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RESPONSES OF THE NERVE TERMINAL OF THE PACINIAN CORPUSCLE

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A number of studies of the Pacinian corpuscle have been made with the aim of analysing the mechanisms underlying the initiation of impulses by this sense organ (Gray & Sato, 1953; Diamond, Gray & Sato, 1956; Loewenstein, 1958) and the characteristics of its response to mechanical stimuli (Gray & Matthews, 1951; Loewenstein, 1958; Hunt, 1961; Sato, 1961). In the studies of Gray & Sato (1953), recording by means of an air gap revealed the potential differences between the axon at its point of emergence from the corpuscle and a point approximately 0·25 mm central on the axon. Such records revealed many features of the potential changes occurring in the nerve terminal in response to mechanical stimulation, in particular the characteristics of the receptor or generator potential. A somewhat similar type of recording has been employed by Loewenstein (1958), in which the potential difference between the corpuscle and a more central point on the axon was recorded in paraffin oil. These experiments showed that impulse activity as well as graded receptor potentials occur in the nerve elements within the corpuscle. However, anatomical studies have shown that the first node is intracorpuscular (Quilliam & Sato, 1955) so that impulse activity within the corpuscle need not be attributed to the non-myelinated ending. On the basis of other evidence, it has been suggested that the non-myelinated axon produces only a generator potential which initiates impulse activity in the first node by electrotonic spread (Diamond *et al.* 1956; Loewenstein & Rathkamp, 1958; see Discussion).

The non-myelinated axon of the Pacinian corpuscle has some unusual characteristics. It is exceptionally long, often between 500 and 1000 μ, of nearly uniform diameter (3–4 μ) and is, for most of its length, unbranched. Bifurcation of the axon sometimes occurs but only near the distal end of the corpuscle (Quilliam & Sato, 1955). In view of the exceptional length of the unmyelinated axon in this receptor, it seemed possible that external recording of potentials along the length of the axon might provide further information as to the properties of this region.

Although technical limitations made it unlikely that the bare axon could be isolated, there was some possibility that potential changes originating in the axon might be recorded by external electrodes after the outer lamellae had been removed, in the manner described by Loewenstein & Rathkamp (1958). The lamellae immediately surrounding the non-myelinated axon form a distinct zone, the inner core, in which the lamellae are not complete but are separated by two symmetrically distributed longitudinal clefts running along the length of the axon (Pease & Quilliam, 1957). Presumably, these clefts might furnish a relatively low-resistance path for current flow which could be recorded external to the inner core.

By recording with fine platinum-iridium wires, external to the inner core, it proved possible to record potential changes of the nerve ending in response to mechanical stimuli and to antidromic impulses initiated by nerve stimulation. The characteristic responses to both antidromic and orthodromic impulses, which are described, indicate that the non-myelinated ending normally conducts propagated impulses both in response to above-threshold mechanical stimulation and to antidromic stimulation of the nerve.

METHODS

Pacinian corpuscles were removed, together with the nerves supplying them, from the mesentery of cats anaesthetized with sodium pentobarbital (Nembutal, Abbott). The corpuscles were then placed on a glass plate in Locke's solution (composition mM: NaCl 155, KCl 1, $CaCl_2$ 1·9, $NaHCO_3$ 1·2). Under a dissecting microscope the outer lamellae were removed, as far as possible, using sharpened needles. This left the inner core, a cylindrical

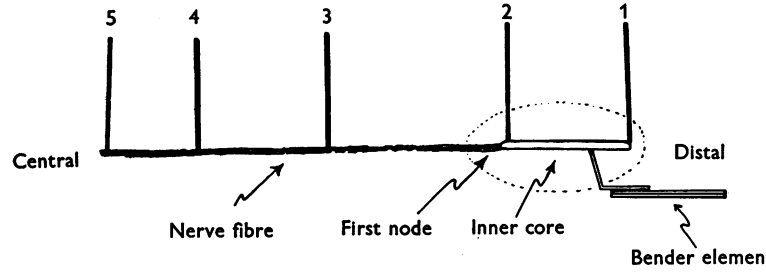

Fig. 1. Schematic view of recording and stimulating arrangement. 1, stationary recording electrode; 2, roving recording electrode; 3, earthed electrode; 4 and 5, stimulating electrodes. Interrupted line indicates approximate original outline of corpuscle.

