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# CONDUCTION THROUGH THE INFERIOR MESENTERIC GANGLION OF THE RABBIT

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In recent years a considerable volume of information has accumulated about conduction through the ganglia of the sympathetic nervous system. The pathways through the superior cervical ganglion, the stellate and the inferior mesenteric ganglion of the cat have been studied in detail (Eccles, 1935, 1943; Lloyd, 1937; Bronk, Tower, Solandt & Larrabee, 1938), and accurate figures are available for conduction velocities in afferent and efferent fibres for refractory periods and for synaptic delays in these ganglia.

Our attention was originally directed towards the inferior mesenteric ganglion of the rabbit by our need to secure, for another purpose, a ganglion with a long post-ganglionic trunk and capable of survival for long periods after isolation from the body. Preliminary tests revealed fibre connexions in this ganglion of greater complexity than we had suspected, and transmission phenomena which distinguished it in some respects from those previously studied. A preliminary account of some of the experiments has already appeared (Brown & Pascoe, 1951).

## METHODS

All our experiments have been made on the inferior mesenteric ganglion of the rabbit, isolated from the body and suspended in Locke's solution.

### *Gross anatomy and nomenclature*

The inferior mesenteric ganglion of the rabbit is a single (unpaired) structure lying within the mesocolon in the cranio-ventral angle between the inferior mesenteric artery and the aorta (Fig. 1). It is connected with the sympathetic ganglionated chain through the inferior splanchnic nerves. The only one of these large enough for dissection and convenient manipulation runs from the cranial pole of the ganglion, cranio-dorsally and may be 1–1·5 cm in length. A smaller splanchnic nerve is sometimes visible running ventrally from the chain to enter the middle of the ganglion. Only on a few occasions have we succeeded in dissecting this in a viable condition. Other minute filaments can also be seen running from the chain towards the ganglion or its connexions and are presumably subsidiary inferior splanchnic nerves.

Running from the caudal pole of the ganglion is a complex network of branches, some emanating from the ganglion itself and others from nerve fibres on the colonic vein and inferior

mesenteric artery. This network often forms two distinct trunks which embrace the inferior mesenteric artery and then unite to join the accessory inferior mesenteric ganglion, from which arise the hypogastric nerves proper.

On the ventral side of the main ganglion there is a dense plexus of nerves, the main strands of which form the ascending mesenteric nerve, running cranio-ventrally along the colonic vein. In many animals a separate subdivision of the ascending mesenteric nerve, the aortic branch, arises from the cranial pole of the ganglion, runs dorsally in the mesocolon and then turns ventrally to join the main trunk of the ascending mesenteric nerve. Running along the colonic vein, in close association with the fibres arising from the ganglion, are numerous strands which may either run into the accessory ganglion, turn ventrally with the colonic vein or inferior mesenteric artery, or mingle inextricably with the plexus on the ventral side of the main ganglion.

We have adhered closely to the nomenclature used by Langley & Anderson (1896); the term intermesenteric nerve is used by Kuntz (1940) apparently to describe the ascending mesenteric nerve and its branches.

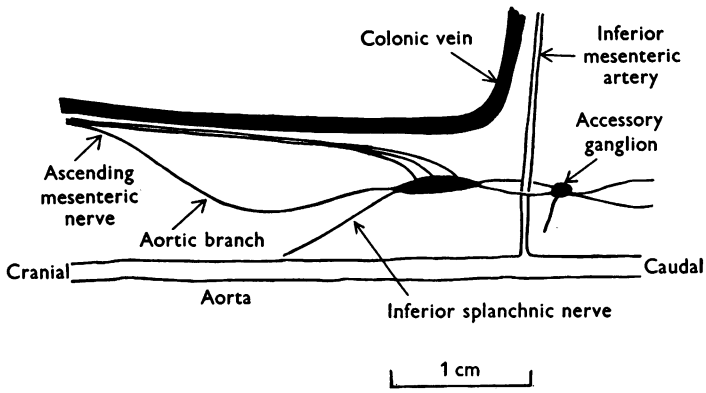


Fig. 1. Diagram of connexions of inferior mesenteric ganglion in the rabbit, as seen from the right side of the supine animal.

