) P *wave and inhibition*

With regard to the *P* wave and inhibition the evidence is uncertain, for there usually are discrepancies between the respective series of observations in both of the following respects.

(1) The *P* wave set up by a maximal antidromic volley is always smaller and often much smaller than that set up by a maximal preganglionic volley (Text-fig. 3; Pl. I, fig. 2), while the intensity of the antidromic inhibition is never much smaller and often is as large or a little larger, even at such long intervals that the complicating effect of the more intense preganglionic facilitation must have passed off (Text-figs. 17 A and 18 A). This discrepancy is illustrated in Pl. III, fig. 10, and in Text-fig. 17. Since the antidromic slow positivity is considerably distorted by the stimulus artefact, the course of the slow positivity of both the initial preganglionic and antidromic responses has been determined in Text-fig. 17 B by plotting against the stimulus intervals the corresponding increases in the slow negativities of the subtracted curves of the testing preganglionic responses, a procedure which has been justified in section C (3). Except at short intervals, where the larger preganglionic *N* wave interferes, the preganglionic slow positivity is much greater than the antidromic slow positivity, hence the preganglionic *P* wave is also much greater. But for these same observations the preganglionic inhibition is smaller (Text-fig. 17 A), and the complicating effect of the more intense preganglionic facilitation certainly seems to have passed off at the longest intervals.

(2) When set up either preganglionically or antidromically, the *P* wave usually decays more rapidly than the inhibition. It was suggested [Eccles, 1935 *c*] that such a discrepancy could perhaps be due to an effect on *P* by amplifier distortion or tissue polarization, but such suggestions are of course invalid when an identical course for the *P* wave is indicated by the increase of the slow negativity set up by a testing preganglionic volley. Moreover, this discrepancy is sometimes absent or even slightly in the reverse direction [Eccles, 1935 *c*, Text-fig. 20], variations which are inexplicable by the above suggestions.

Hence it must be concluded that the *P* wave and the inhibition do not usually run identical time courses, and that, relative to the effect of a preganglionic volley, an antidromic volley sets up a *P* wave proportionately smaller than its inhibitory effect. This conclusion of course does not signify that these two reactions are absolutely distinct activities of the ganglion

cell, for in many ways they are closely related. To the evidence on this point already adduced from the action of a preganglionic volley [Eccles, 1935 *c*, Discussion] must now be added the similar evidence adduced in this paper both from the action of an antidromic volley and from all possible interactions of antidromic and preganglionic volleys (sections C and D), e.g. the *N* and *P* wave interaction of Pl. II, fig. 7, is very similar to the interaction of facilitation and inhibition in Text-fig. 21.

Evidence has already been brought forward [Eccles, 1935 *c*, Section F] which suggested a hypothetical *P* process of the ganglion cell which gave rise to the potential change (presumably in the surface membrane) which is recorded as the *P* wave. The evidence strongly suggested that this hypothetical process was also the basis of the raised threshold of the ganglion cell, which is of course indicative of c.i.s., i.e. that the *P* process was identical with c.i.s. With the technique at present available for investigating the living ganglion cell we can only determine its responses in terms of changes in its threshold and in an electrical potential which, on analogy with peripheral nerve and other isolated tissues that have been investigated, is largely if not entirely produced across its surface membrane. It is important to regard such changes as no more than special aspects of fundamental reactions of the cell. Complicating factors may prevent such a fundamental reaction from being expressed to a comparable degree in two aspects such as the *P* wave and the raised threshold. For example, the coexistent fundamental reaction (hypothetical *N* process or c.e.s.) which probably similarly underlies the *N* wave and the lowered threshold of facilitation may diminish the expression of the hypothetical *P* process or c.i.s. in terms of the raised threshold more than in terms of the *P* wave, hence the explanation of the discrepancy illustrated in Text-fig. 17, for more of the hypothetical *N* process or c.e.s. is set up by a preganglionic volley than by an antidromic volley.

Hence it may be concluded that there is no reliable experimental evidence suggesting that a maximal preganglionic volley sets up less c.i.s. than a maximal antidromic volley. Now it has been shown that the discharge of an impulse by a ganglion cell probably inactivates some of the c.e.s. of that cell [Eccles, 1935 *b*, section E], an action which undoubtedly is to be correlated with the production of c.i.s. by a preganglionic volley, i.e. a preganglionic volley gives rise to c.i.s. by an action secondary to the impulses which it sets up, and this c.i.s. may not be less than that set up by an antidromic volley. Thus the experimental evidence qualita-

tively supports and quantitatively does not contraindicate the original suggestion that an antidromic impulse has the same action on a ganglion cell as an impulse discharged by that cell.

