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THE ORIGIN AND NATURE OF GANGLION AFTER-POTENTIALS

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In a previous paper [Lloyd, 1937] it was shown that a complex action potential may be recorded from the inferior mesenteric ganglion when leads are placed on the ganglion and the postganglionic trunk. This potential resembles in general that recorded from the superior cervical ganglion [Eccles, 1935*a*, *b*], and may be analysed in a similar manner into its components: the spike potentials, the negative after-potential and the positive after-potential. The decision to refer to the slow potential waves of ganglion as ganglion after-potentials is based on the trend of current usage, which seems to be entirely justified since in no essentials do they differ from after-potentials recorded from other nervous structures.

The present paper deals largely with ganglion after-potentials as they appear in the inferior mesenteric ganglia. This choice of ganglion has the advantage of eliminating possible differences in the after-potentials following preganglionic and antidromic volleys, due to the presence of subliminal fringe. An attempt is made to clarify the origin and nature of these potentials.

A preliminary account of some of these results has been presented to the Canadian Physiological Society [Lloyd, 1938*a*].

Method

Cats have been used in all the present experiments. These were either decerebrated under deep ether anaesthesia or anaesthetized with nembutal, and not allowed to recover following experimentation. In some of the experiments involving degeneration of preganglionic fibres, the superior cervical ganglion was used because of the ease and surety of total preganglionic section. These degeneration experiments were all

done in Toronto, the cervical sympathetic or both sympathetic and vagus nerves being crushed or cut low in the neck with aseptic precautions and under ether anaesthesia. Records from the superior cervical ganglia were obtained 5–22 days following preganglionic section.

The amplifiers and recording systems have been the same as used in previous experiments [Lloyd, 1937, 1938*b*, 1939*a*]. The coupling condensers and grid resisters of the amplifier are of large enough value (6×1) to give reasonably faithful records of the after-potentials.

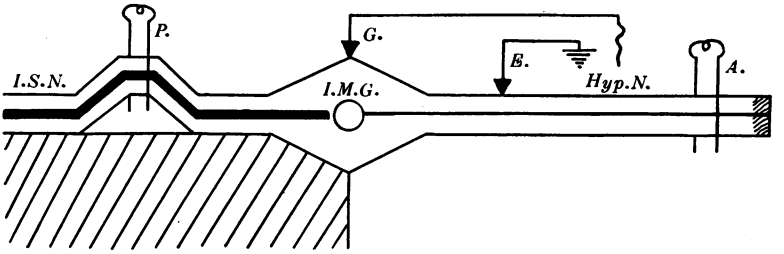

Fig. 1. Diagram of the inferior mesenteric ganglion to show conditions under which ganglion after-potentials are recorded following preganglionic and antidromic volleys. *I.S.N.* inferior splanchnic nerve; *Hyp.N.* hypogastric nerve; *I.M.G.* inferior mesenteric ganglion; *E.* and *G.* earth and grid amplifier input leads; *P.* preganglionic stimulating electrodes; *A.* antidromic stimulating electrodes. The hatched area indicates the extent of attachment of the ganglion to the animal. The blood supply to the ganglion is maintained intact.

Fig. 1 shows the position of the stimulating electrodes and recording leads with respect to the ganglion. The postganglionic hypogastric nerve and distal pole of the ganglion have been isolated up to the position of the ganglionic lead (*G*). A short stretch of the preganglionic nerve has been isolated for the placement of the stimulating electrodes (*P*). In all experiments, the animal was earthed via the earth lead, and not separately.

Results

Fig. 2, observation 1, shows the action potential set up by a single maximal antidromic volley applied to the hypogastric nerve, with one lead on the inferior mesenteric ganglion, the other being on the postganglionic trunk as in Fig. 1. Fig. 2, observation 2, shows the action potential set up by a single maximal preganglionic volley applied to an inferior splanchnic nerve, with the same recording leads. In all the observations of this paper an upward deflexion denotes negativity of the ganglion relative to the postganglionic trunk. Following the spike negativity in both observations 1 and 2 of Fig. 2, the potential drops

slowly to a maximum positivity at 100–120 msec. and returns to normal only after some 400–500 msec. Following preganglionic activation, diphasicity cuts into the early course of the after-potential and is difficult to obviate, since the postganglionic fibres belong to the C group. Following antidromic activation the after-potential overlaps the descending limb of the spike potential. For these reasons the early potential value of the after-potential is almost impossible to determine. However, the best