For dissection of the ganglion and its nerves the rabbits were anaesthetized with urethane (1·8 g/kg), the abdomen was opened, and the mesocolon in the region of the inferior mesenteric artery was spread on a black glass plate. This procedure, in thin rabbits, exposes clearly the ganglion and its connexions. In animals with copious retroperitoneal fat, the ganglion may not be visible until the uppermost layer of mesocolon has been removed. When the ganglion and its branches had been identified, the inferior splanchnic was dissected and tied, then the aortic branch was dissected, and the ascending mesenteric nerve was stripped from the vein. The final procedure was to ligate the caudal branches of the ganglion and to free it from its bed. By proceeding in this order we were able usually to preserve all branches in a conducting condition, and the ganglion itself retains its blood supply until the end; the artery of the ganglion is usually a branch of the inferior mesenteric vessel, and its veins appear to drain directly into the inferior vena cava. Most of the dissection was made with steel needles ground to knife edges, and with the aid of a binocular-dissecting microscope giving a magnification of $\times 7$.

*Recording*

The ganglion was placed in Locke's solution at room temperature and eventually set up in the recording bath. This consisted of a Petri dish surrounded by a brass frame which carried in ball joints sufficient platinum hooks to provide suspensions for the four branches of the ganglion and stimulating, recording and earth leads for any three of them. The brass frame was closed at the top and bottom with glass plates, the whole forming a reasonably gas-tight chamber. The Locke's

solution in the Petri dish was aerated and circulated continuously with a 95% $O_2$–5% $CO_2$ mixture, and its level could be changed to allow suspension of the preparation in the gaseous atmosphere for recording, and immersion in the solution at intervals.

In some of our early experiments we dissected under light liquid paraffin and attempted to record in paraffin or in a paraffin-Locke's solution interface. We found that the preparations in paraffin decayed rapidly, and accordingly abandoned its use.

The potentials from the ganglion and branches were led through cathode followers into an amplifier with variable time constant, d.c. recording being available if necessary. The amplified potentials were displayed and recorded from a double-beam cathode-ray oscilloscope.

*Stimulation*

The stimuli used were rectangular voltage pulses, floating from earth, and of a duration of 0·5 msec.

## RESULTS

### *Conduction from inferior splanchnic to ascending mesenteric nerve*

Stimulation of the inferior splanchnic causes the appearance of a spike in the ascending mesenteric nerve. The shortness of the inferior splanchnic nerve usually prohibited determination of the velocity of the ingoing volley. In two experiments, in which a sufficient length of nerve was available, we measured the velocity of the component of the ingoing volley responsible for the main spike of the outcoming volley in the ascending mesenteric nerve by moving the stimulating electrodes on the inferior splanchnic. The ingoing fibres conducted at a velocity not less than 5 m/sec at 20° C. In the other experiments the stimulating cathode was so close to the ganglion that no allowance for the velocity of the inferior splanchnic volley was necessary in making subsequent calculations of ganglionic delay.

Stimulation of the ascending mesenteric evoked in the inferior splanchnic only a minute spike; the major part of the volley produced in the ascending mesenteric by stimulating the splanchnic is thus postganglionic. This conclusion was confirmed by the almost complete disappearance of the ascending mesenteric spike when the ganglion was blocked with either D-tubocurarine or nicotine acid tartrate.

*Velocity of outcoming ascending mesenteric volley.* A number of determinations was made of the velocity of the main spike appearing in the ascending mesenteric nerve when the inferior splanchnic was stimulated; the velocities at temperatures 20–22° fell between 0·37 and 0·56 m/sec (mean 0·43, 9 determinations, S.E. ±0·02).