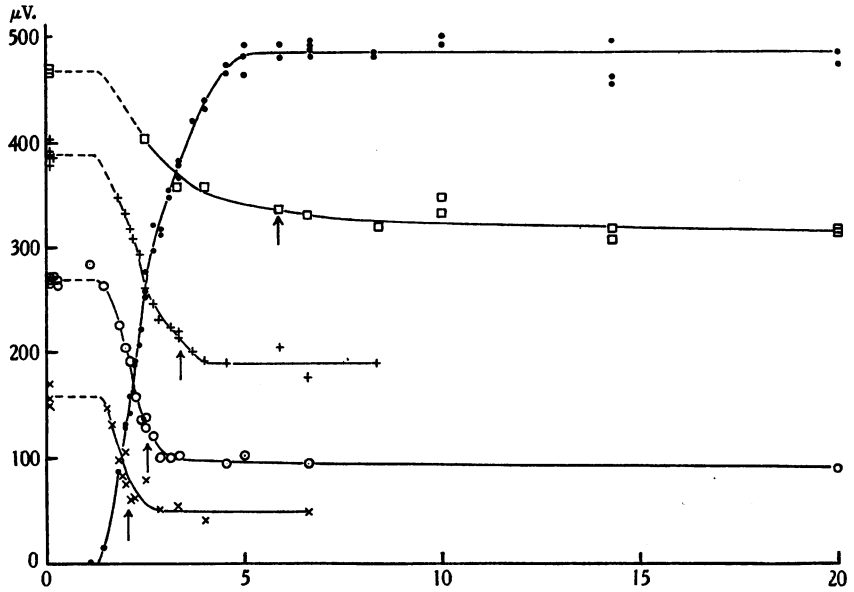
Specific inhibitory preganglionic fibres?

In some experiments, e.g. Text-fig. 18 A, it seems that a maximal preganglionic volley sets up a more intense inhibitory effect than can be set up by an antidromic volley. Though it is possible that this is due to the antidromic volley not being maximal, e.g. the postganglionic trunk may be injured (cf. section A), this does suggest that in such experiments more c.i.s. is set up by the preganglionic volley, for the preganglionic P wave is also larger than the antidromic P wave. If it be granted that the antidromic impulse has the same action on a ganglion cell as an impulse discharged by that cell, such experiments suggest that preganglionic impulses themselves directly set up c.i.s. additional to that set up secondarily to the discharge of an impulse from a cell. Such impulses would have the classical inhibitory action on that cell, setting up an inhibitory process as a primary response of the cell and not as a sequel to the discharge of an impulse. From the experimental evidence available such an action must be regarded as no more than doubtful in some experiments, e.g. Text-fig. 18 A, and probably not existing in others, e.g. Text-fig. 17 A.

In a previous paper [Eccles, 1935 *b*] specific inhibitory fibres were assumed to exist, for it was not then recognized that an antidromic impulse (and hence probably the discharge of an impulse from a cell) could set up such an intense long-lasting depression of excitability. However, none of the evidence presented in that paper proves that any of the inhibition is produced by specific inhibitory fibres, for even the almost complete restriction of the inhibition to the S_2 ganglion cells can be explained by the preponderating facilitatory type of response of the S_1, S_3 and S_4 ganglion cells, and the larger P wave (and hence probably c.i.s.) produced in S_2 ganglion cells both by antidromic volleys (cf. Text-fig. 2) and preganglionic volleys [cf. Eccles, 1935 *c*, Text-figs. 3, 4 and 5], though of course the reason for this unique behaviour of S_2 ganglion cells is still obscure. Again none of the experimental observations on the slow potential waves set up by preganglionic volleys [Eccles, 1935 *c*] proves that the P wave is set up by specific preganglionic fibres, *e.g.* as the intensity of the preganglionic stimulus was varied, the size of the P wave closely paralleled the size of the S_1 and S_2 spike potentials, the apparent absence of a P wave with very weak S_1 responses probably being

due to the preponderating N wave set up under such conditions [cf. Eccles, 1935 *c*, Text-figs. 3, 4 and 5].