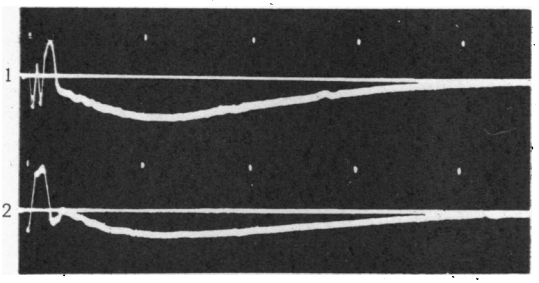

Fig. 2. Ganglionic action potentials recorded with the leads shown in Fig. 1. Observation 1 is the potential recorded following an antidromic volley through electrodes *A* in Fig. 1. Observation 2 is the similar potential following preganglionic stimulation through electrodes *P* in Fig. 1. The horizontal lines represent the approximate electrical base line. Time: 100 msec. Slightly retouched.

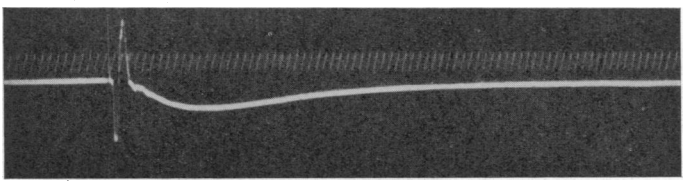

Fig. 3. Ganglionic action potential set up by a maximal antidromic volley as in Fig. 2, observation 1, but in another experiment. Time: 1 d.v. = 10 msec.

preparations (Fig. 3) indicate that the onset of the after-potential following antidromic activation is not far below, and occasionally above the resting potential level, while that following preganglionic activation may more often attain an absolute negativity, as in the control observations of Fig. 7. The negative after-potential then is usually represented by a slowly progressing positivity, which contrasts with the abrupt positivity encountered when a positive after-potential alone is present [cf. Eccles, 1935*b*, 1936].

The negative after-potential of the inferior mesenteric ganglion is represented, in terms of excitability, by a well-defined peak of excita-

bility to synaptic stimulation following both preganglionic conditioning [Lloyd, 1939*a*] and antidromic conditioning [Lloyd, 1939*b*]. The after-potentials, however initiated, bear a remarkable similarity and constancy with respect to their time course in the normal resting ganglion and are not sufficiently disparate in potential to warrant the assumption that they arise from different sources, or that a common source is behaving in an essentially different manner in the two instances. Some of the difference in amplitude may be attributed to the obvious impossibility of exciting an equal number of ganglion cells in this ganglion by the two methods. Such differences have no special significance.

An indication of a true difference in the potential value of the after-potentials may be obtained by a comparison of the excitability cycle of the inferior mesenteric ganglion cells following preganglionic and antidromic volleys [Lloyd, 1939*a*, *b*]. The supernormality peak is higher in the former case than in the latter, which suggests the differential influence of factors external to the cell (possibly acetylcholine liberation) or incidental factors such as the direction in which the conducted disturbance sweeps over the cell. Such influences might well be expected to introduce secondary discrepancies between ganglion after-potentials and excitability cycles as recorded following preganglionic and antidromic activation.

The illustrations of after-potentials from the superior cervical ganglion presented by Eccles [1936] show differences such as are seen in the inferior mesenteric ganglia. The great disparity observed in the excitability cycle following preganglionic and antidromic volleys in the superior cervical ganglion is related to the subliminal fringe set up by preganglionic conditioning in this ganglion and the subsequent recruitment.