*Ganglionic delay.* The ganglionic delay was determined graphically from a plot like that shown in Fig. 2. The distance shown as 0 was taken as the position of the recording electrodes when that nearest to the ganglion was touching the junction of the ascending mesenteric nerve and the ganglion. It is obvious that this point can only give an approximation to the position of the actual synapse, since the ganglion extends over several mm, and it is well known that ganglion cells may be found in sympathetic nerve trunks at considerable

distances from an anatomically circumscribed ganglion. The spatial extent of the ganglion, therefore, together with the low velocity of conduction of the outcoming volley, led to inaccuracies in calculation of the delay in the passage of the impulse through the ganglion.

At temperatures of 20–22°, delays between 26 and 43 msec have been observed (mean 33, 9 determinations, S.E. ±3).

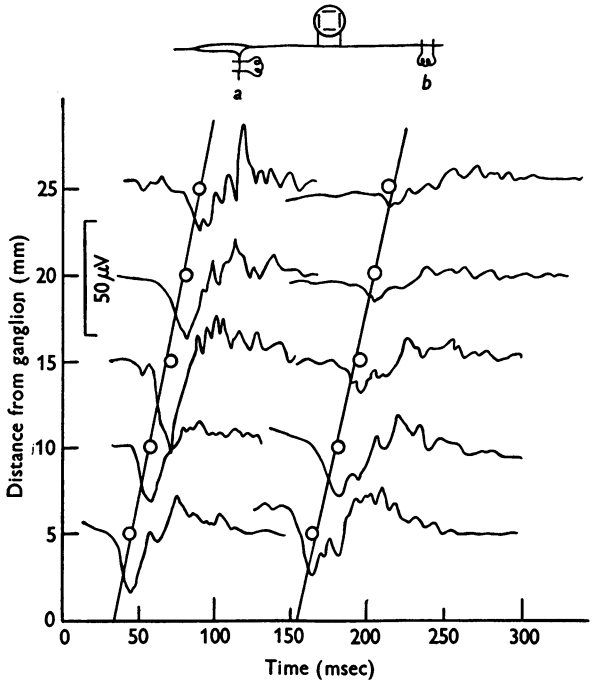


Fig. 2. Example of plot used to determine ganglionic delay and velocity of outcoming volley in ascending mesenteric nerve, excited (*a*) by inferior splanchnic stimulation, and (*b*) by ascending mesenteric ingoing volley. In this and all subsequent figures a downward deflexion indicates negativity of the recording electrode nearer to the ganglion.

### *Effects of stimulation of ascending mesenteric nerve*

When we started these experiments we had assumed that the ascending mesenteric nerve would contain mainly postganglionic fibres with cells in the inferior mesenteric ganglion supplied by the inferior splanchnic, together with a few 'straight through' fibres like those reported by Lloyd (1937) as occurring in the cat. This proved to be incorrect, since excitation and recording from the nerve showed that a volley entering the ganglion (the ingoing volley) gave rise to a smaller and less synchronous outcoming volley after a delay in the ganglion (Fig. 3).

*The ascending mesenteric ingoing volley.* Maximal stimulation of the ascending mesenteric nerve gives rise to a large, synchronous and apparently

homogeneous diphasic spike conducted at velocities between 0·35 and 0·67 m/sec at 20–22° (mean 0·45 m/sec, 14 determinations, S.E. ±0·013). In some experiments the large spike was preceded by a much smaller spike representing a group of fibres with a lower threshold, conducting at 2 m/sec. With higher amplification a third spike becomes evident, produced by a group of fibres with higher threshold and a conduction velocity near 0·25 m/sec. The method used in determining the velocities of the ingoing components of the ascending mesenteric nerve and of the outcoming volley is shown in Fig. 4.

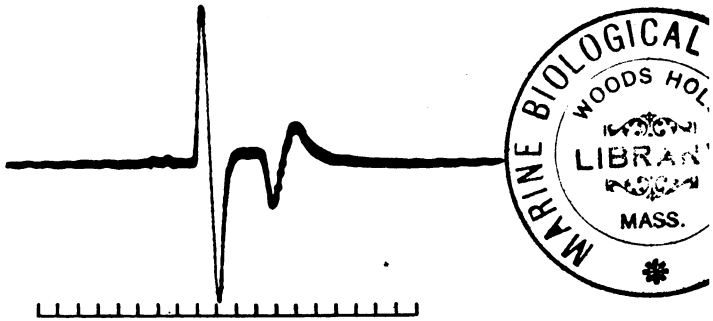



Fig. 3. Response of ascending mesenteric nerve to maximal single shock, showing ingoing spike and spike returning from ganglion. Stimulating cathode 26 mm from ganglion and one recording electrode on pole of ganglion. Time, 20 msec.