The question of the existence of the classical inhibitory fibres may be investigated by a development of the procedure adopted in testing for the threshold of the inhibitory preganglionic effect [Eccles, 1935 *b*, Pl. III, fig. 9, and section I]. An initial (inhibitory) preganglionic volley



Text-fig. 22. In each of the series of observations (shown by the squares, upright crosses, circles, and oblique crosses) the potentials of the postganglionic S_2 responses evoked by a constant testing preganglionic stimulus are plotted as ordinates against as abscissæ the strengths of a varied preganglionic stimulus applied at a constant interval previously. The strength of the second preganglionic stimulus is shown for each series by the arrows immediately below the curve. The dots show the potentials of the S_2 responses evoked by the first stimuli plotted as ordinates against the corresponding stimulus strengths.

is set up by a stimulus of varied strength and at the same electrodes a second (inhibited) volley of constant size is set up at a fixed interval later, this stimulus interval being made longer than the optimal interval for inhibition in order to avoid complications arising from the c.e.s. which is of course also set up by the first volley. In Text-fig. 22 the potentials of the inhibited S_2 responses (recording as in Text-fig. 1 B) are plotted as ordinates against as abscissæ the strengths of the corresponding first preganglionic stimuli for each of the four series of observations, the

strength of the second preganglionic stimulus, which was constant for each series, being indicated by the arrow immediately below the curve drawn through the points of the corresponding series. In addition the curve expressing the relation between the potentials of the initial S_2 responses against the corresponding stimulus strengths is also drawn [cf. Eccles, 1935 *c*, Text-figs. 3, 4 and 5], and close to zero stimulus strength are plotted the S_2 potentials evoked by the second volley alone for each of the series of observations.

The interpretation of Text-fig. 22 depends upon the following argument. As the first preganglionic stimulus is strengthened to equal eventually the constant second stimulus (submaximal) for that series of observations, the field of ganglion cells excited to discharge impulses by the first volley will increase *pari passu* until it becomes identical with the field responding to the second volley alone, for both volleys should then be identical, being set up as they are by identical stimuli applied through the same electrodes. Any further increase in the first volley will excite in addition a discharge from ganglion cells whose inhibition is not being tested by the second volley, for inhibition is only indicated by a diminution in the number of ganglion cells responding to this testing volley. Thus if the inhibition of the response to the second volley is solely due to the depression of excitability resulting from the discharge of impulses set up by the first volley, there should be, as the first stimulus is strengthened to equal the second, a progressive increase in the inhibition to a maximum which is not altered by any further increase in the first stimulus.

Actually, however, the following three factors would combine to delay the attainment of such a maximum until the first stimulus is slightly stronger than the second, for only then would the first stimulus set up a discharge from the whole field of ganglion cells excited by the second volley.

(1) There are probably small spontaneous variations in the excitability of the preganglionic fibres similar to those described by Blair & Erlanger [1933, 1936].

(2) Again there are presumably also small spontaneous variations in the thresholds of the ganglion cells.

(3) When preceded by the first volley, the second volley may set up the discharge of impulses from additional ganglion cells on account of a small facilitatory effect surviving during the long stimulus interval.

There is no way at present of determining the magnitude of these three effects, and it seems doubtful if they would be sufficiently large to

account for the maximum inhibition not being attained until the first stimulus is about 20 p.c. stronger than the second, as is shown in Text-fig. 22, which is typical of the series of observations in the four other experiments. Failing that explanation the presence of specific inhibitory fibres provide the only conceivable mechanism by which a delay in the attainment of a maximum could be brought about, the thresholds of some of these fibres being higher than those of the excitatory preganglionic fibres for the field of ganglion cells investigated. Thus the existence of specific inhibitory preganglionic fibres must be left undecided, but on account of the closeness with which the size of the first response parallels the inhibition of the second (Text-fig. 22), and of the magnitude of the antidromic inhibitory action, it must be concluded that such fibres, even if they exist, exert a much smaller inhibitory effect than that produced secondary to the discharge of impulses by the ganglion cells.