structure of nearly uniform diameter (50–100 μ) containing the non-myelinated nerve ending and connected to the parent myelinated nerve axon. The nerve and the dissected corpuscle were then mounted on fine platinum-iridium electrodes in paraffin oil. The electrode arrangement is shown schematically in Fig. 1. One recording electrode was kept at the distal end of the inner core (1, stationary electrode) while the other (2, roving electrode) was placed at varying positions along the inner core. Another pair of electrodes (4 and 5) was located proximally on the nerve, for stimulation. An earthed electrode (3) was placed

between the stimulating and recording pairs in such a position as to minimize artifact. Capacity-coupled amplifiers were generally used, the time constant being adjusted so as to produce no distortion of the potential changes. Potentials were displayed and photographed on a Tektronix model 502 oscilloscope. Occasionally isotonic sucrose was washed briefly over the region of the inner core and then removed in order to decrease shunting by external fluid. In the amount applied, this did not produce detectable changes in electrical response other than in increase in amplitude. In some experiments 0·05 % procaine HCl in Locke's solution was applied briefly to the inner core and then washed off.

A consideration of the recording conditions is necessary for interpretation of the records that follow. The potentials recorded were due to current flow along the external longitudinal resistance between the stationary and roving electrodes. In one case, with the roving electrode at the proximal end of the inner core, the resistance between electrodes was found to be 300,000 Ω. In all records, negativity at the roving electrode relative to the stationary electrode produced an upward deflexion. This negativity indicated a net current flow along the external resistance from the stationary to the roving electrode. Conversely, a positive deflexion resulted from a net current flow in the opposite direction.

Mechanical stimulation of the corpuscle was applied by a fine glass stylus attached to a barium titanate bender bimorph element (Gulton Industries). The characteristics of this element were similar to those described by Sato (1961). Rectangular pulses of varying amplitude and duration were used to excite the electromechanical transducer.

RESULTS

Responses to antidromic impulses

Stimulation of the axon at some distance from the corpuscle evoked the potential changes, recorded externally from the inner core, such as those shown in Fig. 2. The stationary electrode remained fixed at the distal end of the inner core while the roving electrode was placed at various positions more proximal. The principal deflexion was an all-or-none spike-like negativity of the roving electrode relative to the stationary electrode. This was usually followed by a smaller positive deflexion (see below). Typically, the amplitude of the negative deflexion fell as the roving electrode was moved distally and as inter-electrode distance was consequently reduced. However, the duration of the negative deflexion remained substantially the same at different positions of the roving electrode. The duration of the negative deflexion ranged between 0·5 and 1·0 msec, from onset to return to base line.

A plot of the peak amplitude and duration of the rising phase of the negative deflexion as a function of recording position is shown in Fig. 3, taken from another preparation in which outer lamellae had been removed. The amplitude (filled circles) fell approximately linearly with distance as the roving electrode was moved distally, but the time from onset to peak (open circles) remained essentially constant. These findings are typical for the large number of preparations examined. The fall of amplitude as the roving electrode was moved distally may be attributed to the accompanying decrease in inter-electrode resistance. The fact that the amplitude

is approximately linearly related to distance of the roving electrode from the distal end, while the rise time of the potential remains the same, suggests that the spike-like deflexion results from impulse propagation in the nerve axon of the inner core. However, these effects could conceivably

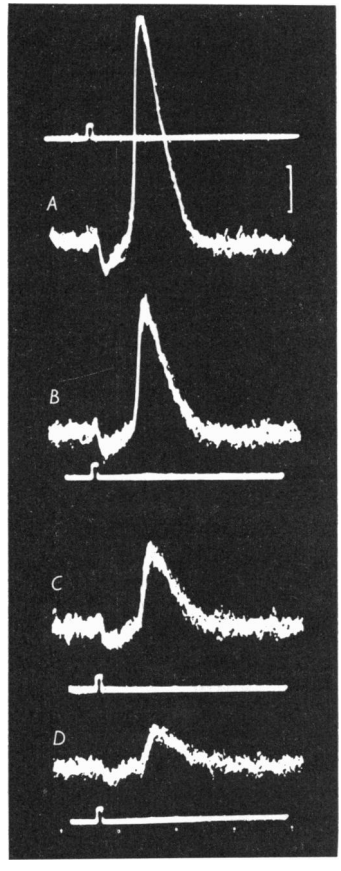

Fig. 2. Antidromic responses recorded with roving electrode at various positions along inner core. Distance of roving from stationary electrode: *A*, 0·84; *B*, 0·64; *C*, 0·52; *D*, 0·44 mm. Length of inner core 0·90 mm. Second beam in each record shows stimulus artifact. Dots below *D* show time intervals of 0·5 msec. Vertical calibration alongside *A* equals 40 μV. Amplifier 3 db points 10 kc/s and 8 c/s.

result from electrotonic spread of potential changes from an antidromic impulse which propagated only to the first node, if the length constant of the unmyelinated axon were considerably longer than its actual length.