*The ascending mesenteric outcoming volley.* The outcoming volley recorded in the ascending mesenteric nerve shows a spike which is seldom more than 20% of the main ingoing spike and is followed by an asynchronous discharge of variable magnitude and duration. An example of a particularly clear asynchronous discharge is given in Fig. 5. Measurements of the velocity of the outcoming volley show that the main spike is conducted at 0·20–0·53 m/sec at 20–22° (mean 0·37, 16 determinations, S.E. ±0·02). In those experiments in which all determinations were made, the outcoming volley was always found to travel a little slower than the main ingoing spike, but faster than the third component of the ingoing spike.

*Preganglionic fibres exciting outcoming ascending mesenteric volley.* In our earlier experiments we assumed that the main ingoing volley contained the fibre group responsible for the outcoming discharge in the ascending mesenteric nerve (cf. Brown & Pascoe, 1951). We were led to doubt this by the observation that the outcoming spike did not appear until the stimulating voltage was increased beyond that necessary to produce a maximal main spike. We therefore determined directly the velocity of the fibres responsible for exciting the outcoming spike by the following method (Fig. 6). Recording electrodes were placed at *A* on the ascending mesenteric nerve, and the tissue under the distal lead was treated with cocaine to produce a monophasic record. The

stimulating electrodes were moved by steps between *B* and *C* on the aortic nerve. This provides a fixed distance of travel for the outcoming volley and a variable distance for the ingoing; the difference in latency between points *B* and *C* thus gives a measure of the velocity of the ingoing volley responsible for the outcoming volley recorded at *A*. The values obtained agreed closely with the velocity of the third, slowest component of the ascending mesenteric complex action potential.

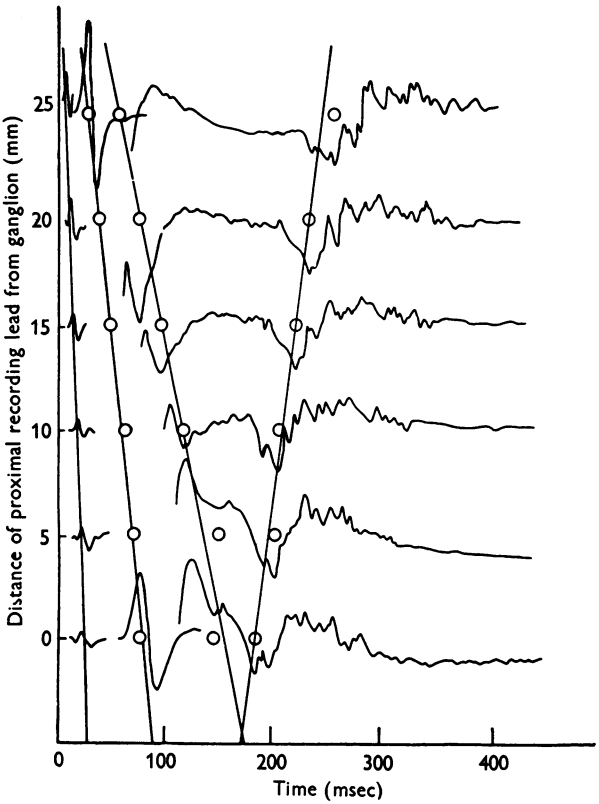


Fig. 4. Determination of velocities of ingoing ascending mesenteric spikes and of the outcoming volley. The main ingoing spike has been deleted except at positions 0 and 25 mm for the sake of clarity. Lower gain was used for recording the main spike. In this experiment the velocities were as follows: 1st spike, 1·4 m/sec; 2nd spike (main spike), 0·47 m/sec; 3rd spike (true ingoing), 0·27 m/sec; outcoming, 0·39 m/sec.