The relationship between antidromic and preganglionic impulses

There is more definite evidence that the *P* wave is to some extent directly set up by preganglionic impulses. Thus the *P* wave set up by a preganglionic volley is probably always larger than that set up antidromically (Text-fig. 3), and, when the refractory period following an antidromic volley prevents a preganglionic volley from setting up a discharge from the ganglion cells, the preganglionic volley still produces an additional *P* wave (Text-fig. 10). This special action of preganglionic impulses does not of course imply the existence of specific preganglionic fibres (which presumably would be of the classical inhibitory type), for the additional *P* wave could be produced directly by the ordinary excitatory preganglionic impulses. However, on account of the larger *N* wave directly set up by a preganglionic volley, the discharge of an impulse by a ganglion cell may itself give rise to a larger *P* wave than an antidromic impulse, for the *P* wave set up by either an antidromic or a preganglionic volley is increased by a pre-existent *N* wave (section C (4)).

Thus it must be concluded that the evidence suggests, but does not prove, that preganglionic impulses directly set up a *P* wave, which as we have seen is probably one aspect of c.i.s., a fundamental response of the ganglion cell. If preganglionic impulses do thus directly set up c.i.s., the direct actions of preganglionic and antidromic impulses on ganglion cells are qualitatively similar, both setting up c.e.s. and c.i.s., but quantitatively they differ,

for a preganglionic impulse directly sets up an intense c.e.s. and no more than a weak c.i.s., and an antidromic impulse (and probably the discharge of an impulse from a ganglion cell) an intense c.i.s. and a weak c.e.s.

General discussion

In this section experimental observations on the action of antidromic impulses on other nerve cells will be considered in the light of the conclusions reached in regard to ganglion cells. In section A, Umrath's results [1933] have suggested that antidromic impulses probably set up *N* and *P* waves in any nerve cell, and presumably such waves indicate the existence of the corresponding fundamental reactions, c.e.s. and c.i.s.

The motoneurones of the flexor reflex. In the original investigation on antidromic impulses any late depression of the excitability of motoneurones corresponding to Umrath's slow positive wave could not have been detected, for no examination of excitability was made at intervals beyond the stage of apparently complete recovery from the refractory period set up by that volley [cf. Eccles, 1931, Text-figs. 2 A, B]. It is now evident that such an apparently complete recovery probably was due to a temporary balance of the c.e.s. and c.i.s. set up by the antidromic volley (cf. Text-fig. 18 B). Such an interpretation has the further advantage of providing an explanation of the removal of facilitation by an interpolated antidromic volley [cf. Eccles, 1931, Pls. 39 and 40, figs. 3, 4 and 5] without drawing the conclusion (as was then done) that an antidromic volley inactivated c.e.s., an action which it does not appear to have on ganglion cells or on the motoneurones of the third nerve [Lorente de Nó, 1935 *b*]. Thus on analogy with the behaviour of ganglion cells a pre-existent *N* wave of the motoneurones would cause an antidromic volley to set up a larger *P* wave and probably a smaller *N* wave (cf. Text-fig. 16), effects which presumably also would be reflected in the corresponding c.i.s. and c.e.s. production with the result that there would be the apparent inactivation of the pre-existent c.e.s. when sampled by a later testing centripetal volley. In 1931 the existence of such an effect was of course not suspected, and its presence would not be indicated by the control observations on the action of the antidromic volley on the testing volley alone.

Motoneurones of the crossed extensor reflex. The action of an antidromic impulse when backfired into a rhythmically discharging motoneurone receives a more complete explanation than has hitherto been possible. Each discharge of the normal rhythmic series would normally set up a short *N* and a longer *P* wave whose course delays the setting up

of the next discharge and so conditions the duration of the normal cycle. An interpolated antidromic impulse would add to the P wave and so delay the subsequent discharge. The maximum beyond which the P wave (and presumably the c.i.s.) of the ganglion cell cannot be increased provides an analogy to the basal level beyond which it was impossible to depress the motoneurone [cf. Eccles & Hoff, 1932]. Moreover, the short N wave and c.e.s. presumably set up by a normal discharge (as well as by an antidromic impulse) provides a possible explanation of the hitherto inexplicable grouped discharges of motoneurones which so often appear after abnormally long cycles or at the beginning of a tetanus.