Careful measurement of the interval between stimulus and onset of the negative deflexion revealed a slight but definite increase in latency as the roving electrode was moved distally along the inner core. The onset of the

spike-like deflexion was usually abrupt and examination of a number of records from each recording position showed the latency to be constant. A plot of the relation between latency and position of the roving electrode is shown for four preparations in Fig. 4. (Differences in latency can also be seen in Fig. 2.) The changes in latency of the antidromic response as a function of recording position are considered to indicate that the potential

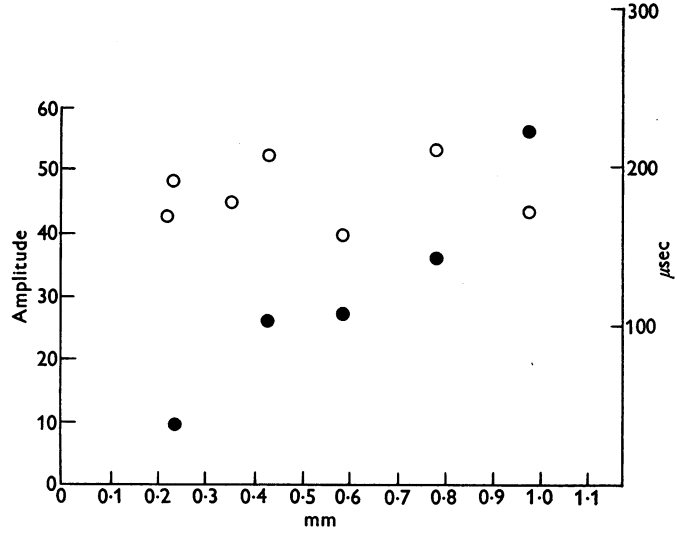

Fig. 3. Relation of amplitude of negative deflexion of antidromic response (filled circles) and time from onset to peak of negative deflexion (open circles) as a function of distance of roving electrode from distal end. Length of inner core 1·18 mm. Ordinates: left, amplitude of negative deflexion; right, rise time.

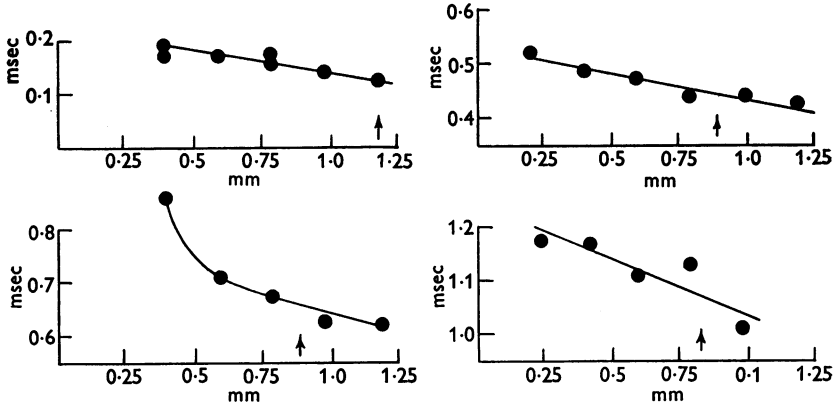

Fig. 4. Latency of onset of negative deflexion of antidromic response as a function of distance of roving electrode from distal end in four preparations. Variations in latency among the four preparations are due to differences in conduction distance from stimulating electrodes. Arrows show position of proximal end of inner core.

changes result from impulse propagation in the non-myelinated axon. Electrotonic spread alone into the non-myelinated axon would not be expected to produce such latency changes. It might be argued that the onset of a potential change due to electrotonic spread could appear to begin later when recording toward the end of the corpuscle because of a slower rise time. This would require a significant electrotonic decrement