The evidence from velocities points to a fundamental change in the conducting pathway after the impulses have passed through the ganglion. As Table 1 shows, the outcoming spike always travels faster than the ingoing spike responsible for it. This, in itself, is good evidence that a synapse is involved. The outcoming volley, moreover, disappears when the ganglion is treated with D-tubocurarine chloride or with nicotine acid tartrate.

The above arguments exclude the possibility that the outcoming volley is due to the discharge of cells excited antidromically, as occurs with the motoneurones of the spinal cord (Renshaw, 1941). The outcoming volley, moreover, can be recorded when the likelihood of antidromic excitation is remote; it occurs, for instance, in the aortic branch of the ascending mesenteric nerve when the main trunk is stimulated and vice versa. The abnormal

Fig. 5. Response of ascending mesenteric nerve to maximal single shock. The main ingoing spike is not visible, since high amplification was used. The third, slowest component of the ingoing spike is clearly shown. The outcoming discharge is unusually asynchronous. Stimulating cathode 29 mm and lead-off electrodes 20 mm from ganglion. Time ,20 msec.

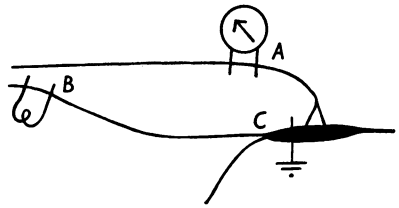


Fig. 6. Method of measuring conduction velocity of ingoing fibres responsible for outcoming volley. For details see text.

TABLE 1. Ascending mesenteric nerve; simultaneous comparisons of velocity of outcoming spike, and that of ingoing spike responsible for it

| Expt. | Outcoming (m/sec) | Ingoing (m/sec) |
|---|---|---|
| 1 | 0·43 | 0·26 |
| 2 | 0·35 | 0·24 |
| 3 | 0·37 | 0·21 |
| 4 | 0·29 | 0·26 |
| 5 | 0·38 | 0·28 |

condition of the tissue in these experiments is not necessary for the appearance of the outcoming spike, since we have observed it in the ascending mesenteric nerve *in situ* and at body temperature.

*Ganglionic delay.* In our earlier experiments we assumed that the main ingoing ascending mesenteric spike was responsible for the outcoming volley. Measurements of ganglionic delay on this assumption gave values much greater than those found in the pathway inferior splanchnic–ascending mesenteric, falling between 48 and 159 msec (Brown & Pascoe, 1951).

The discovery that a much more slowly conducted spike was the true ingoing volley necessitated a redetermination of the ganglionic delay. We have found that the values for the pathway ascending mesenteric–ascending

mesenteric fall within the same range as those for the pathway inferior splanchnic–ascending mesenteric. These figures, however, apply only to the initial spike of the outcoming volley, and much greater delays may occur, if the apparent temporal dispersion of the recorded discharge is not due to repetitive discharge.

*Temporal dispersion of outcoming volley.* As we have already pointed out, the initial spike of the outcoming volley is followed by a long-lasting discharge, the end of which cannot be detected in the ordinary record, since it merges with the background noise of the recording system. We therefore adopted another method of measuring the degree of dispersion of the outcoming discharge. The stimulating and recording electrodes were placed on the ascending mesenteric nerve, with the recording electrodes nearer the ganglion. A maximal stimulus was applied to the nerve, setting up ingoing and outcoming volleys. A second stimulus, applied during the time that the outcoming volley was passing between recording and stimulating electrodes, set up a second ingoing volley of reduced size. The reduction of this second volley was proportional to the number of fibres rendered refractory by the outcoming volley. The results of such an experiment showed that the outcoming volley may be dispersed over more than 200 msec. Blocking the ganglion with D-tubocurarine chloride, by abolishing the outcoming volley, removes the depression of the second response.