Motoneurones of the third cranial nerve. Lorente de Nó [1935 *b*] has shown that an antidromic volley sets up a depression of excitability of these motoneurones for as long as 15 msec., and he regards this as analogous to the late subnormality of peripheral nerve rather than to the classical refractory period (cf. section D). Moreover, such neurones differ from ganglion cells in showing no interpolated period of facilitation. He also concludes that an antidromic volley has no effect on pre-existent facilitation other than by the depression of excitability that it produces, the motoneurone thus resembling the ganglion cell; however, many of the observations supporting this conclusion have been complicated by the antidromic impulses being blocked from reaching many motoneurones on account of the impulses discharged from these motoneurones.

Inhibition. The probable absence of specific inhibitory fibres to the superior cervical ganglion raises the question of their existence in the spinal cord, for the inhibitory phenomena of the ganglion closely resemble those of the flexor reflex [cf. Eccles & Sherrington, 1931 *a*, *c*], though in the flexor reflex a volley exerts an inhibitory action on motoneurones without setting up the discharge of an impulse from them. However, Hughes & Gasser [1934 *b*] have presented a scheme by which this could occur through action on internuncial neurones, which histological observations [Hoff, 1932] and the experimental observations of Lorente de Nó [1935 *c*] have shown probably to be interpolated in the central pathway of the flexor reflex. It seems certain that part at least of reflex inhibition in the spinal cord is due to the depression of such nerve cells secondary to the discharge of impulses, for Hughes & Gasser [1934 *b*] find that the time course of the inhibition of the intermediary potentials resembles the positive wave. Moreover, there is as yet no proof of the existence of specific inhibitory fibres in the spinal cord, though Kato's experiments [1934] certainly suggest their presence in the frog. However that may be, the inhibitory state of ganglion cells, which is

largely if not entirely set up in the absence of specific inhibitory fibres, seems to be analogous to the inhibitory state exhibited by neurones of the spinal cord—at least in the case of the flexor reflex—for in all respects it forms a counterpart to the c.e.s. of ganglion cells, which undoubtedly is analogous to the c.e.s. of the flexor reflex.

Summary

An antidromic volley backfired into the superior cervical ganglion gives rise to the following changes in the ganglion cells.

1. A large spike potential, which suggests that an antidromic impulse traverses the ganglion cell and possibly the dendrites.

2. An absolutely refractory period of no more than 2 msec. and 3 msec. for the fastest S_1 and S_2 ganglion cells respectively. This is followed by a relatively refractory period, which shows that an antidromic impulse must penetrate as far as the locus at which the ganglion cell discharge is set up.

3. A slow potential wave, which analysis by the action of nicotine and by the interaction of antidromic and preganglionic volleys shows to be compounded of a negative wave N running concurrently with a larger and longer positive wave P (ganglion positive to its axon).

4. A prolonged depression of the excitability of the ganglion cells (as tested by a preganglionic volley), which analysis by the action of nicotine and by the interaction of antidromic and preganglionic volleys also shows to be compounded of a short facilitatory effect submerged beneath a longer period of depression.

The interaction experiments show that the antidromic N and P waves are indistinguishable from those waves set up by a preganglionic volley, and in addition confirm the previous findings on the interaction of N and P waves, *i.e.* pre-existent P in excess of N increases the N and diminishes the P wave set up either by an antidromic or preganglionic volley, and conversely pre-existent N in excess of P increases the production of P and decreases N. Similarly the facilitation and depression of excitability of the ganglion cells set up by an antidromic volley are shown to be qualitatively similar to the facilitation and inhibition set up by a preganglionic volley.

A maximal antidromic volley always sets up a much smaller N wave and facilitation than a preganglionic volley, but the P wave may be almost as large and the depression of excitability (inhibition) is often larger than that set up preganglionically. Despite the absence of a complete parallelism between the P wave and the depression of excitability of the ganglion

cells it is still thought that these reactions are aspects of the same fundamental state of the ganglion cells, which may be called the *P* process or c.i.s. Similarly the *N* wave and the facilitatory effect are thought both to be aspects of the fundamental state, c.e.s.

The experimental evidence is regarded as indicating that an antidromic impulse has the same action on a ganglion cell as an impulse discharged by that cell, the much larger *N* wave and facilitation set up by a preganglionic volley being due to the direct action of preganglionic impulses on the ganglion cells. On the other hand most of the *P* wave and inhibition produced by a preganglionic volley are set up secondarily by the discharge of impulses by those cells. The evidence is against the existence of specific inhibitory preganglionic fibres, but the excitatory preganglionic fibres in addition to their indirect action may also directly set up some *P* wave and c.i.s.