The role of presynaptic elements in the development of ganglion after-potentials

Following the analysis of dorsal root potentials by Barron & Matthews [1938] in which presynaptic elements are considered to be of paramount importance in the development of potentials observed in the spinal roots, a suggestion was made (though not by those authors) that presynaptic rather than postsynaptic structures are primarily concerned with the development of ganglion after-potentials. The recording of these after-potentials following antidromic activation in the superior cervical ganglion is, perhaps, not a complete refutation of this suggestion, as the postganglionic trunk is short and the necessarily strong stimuli might

have spread to the preganglionic structures. The long available postganglionic nerve in the inferior mesenteric ganglion minimizes this possibility in the recording of after-potentials following antidromic volleys. The theoretical implications of the suggestion are so great,

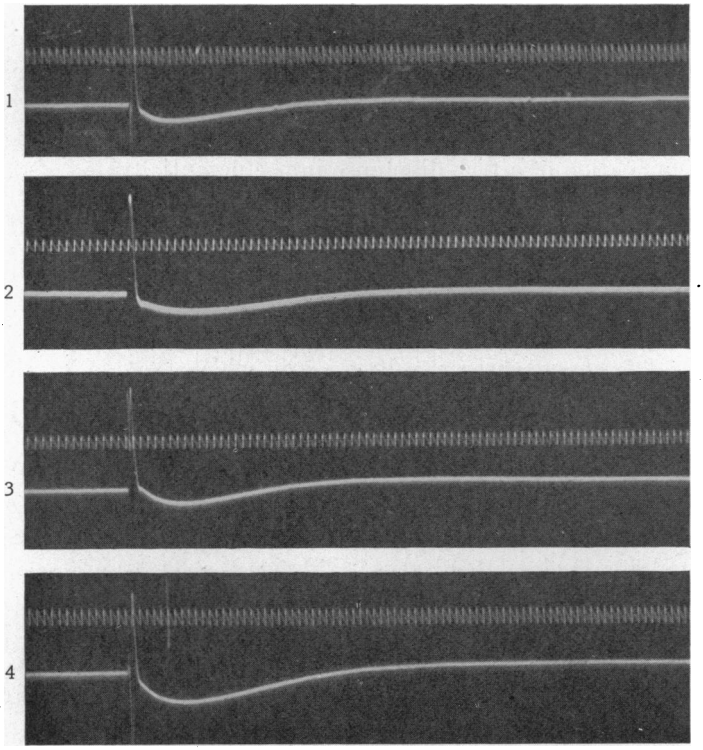

Fig. 4. Action potential set up by maximal antidromic volleys and recorded from the superior cervical ganglion, following preganglionic degeneration. Observation 1, normal ganglion; observation 2, 5 days degeneration; observation 3, 9 days degeneration; observation 4, 22 days degeneration. Amplification similar in all experiments. Time: 1 d.v. = 10 msec.

however, that further evidence has been sought. For this reason ganglion action potentials set up by antidromic volleys were recorded in the superior cervical ganglia under normal conditions and from 5 to 22 days following preganglionic section (Fig. 4). In all cases the stimulating electrodes were on the postganglionic trunk, the recording leads being on the postganglionic trunk and the ganglion.

In Fig. 4, observation 1 is the control recorded from a normal ganglion. Observations 2–4 are from ganglia with degenerated preganglionic fibres. The times of degeneration are given in the legend. In each case the normal after-potential cycle is encountered. There is no progressive alteration that could be correlated with degeneration time and these records both from normal and preganglionically degenerated ganglia compare well with those published by Eccles [1936]. Thus the degeneration of preganglionic elements in the superior cervical ganglion does not disturb the after-potentials set up by antidromic stimulation, which could not be the case if preganglionic elements were an important factor *per se* in the development of ganglion after-potentials.

Modification of the ganglion after-potential by drugs

Nicotine. Fig. 5 shows a series of ganglion action potentials recorded following preganglionic activation. Observation 1 is the normal ganglion action potential. Between observations 1 and 2 dilute nicotine was