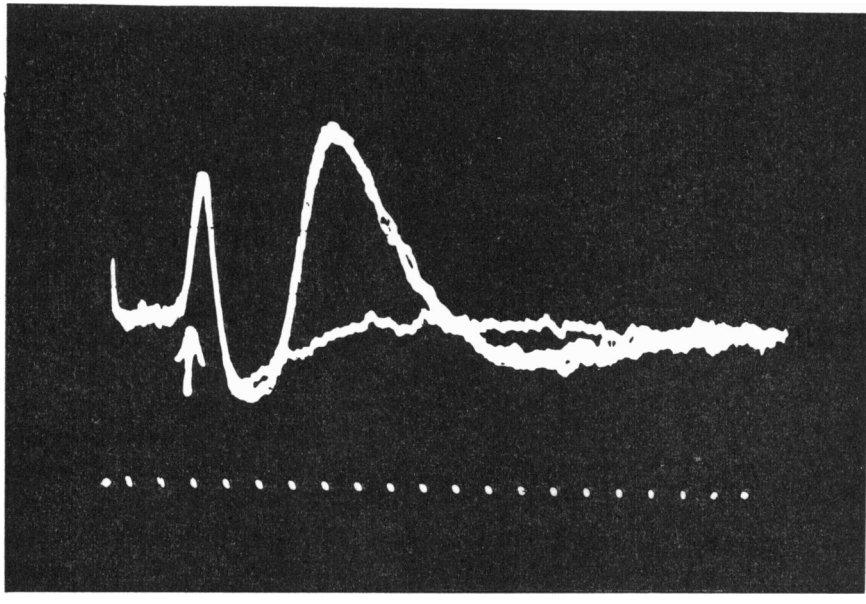

Fig. 5. Response to stimulation of nerve near threshold. Roving electrode at proximal end of inner core (1·18 mm in length). Arrow shows stimulus artifact. On one trace no antidromic impulse was evoked. Time: 0·2 msec.

within the length of the non-myelinated ending, which is not compatible with the findings discussed above, particularly the fact that the rise time of the spike-like response remains the same. Further evidence for impulse conduction is presented below.

On the assumption that the changes in latency of onset of the antidromic spike result from conduction in the non-myelinated axon, velocities of conduction may be estimated from the slope of the relation between latency and distance. Ignoring the point of longest latency in the lower left graph, which may be the result of injury, the slopes for the four preparations shown in Fig. 4 gave the following values for conduction velocity: 4·8, 9·3, 6·2 and 16·3 m/sec. The mean of these values is about 9·1 m/sec. Since the distance over which these observations can be made is quite small (about 500–1000 μ) this measurement should be considered only as an approximation.

In most preparations an antidromic impulse evoked a positive deflexion following the principal negative deflexion when recording with the roving electrode near the central end of the inner core. This positive deflexion had approximately the same duration but was much smaller in amplitude than the negative deflexion. In certain circumstances, such as in ageing preparations or under the influence of procaine, it appeared intermittently and in an all-or-none fashion (see later). An example of the positive phase of the antidromic potential may be seen in Fig. 5, which shows the response to stimulation of the axon at some distance from the corpuscle by a pulse which is near threshold. On one of the repetitive sweeps an impulse was not initiated and the artifact alone may be seen. On the other traces an impulse was evoked causing a negative, then positive, deflexion. The latter may be clearly seen as the response courses below the base line. This positive deflexion was noted when the low frequency response (3 db point) of the amplifier was as long as 0·8 c/s, and hence was not due to differentiation by the amplifier.

Negativity at the roving electrode indicates a net flow of current (along the external resistance) from the stationary to roving electrode. Conversely, positivity indicates a net current flow in the opposite direction. The potential change recorded external to the inner core in response to an antidromic impulse consisted of a negative-positive sequence, both phases of which had all-or-none characteristics and spike-like durations. This suggests that the impulse propagates past the roving electrode, producing an impulsive sink of current flow in the non-myelinated axon. It will be seen below that the potential change recorded in response to an impulse initiated orthodromically shows the opposite sequence, namely a positive-negative deflexion.

The positive phase of the antidromic response was absent in some preparations, possibly owing to ageing. It could also be abolished by procaine. Figure 6 shows the response of a preparation which normally showed no positive phase after the negative antidromic response. *A* shows a series of responses following stimulation of the nerve at a distance from the corpuscle. In *B* similar stimulation was preceded, in some traces, by a brief subthreshold mechanical pulse applied to the inner core. Only when the mechanical stimulus was given before the antidromic response did the latter show a positive phase. On the assumption that the positive phase is due to impulse conduction into the non-myelinated axon, this result suggests that a subthreshold pulse, by depolarizing the non-myelinated axon, may facilitate invasion into this region. An analogous facilitation of antidromic invasion of the cell body of the crustacean stretch receptor by stretch was noted by Eyzaguirre & Kuffler (1955).