The action of antidromic impulses on other nerve cells and inhibition in the spinal cord is discussed in the light of these results.

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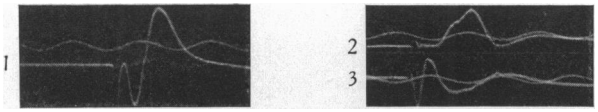

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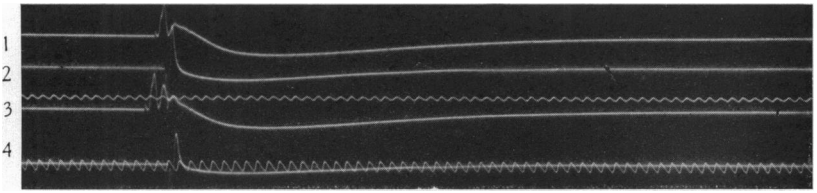

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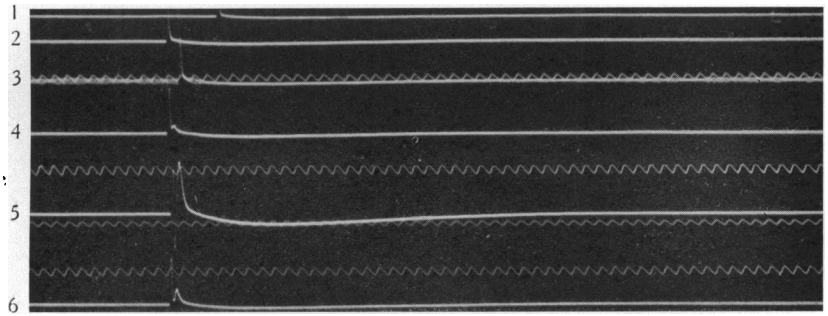

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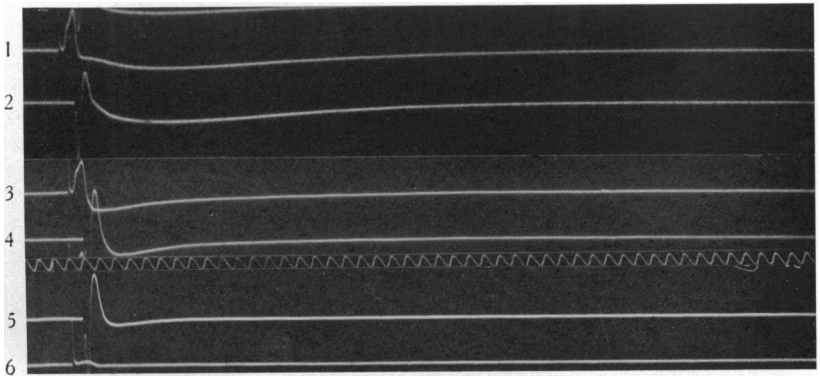
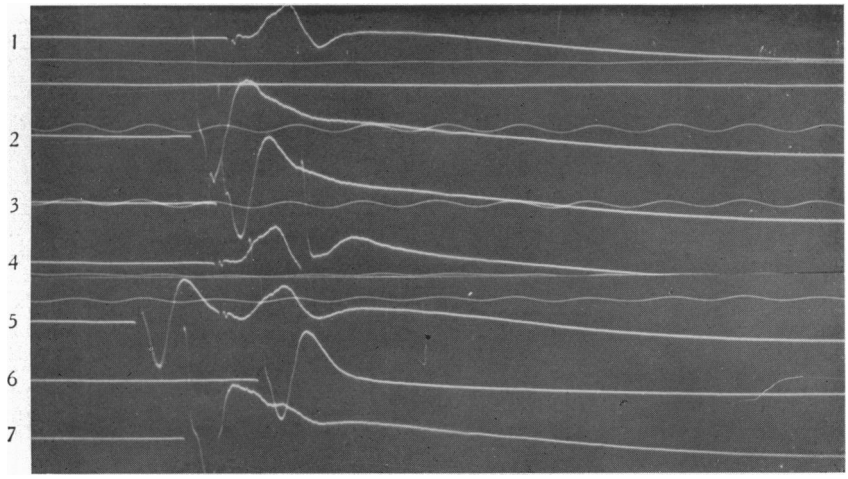


Fig. 4.