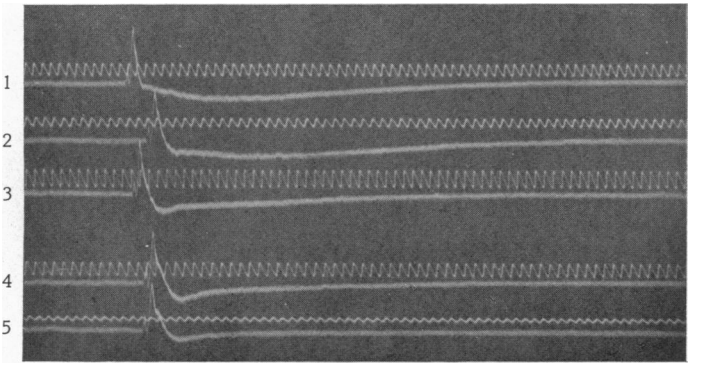

Fig. 5. Ganglionic action potentials set up by single maximal preganglionic volleys. Observation 1 is the normal action potential. Between observations 1 and 2 dilute nicotine was painted on the ganglion. Observations 2–5 show stages in the effect of the nicotine on slow wave production. The spike potential is slightly diminished in the later observations (Langley's block). Time: 1 d.v. = 10 msec.

painted on the ganglion. Observations 2–5 are successive stages in the action of nicotine. As in the superior cervical ganglion [Eccles, 1935*b*] the first effect is the removal of the negative after-potential. Subsequently the positive after-potential is greatly diminished. The differential action of nicotine supports the view that the negative and positive after-potentials are distinct though simultaneously developed and partially

cotemporaneous entities as in the superior cervical ganglion [Eccles, 1935*b*]. Grundfest & Gasser [1938] have recently described the negative and positive after-potentials of C fibres in mammalian sympathetic nerves as developing simultaneously, which emphasizes a parallelism between the after-potentials of ganglion and C fibres.

In view of this action of nicotine on ganglion after-potentials it is of particular interest that Bronk & Larrabee (personal communication) have shown that nicotine reduces the after-potential of postganglionic (C) fibres.

Veratrine. The negative after-potential recorded from ganglia is extremely sensitive to the action of veratrine. Following a local application of this drug to the ganglion, the negative after-potential begins at

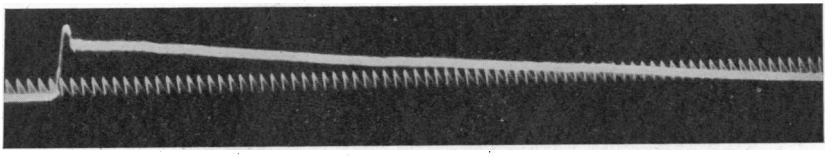

Fig. 6. Ganglionic action potential elicited by a single preganglionic volley after the application of dilute veratrine to the ganglion. Time: 1 d.v. = 10 msec.

about 75 % of the spike height (not corrected for temporal dispersion) and maintains an absolute negative value for more than a second (Fig. 6). There is a hint of spontaneous firing during this large negative after-potential.

The greater negativity developed by veratrine is not reflected by the appearance of facilitation, presumably since further lowering of threshold (as demonstrated in nerve) does not further enhance the effectiveness of an already adequate synaptic stimulus.

The modification of after-potentials by previous activity

Fig. 7 shows a series of ganglion action potentials set up by two successive volleys applied to an inferior splanchnic nerve. Observation 5 is the control observation from the first volley alone, observation 6 being a similar control from the second volley alone. In observations 1–4 there is an obvious increase in the negative after-potential set up by the test volley, which reaches a maximum when the test volley falls at the point of maximum positivity. This effect is sufficiently large to establish an absolute negativity of the ganglion, though this is not long lived. Accompanying the increase in negative after-potential as a result of previous activity there is a deficiency in the development of the positive

after-potential, the combined positivity being little greater than in a single control observation. With very short intervals these effects are precisely reversed [cf. Eccles, 1935*b*].

Gasser [1938] has recently described the higher and longer negative after-potential set up by a single volley falling during the intercurrent positivity following a tetanus in peripheral nerve. Furthermore, Gasser [1937] has shown that the after-positivity set up by two stimuli in nerve is greatest at short stimulus intervals. These observations indicate the comparable effects of previous activity on the after-potentials of ganglion and nerve fibre.