In some preparations the positive phase of the antidromic response

occurred intermittently. In such cases, the occurrence of the positive phase was followed by a period during which a mechanical pulse failed to evoke any spike-like response. However, when the antidromic response failed to have a positive phase, a subsequent mechanical pulse produced apparently a conducted response in the unmyelinated axon without any evident refractoriness (see later, Fig. 13).

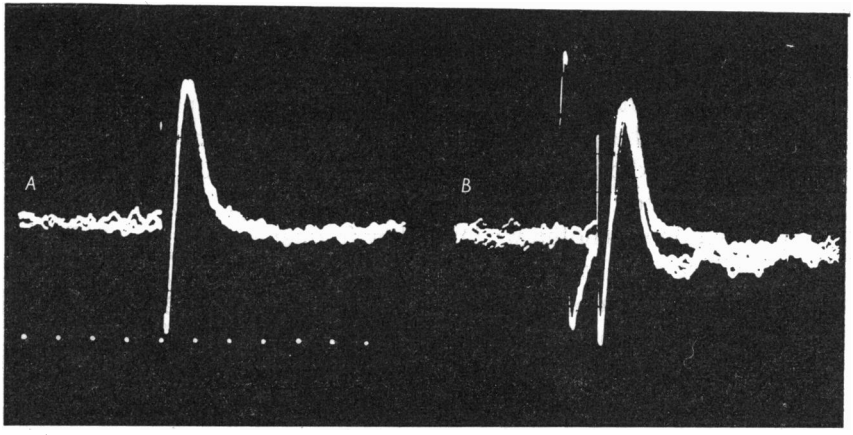

Fig. 6. Facilitation of impulse invasion of non-myelinated axon by subthreshold mechanical pulse. *A*, antidromic response showing lack of positivity following negative spike. *B*, antidromic response, preceded in some traces by subthreshold mechanical pulse. Following the latter a positive deflexion occurred in an all-or-none manner. Time, 1 msec. Roving electrode at central end of inner core.

Responses to mechanical stimuli

The potential changes recorded when an orthodromic impulse was initiated by mechanical stimulation of the receptor showed distinct differences from those accompanying an antidromic impulse. With the roving electrode near the central end of the inner core and the stationary electrode in its usual position at the distal end, a supra-threshold mechanical pulse applied toward the distal end of the inner core produced a positive-negative potential change (Fig. 7*A–D*). At threshold this potential appeared in an all-or-none manner. The initial positive deflexion was normally brief, being terminated by a rapid negative deflexion about 0·1–0·2 msec after its onset. The negative deflexion was generally larger than the preceding positive potential, but the over-all amplitude of the orthodromic response was less than the antidromic response.

Amplitude of orthodromic and antidromic responses following mechanical stimulation. Figure 7 (*A–D*) shows orthodromic responses to mechanical stimuli, decreasing in strength from *A* to *D*. *A* is several times threshold while *D* is near threshold. The total amplitude of the negative deflexion,

from its origin in the positive phase to maximal negativity, was inversely related to stimulus strength, being significantly smaller in *A* than in *D*. The increase in latency as stimulus strength was reduced may also be noted. The amplitudes of all the orthodromic responses are smaller than the antidromic response, shown in *I*. Records *E–H* show antidromic responses delivered at a constant interval after the onset of the mechanical pulses. In each of these records the strength of mechanical stimulation was