To face p. 38



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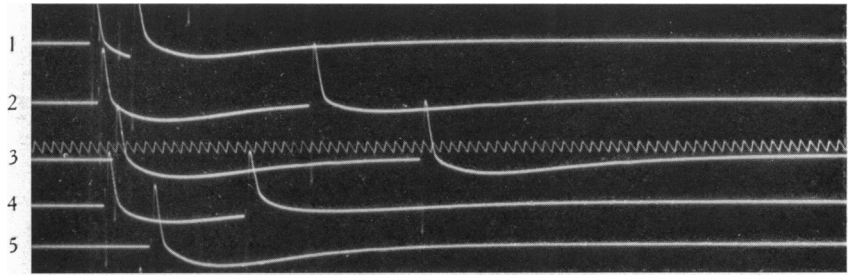

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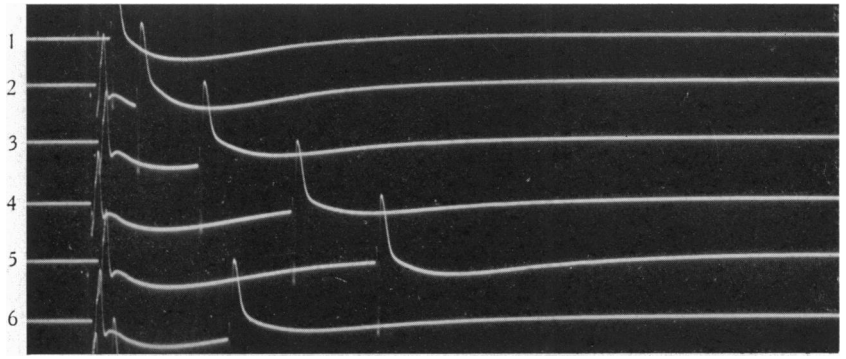

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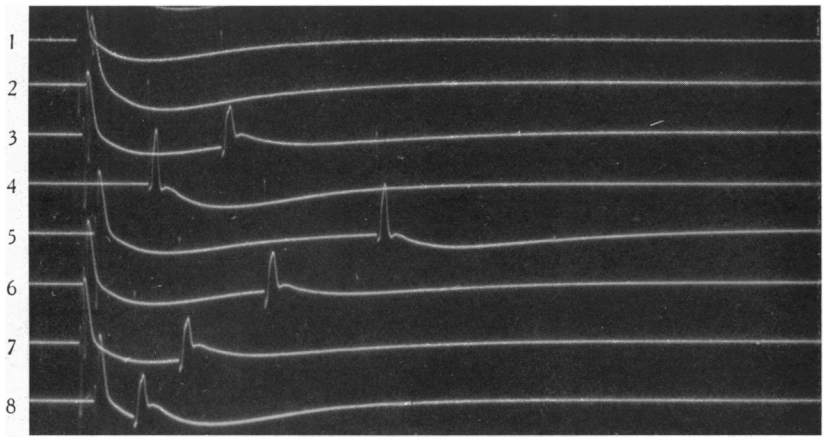

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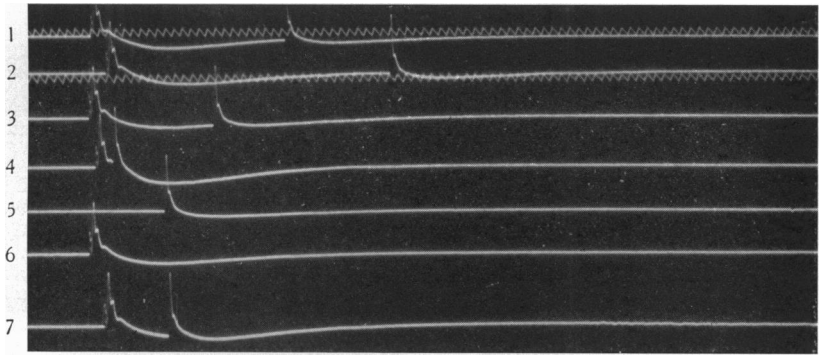