### *Interaction between ingoing ascending mesenteric and inferior splanchnic volleys*

Our experiments have shown that the cells of the inferior mesenteric ganglion receive preganglionic impulses from two sources, the ascending mesenteric nerve and the inferior splanchnic nerve, the discharge of the postganglionic fibres being detectable in the ascending mesenteric nerve in each instance. We had to decide whether the two preganglionic pathways excited common ganglion cells or were discrete. To settle this point, a preparation was needed with three separate functioning pathways: the inferior splanchnic, an ascending mesenteric branch for exciting an ingoing volley, and a separate ascending mesenteric component for recording the outcoming impulses. Only by using this preparation could we avoid the complication of antidromic excitation of the cells from whose postganglionic fibres we were recording. Fig. 7 shows the general disposition of stimulating and recording electrodes. A completely satisfactory preparation was only achieved in a few instances, since in many animals a convenient subdivision of the ascending mesenteric was absent, in others the inferior splanchnic did not conduct after dissection, and often the outcoming spikes were too diffuse to permit accurate measurement.

Experiments to assess the presence and degree of overlap of the two

preganglionic fields were made as follows. A maximal stimulus was applied at *S* to the inferior splanchnic nerve, and at intervals before and after it, a second stimulus was applied to a branch of the ascending mesenteric nerve at *A*. The outcoming volley was recorded monophasically in the ascending mesenteric nerve at *M*. Drawings of the responses to *S* alone and *A* alone, and to *S*+*A* at a variety of intervals were made, and the time-potential integrals were estimated with a planimeter. When the preganglionic volleys were so timed that the outcoming volleys were approximately synchronous, we obtained evidence in one experiment alone of some degree of facilitation, i.e. the area of *S*+*A* was greater than the sum of *S* alone and *A* alone. The difference was less than 10% and therefore of doubtful significance.

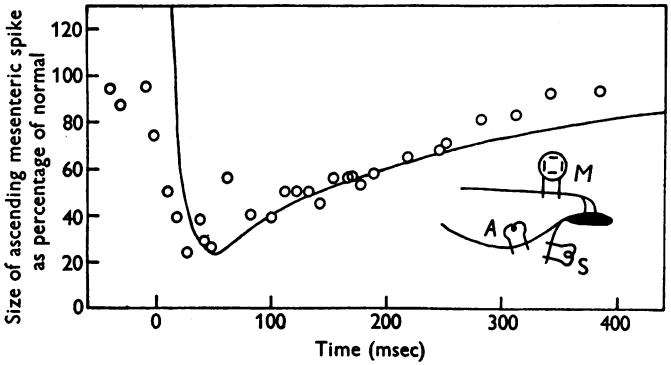


Fig. 7. Effect on outcoming ascending mesenteric volley of discharge of cells excited by inferior splanchnic. Time 0 represents point at which the peak of the inferior splanchnic volley leaves the ganglion. The continuous curve shows the ganglionic slow potentials, evoked by inferior splanchnic stimulation, fitted to the present time scale.

In all the other experiments the area of *S*+*A* equalled or was less than the sum of *S* alone and *A* alone; this suggests that occlusion was occurring. The degree of occlusion we observed varied from preparation to preparation between 16 and 39% but was constant in any one preparation.

Although this depression of the summed spike of the apparently simultaneous discharge of the two groups of ganglion cells may be due to a genuine occlusion, we have had difficulty in dissociating it from other, 'inhibitory', phenomena which follow the discharge of the ganglion cells. It appears that the discharge of one group of ganglion cells depresses the excitability of those supplied by another preganglionic trunk. For instance, in one experiment in which there was no evidence of occlusion and less than 10% of facilitation between the ascending mesenteric and inferior splanchnic pathways, the discharge of the ganglion cells supplied by the inferior splanchnic produced a depression of the response to ascending mesenteric stimulation which lasted some 250 msec. The depression follows closely the time course of the ganglionic slow positive potential (Fig. 7).