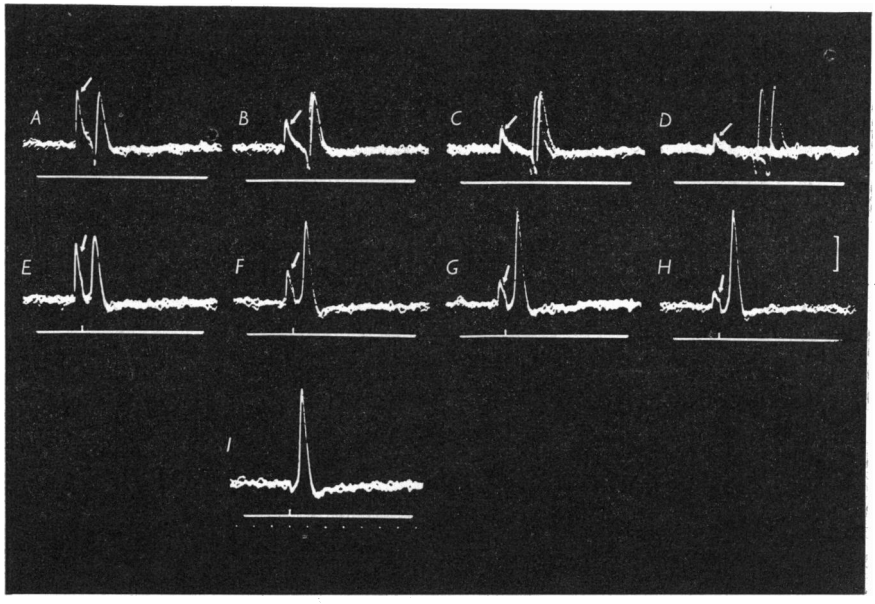

Fig. 7. Responses to mechanical and antidromic stimulation. Mechanical stimulation of decreasing strength from *A* to *D*. Stylus of bender element 0·15 mm from distal end of inner core. *E–H*, mechanical stimuli of same strength as in records above (*A–D*) followed by antidromic response which precedes usual orthodromic response. *I*, control antidromic response. Nerve stimulus artifact shown on lower records. Time (below *I*), 1 msec intervals. Vertical calibration (alongside *H*), 40 μV. Length of inner core 0·9 mm. Roving electrode 0·95 mm from distal end, stationary electrode at distal end. Arrows show artifacts from onset of mechanical stimuli.

the same as in the corresponding record of *A–D*. The antidromic responses were timed to occur before the normally occurring orthodromic responses and the latter failed to appear. The amplitudes of the responses in *E–H* were less than the control antidromic response (*I*). Further, the reduction was proportional to strength of the mechanical stimulus. Both orthodromic and antidromic responses therefore show a reduction in amplitude as a result of mechanical stimulation of the receptor.

In preparations with a higher threshold to mechanical stimulation,

changes in amplitude of an antidromic impulse could be detected following a subthreshold mechanical pulse. An example is shown in Fig. 8. The control response to antidromic stimulation is shown in *A*, while *B* illustrates the response to a brief subthreshold mechanical pulse. In *C* and *D*, antidromic responses were timed to occur at two different intervals after the same mechanical stimulus. The antidromic response in *C* was approximately 87%, and that in *D* 99% of the control. The relation between

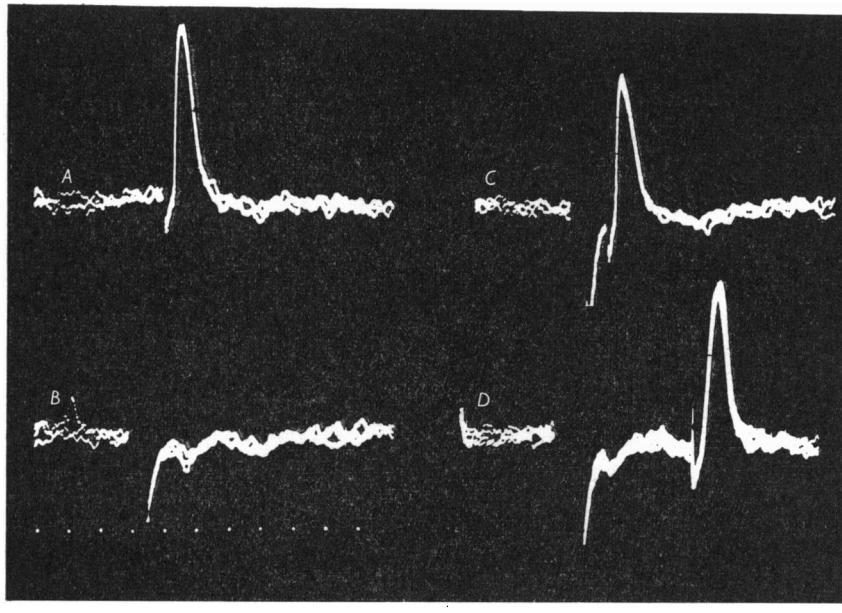

Fig. 8. Effect of brief subthreshold pulse (0·2 msec duration) on antidromic response. *A*, antidromic response alone. *B*, mechanical pulse alone. *C* and *D*, antidromic responses following mechanical pulses at two intervals. Time, 1 msec. Roving electrode at central end of inner core, 0·59 mm in length.

antidromic response amplitude and interval after a brief subthreshold pulse may be seen in Fig. 9. The reduction in response amplitude decayed along a time course roughly comparable to the decay of receptor or generator potential (see Discussion).