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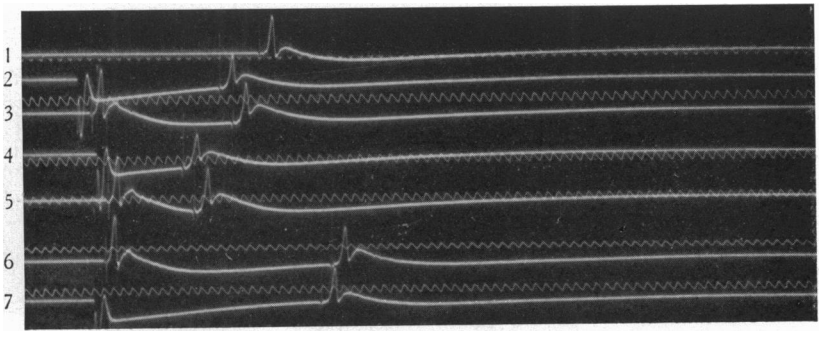

Fig. 10.

EXPLANATION OF PLATES I–III

PLATE I

Fig. 1. Ganglionic action potentials evoked by an antidromic volley (observations 1 and 3) or by a preganglionic volley (observation 2), the amplification with observation 3 being 2·7 times that of observations 1 and 2. With an upward deflection in this and all subsequent records the ganglion is negative to the postganglionic trunk. In all figures 1 d.v. equals 10 msec.

Fig. 2. As in fig. 1, but at a much slower speed so as to show the full course of the slow potential waves set up by an antidromic volley (observations 2 and 4, stimulus strengths 20 and 14·3 arbitrary units respectively), and by a preganglionic volley (observations 1 and 3, stimulus strengths 10 and 20 arbitrary units). The antidromic stimulus of 20 units was almost maximal, for strengthening it by 50 p.c. only slightly increased the spike and did not alter the positive wave, which in all observations is the slow downward deflection.

Fig. 3. As in fig. 3, but with weaker stimulus strengths—0·67 for observation 1; 1·0 for 2; 1·25 for 3; 1·67 for 4; 3·3 for 5; 2·0 for 6.

Fig. 4. Observations 1 and 2 as in fig. 2, but observations 3 and 4 were taken about 3 min. after painting the ganglion with 0·005 p.c. nicotine, and observations 5 and 6 after a further painting with 0·05 p.c. nicotine. Observations 1, 3 and 6 show the responses elicited by a maximal preganglionic volley, and observations 2, 4 and 5 by a maximal antidromic volley.

PLATE II

Fig. 5. Action potentials produced in the ganglion by maximal antidromic, *A*, and preganglionic, *P*, volleys at the following intervals—1, *P* alone; 2, *A* 2·5 msec. *P*; 3, *A* 0·0 msec. *P*; 4, *P* 11·9 msec. *A*; 5, *A* 11·4 msec. *P*; 6, *A* alone; 7, *A* 4·0 msec. *P*.

Fig. 6. Ganglionic action potentials produced by two maximal antidromic volleys at the following intervals—observation 1, 43 msec.; 2, 227 msec.; 3, 326 msec.; 4, 151 msec.; 5, control of second alone.

Fig. 7. Ganglionic action potentials produced by a maximal preganglionic volley followed by a maximal antidromic volley at the following intervals—observation 1, control of *A* alone; 2, 43 msec.; 3, 108 msec.; 4, 217 msec.; 5, 299 msec.; 6, 147 msec.

PLATE III

Fig. 8. Ganglionic action potentials produced by a maximal antidromic volley followed by a maximal preganglionic volley at the following intervals—observation 1, control of *A* alone; 2, 0·0 msec.; 3, 147 msec.; 4, control of *P* alone; 5, 309 msec.; 6, 199 msec.; 7, 110 msec.; 43 msec.

Fig. 9. As in fig. 7, but for submaximal preganglionic and antidromic volleys (almost maximal for S_1) at the following intervals—observation 1, 231 msec.; 2, 338 msec.; 3, 148 msec.; 4, 21 msec.; 5, *A* alone; 6, *P* alone; 7, 77 msec.

Fig. 10. Ganglionic action potentials evoked by a submaximal preganglionic volley (control response in observation 1) at intervals of 143, 87 and 231 msec. respectively after either a maximal preganglionic volley (observations 3, 5 and 6) or a maximal antidromic volley (observations 2, 4 and 7).