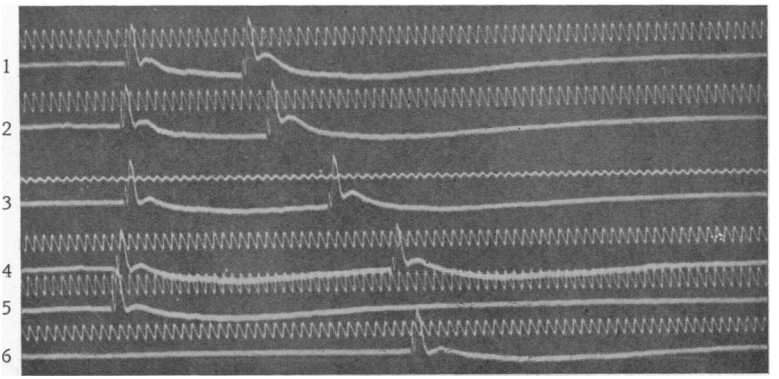

Fig. 7. Action potentials recorded from the inferior mesenteric ganglion and set up by two successive maximal preganglionic volleys. Observations 1–4 have inter-stimulus intervals of 140–325 msec. Observations 5 and 6 are controls from the conditioning and test volleys respectively. Time: 1 d.v. = 10 msec.

When a ganglionic lead is used (Fig. 7) there is regularly an apparent increase in spike amplitude of the response to a test volley, which follows a time course identical with that of the inverted after-potential of the conditioning response. This effect has been noted by Rosenblueth & Simeone [1938] and apparently taken to indicate the presence of facilitation during the "inhibitory period", and hence a lack of correlation between the after-potentials and the excitability of the ganglion cells. The increase in spike height is illusory, and is due entirely to increase in the negative after-potential as shown in Fig. 8. Since the amplitude-time plots of the spike and negative after-potential are exactly parallel, the spike potential is in reality constant throughout. This contention is borne out by the complete absence of any amplitude changes in the spike potential recorded with truly postganglionic leads, in the same ganglion

with all other conditions similar. Thus in experiments purporting to show facilitation and inhibition either postganglionic leads must be used or proper allowance should be made for alteration in the after-potentials due to previous activity.

That a lack of correlation sometimes exists is not doubted, but this lies between facilitation and inhibition on the one hand, and the after-potentials with associated threshold changes (supernormality and subnormality) on the other [Lloyd, 1939*a*]. This lack of correlation is due to

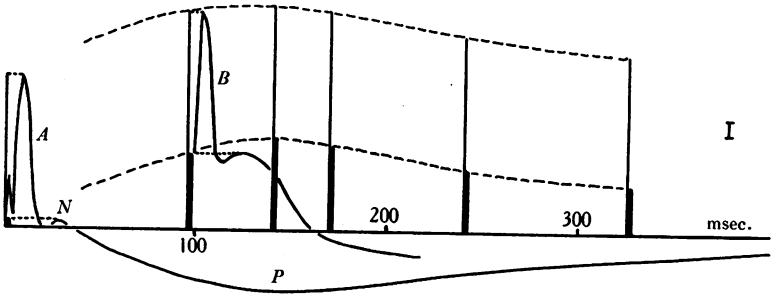

Fig. 8. A semidiagrammatic representation constructed from observations, some of which are shown in Fig. 7. Curve *A* is a plot of a control ganglionic action potential to show particularly the course of the negative and positive after-potentials developed on a resting background. Curve *B* is plotted similarly but represents the action potential set up 96 msec. following a similar preganglionic conditioning volley. The thin vertical lines represent the amplitude of the spike response, the heavy vertical lines that of the negative after-potential, plotted against the stimulus interval. These are derived by projecting the true potentials into the appropriate time ordinate as indicated by the horizontal dotted lines from curves *A* and *B*. The upper hatched curve thus represents the variation in spike height, the lower hatched curve that in negative after-potential at various intervals following a conditioning volley. A measure of the relative spike height is obtained in such experiments by measuring from the crest to the diphasic artefact. The calibration line to the right gives the variation in control responses from beginning to end of the experiment.

the fact that synaptic stimulation tests the excitability changes of the ganglion cell only within the limits fixed by the density of active preganglionic endings, and is the same as that which may be observed in nerve if the test stimulations are liminal or supraliminal for all the axones. Reversal effects, such as facilitation during the positive after-potential and associated subnormal period, are not encountered.