The most likely explanation of the effect of mechanical stimulation, both sub- and suprathreshold, on the amplitude of the antidromic response is that depolarization of the receptor by generator action decreases the potential difference between the non-myelinated axon and the first node. Hence, when the first node becomes active, less current flows along the external resistance of the inner core during generator activity. This would also explain the fact that the orthodromic response is smaller than the

antidromic response and varies in size with the strength of mechanical stimulation (Fig. 7).

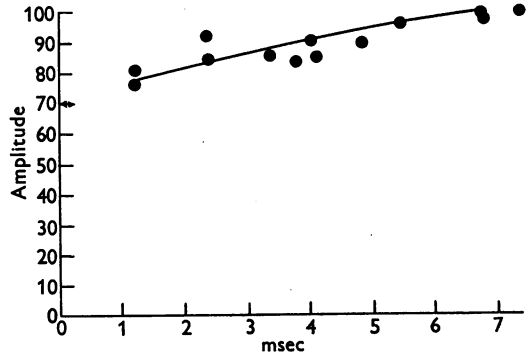

Fig. 9. Relation between amplitude of antidromic response and interval after a brief subthreshold mechanical pulse (as in Fig. 8). Double arrow shows duration of mechanical pulse. Ordinate: amplitude of antidromic response in percentage of control. Abscissa: time.

Positive component of the orthodromic response. The positive phase of the orthodromic response could be elicited in isolation when a strong mechanical pulse was given at a critical interval after an antidromic response. An example may be seen in Fig. 10, in which *A* is the antidromic response, *B* the normal orthodromic response, and *C* the response produced by delivering the mechanical stimulus after an antidromic response. The roving electrode was located near the central end of the inner core. The positive potential seen in *C* has a slower rising phase than the positive deflexion in *B* and is not followed by the normal negative phase of the orthodromic potential sequence.

Further details of the responses to mechanical stimulation following antidromic impulses are shown in Fig. 11, taken from another preparation. Recording conditions were similar to those of Fig. 10, but amplification was greater. The interval between antidromic impulse and mechanical stimulus was increased between *A* and *B* and between *B* and *C*. In *A*, the mechanical pulse produced a small generator potential and, on some traces, a positive spike-like deflexion. In *B*, the brief positive spike was always evoked and in two instances was followed by a large spike-like negative deflexion. In *C*, the positive spikes were usually succeeded by negative spikes. The latter were not followed by an after-positivity (as was noted in the experiment using procaine, see below Fig. 12*C*).

These responses to mechanical stimulation may be explained by the following hypothesis: At a certain interval after an antidromic response, the first node and the non-myelinated ending are refractory and mechanical

stimulation evokes only a generator potential. At a slightly longer interval, the non-myelinated axon has recovered sufficiently to give an impulsive response to a *strong* generator potential but the currents thereby produced are not sufficient to excite the still partially refractory first node. When the interval is further lengthened the first node has recovered sufficiently to be excited by currents flowing between it and the non-myelinated axon.

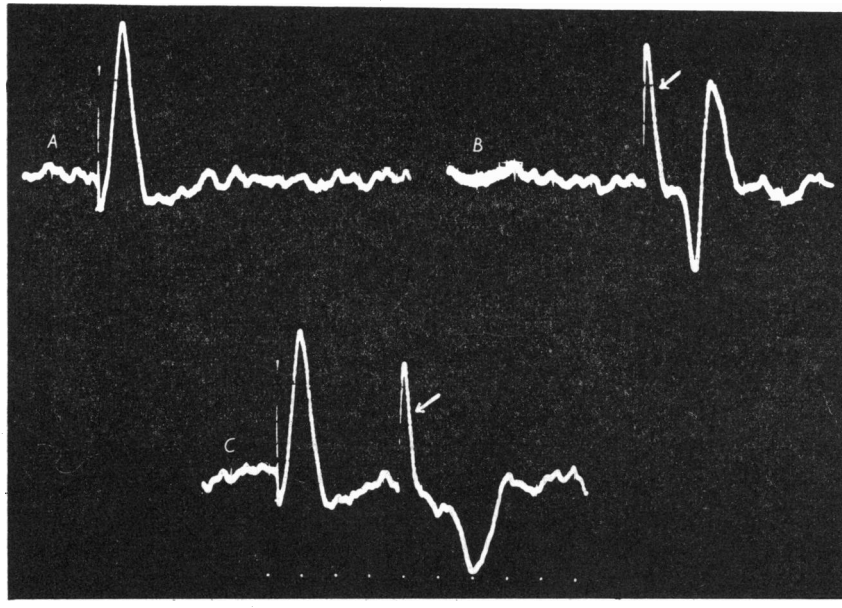

Fig. 10. Response to a mechanical pulse at a critical interval after an antidromic response. *A*, control antidromic response. *B*, response to mechanical pulse alone. *C*, mechanical stimulus as in *B* but following antidromic response. Time, 1 msec. Roving electrode near central end of inner core. Arrows show artifact from mechanical stimulus.