## DISCUSSION

Examination of what might be called the conventional pathway through the inferior mesenteric ganglion—from the inferior splanchnic nerve to the ascending mesenteric nerve—reveals no peculiar features; the preganglionic conduction velocity, ganglionic delays and postganglionic velocity agree closely with values obtained in other ganglia if allowance is made for temperature. The other pathway through the ganglion—ingoing ascending mesenteric, outcoming ascending mesenteric—shows features of interest. One of the most striking is the extremely slow conduction velocity—and presumably small size—of the ingoing fibres responsible. The velocity of conduction (mean 0·25 m/sec) is about one-twentieth of that of the inferior splanchnic preganglionic fibres and one-fortieth of that of the cervical sympathetic trunk determined under similar conditions. The postganglionic fibres of the splanchnic pathway conduct at 0·43 m/sec and those of the ascending mesenteric at 0·37 m/sec. It follows that the mean velocity of the ascending mesenteric preganglionic fibres is much less than that of the postganglionic fibres which they supply.

The small size of these preganglionic fibres naturally raises speculation about their origin. Langley & Anderson (1896) assumed that the ascending mesenteric nerve, in addition to supplying the colon, made connexions with the superior mesenteric ganglia. Kuntz (1940) has claimed that visceral reflexes take place through mesenteric nerves and the inferior mesenteric ganglion. If Kuntz's claim is correct, then these slow fibres might well be the afferents of this system. Experiments are in progress to determine the origin of these fibres; it is sufficient to report at this stage that degenerative decentralization of the inferior mesenteric ganglion removes neither the slow component of the ingoing volley, nor the outcoming response. Degenerative section of the ascending mesenteric nerve removes the ingoing slow component from the ganglionic stump, but it persists in the distal stump. It follows from this that, whatever is the origin of these fibres, the cell somata lie somewhere in the headward distribution of the ascending mesenteric nerve.

Our evidence on the degree of overlap of the two ganglionic fields is not conclusive. If facilitation does occur it does not exceed 10% and is near the limits of accuracy of the method of measurement. The depressant effects of the discharge of one group of ganglion cells make measurements of occlusion of doubtful value. The curve reproduced in Fig. 7 shows that the onset of the depression is abrupt. It follows then that the cells of one group are already likely to be exposed to the depressant action of cells of the other group, discharging slightly before them, and that slight temporal shifts of the two volleys might produce effects indistinguishable from true occlusion. In a number of experiments neither facilitation nor occlusion has been observed,

and it seems possible to conclude that the two groups of cells can exist without overlapping connexions and, if overlap does exist, it seldom is extensive.

SUMMARY

1. The inferior mesenteric ganglion of the rabbit survives for many hours when suspended in Locke's solution at room temperature.

2. Stimulation of the inferior splanchnic nerve causes the appearance in the ascending mesenteric nerve of a spike, conducted at 0·43 m/sec, after a ganglionic delay of 30 msec.

3. The ascending mesenteric nerve contains three main fibre groups: a fast group conducting at 2 m/sec, a main group (0·45 m/sec) and a slow group (0·25 m/sec). The fast group is made up of fibres which do not form synapses in the ganglion. The main group is composed of postganglionic fibres.

4. The slow group (0·25 m/sec) is composed of preganglionic fibres having synaptic connexions in the inferior mesenteric ganglion and causing the appearance of a spike in the ascending mesenteric nerve after a ganglionic delay of 30 msec.

5. The two pathways through the ganglion appear to be largely separate, facilitation and occlusion being small. The discharge of one group of ganglion cells, however, causes a long-lasting depression of excitability in the other. The time-course of the depression follows that of the ganglionic positive after-potential.

6. The cells of origin of the small preganglionic fibres in the ascending mesenteric nerve lie in the headward distribution of the nerve.

The expenses of this investigation were partly met by a grant from the Medical Research Council.

*Note added in proof.* After this paper had been submitted for publication we learnt that C. Job and A. Lundberg of the Nobel Institute of Neurophysiology, Stockholm, had observed similar phenomena in the inferior mesenteric ganglion of the cat. Their paper is appearing in *Acta physiol. scand.* 1952.

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