The analogy between ganglion and nerve fibre after-potentials

The analogy between the after-potentials recorded from ganglion and those recorded from a simple nerve, containing only axones, has not been completed, but all the observations which have as yet been made on

TABLE I

Ganglion	Nerve
Single action followed by N and P after-potentials	Do. [Gasser, 1937]
N and *P* after-potentials developed simultaneously	Do. [Grundfest & Gasser, 1938]
N after-potential associated with threshold lowering process (supernormality)	*N* after-potential associated with supernormality. [Gasser & Erlanger 1930; Graham, 1934]
P after-potential associated with threshold raising process (subnormality)	*P* after-potential associated with subnormality. [Graham & Gasser, 1934; Graham, 1935]
N after-potential increased by background of *P* after-potential	*N* after-potential increased during positivity following tetanus [Gasser, 1938]
P after-potential increased by background of *N* after-potential (short intervals)	Positivity set up by two volleys greatest at short intervals [Gasser, 1937]
N after-potential increased by veratrine	Do. [Graham & Gasser, 1931]
After-potentials removed by nicotine	Do. [Bronk & Larrabee, personal communication]
After-potential of S_2 cells predominantly positive	Positive after-potential predominates in C fibres [Grundfest & Gasser, 1938]

ganglion after-potentials have their counterparts in nerve. These may be seen in Table I.

In the light of these similarities, the assumption that ganglion and nerve after-potentials are analogous processes is difficult to avoid.

The origin of ganglion after-potentials

In 1935 Bronk, Tower & Solandt raised the question as to whether the after-potentials recorded by Eccles from the superior cervical ganglion could not be attributed to the activity of intraganglionic nerve fibres and not primarily to the ganglion cells. Later Bishop [1936] criticized Eccles' findings on the basis that a ganglion might behave as an inert mass of conduction tissue applied to the postganglionic fibres, which might be solely responsible for the recorded potentials. At the present time Bronk, Tower, Solandt & Larrabee [1938] maintain that "mere size of after-potential is not an adequate criterion for identifying a cell potential", a view with which the author is in complete agreement. In the face of the uncertainty with which ganglion after-potentials have been regarded, it is well to summarize here the principal evidence for the view that the ganglion after-potentials are truly cell body potentials:

(1) The ganglion after-potentials are recorded when one lead is on the ganglion and the other on the *intact* postganglionic trunk. Eccles [1937] maintains that postganglionic fibre after-potentials could not be recorded to an appreciable extent with diphasic leads.

(2) As the ganglionic lead is moved progressively along the post-ganglionic trunk there is a rapid decrement in the after-potentials not associated with the "killed end effect".

(3) Ganglion after-potentials are recorded following antidromic volleys. Furthermore, the after-potentials are still present after degeneration of preganglionic elements.

(4) The excitability cycle of the ganglion cells follows closely the course of the after-potentials.

The last consideration forms probably the best evidence for the existence of true cell body after-potentials. There can be little doubt that the threshold changes observed following preganglionic and antidromic conditioning volleys take place at the site of synaptic stimulation of the cell by the testing preganglionic volley [Eccles, 1936; Lloyd, 1939*b*], i.e. in the region of the dendrites and cell body (cf. also evidence presented by Lorente de Nó for motoneurones [1935, 1938]). The after-potentials which would be expected to accompany these threshold changes are similar to those which are in fact recorded from the ganglion.

Summary

Similar after-potentials are recorded from the inferior mesenteric ganglion following single preganglionic and antidromic volleys. Such differences as exist suggest the influence of differentiating factors incidental to the direction and mode of activation of the ganglion cells in the two instances.

Preganglionic structures are not important *per se* in the development of ganglion after-potentials, as shown by degeneration experiments.

Ganglion after-potentials and nerve after-potentials react in the same way to drugs and previous activity, and by a considerable weight of evidence appear to be analogous processes.

A satisfactory agreement between ganglion after-potentials and ganglion cell excitability is found within the range of cellular threshold that can be tested by the relatively fixed synaptic excitation. Reversal effects, such as increased responsiveness (supernormality) during the positive after-potential, do not occur.

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