By exposing the preparation to procaine ($< 0{\cdot}05\,\%$), it was also possible to evoke the positive phase of the orthodromic response without the usual subsequent negative phase. Figure 12 shows such an example. Procaine ($0{\cdot}05\,\%$) was applied to the inner core leading to block of responses to mechanical stimuli. The inner core was then briefly rinsed with Locke's solution to reduce the effect of procaine. The roving electrode was then placed near the central end of the inner core, the stationary electrode in its usual position at the distal end. Mechanical stimuli were delivered as usual by a stylus applied toward the distal end of the inner core. The amplitude of the mechanical pulse was increased from *A* to *B* and from *B* to *C*. In *A*, a small generator potential was recorded, resulting in positivity of the roving electrode and in a few traces small, spike-like, all-or-none positive deflexions occurred. In *B*, brief spike-like positive deflexions resulted in

all sweeps but no negative deflexions followed. In *C*, the positive spikes occurred with shorter latency and in two traces gave rise to a subsequent spike. In Fig. 12*C*, the two negative spikes are followed by an after-positivity of considerably longer duration than the negative deflexion;

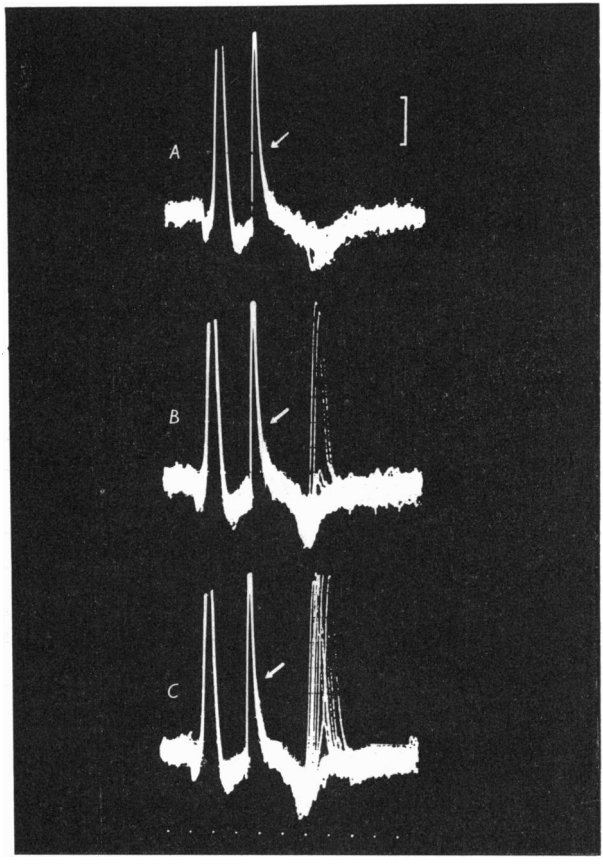

Fig. 11. Response to mechanical stimulus following antidromic response. Interval between antidromic and mechanical pulse increased from *A* to *B* and from *B* to *C*. Arrows show artifact from onset of mechanical pulse which lasts for remaining duration of sweep. Time 1 msec intervals. Roving electrode at central end of inner core (0·90 mm in length). Stylus 0·3 mm from distal end. Vertical calibration (alongside *A*) 20 μV.

this was not seen in the absence of procaine (see above) and its basis is not known. Procaine apparently increased the threshold of the first node, permitting a spike-like process in the unmyelinated axon to be observed in isolation (*B*). While it is not obvious from Fig. 12, observation of the oscilloscope traces showed that a small negative deflexion followed the positive spike-like deflexion (compare *A* and *C*). This may indicate that an

impulse event in the non-myelinated axon produces a diphasic potential sequence due to a reversal of current flow. Another factor may be elimination of the passive component of the generator potential by impulse activity in the non-myelinated axon. With stronger mechanical stimulation (*C*), the first node may have undergone stronger depolarization by current

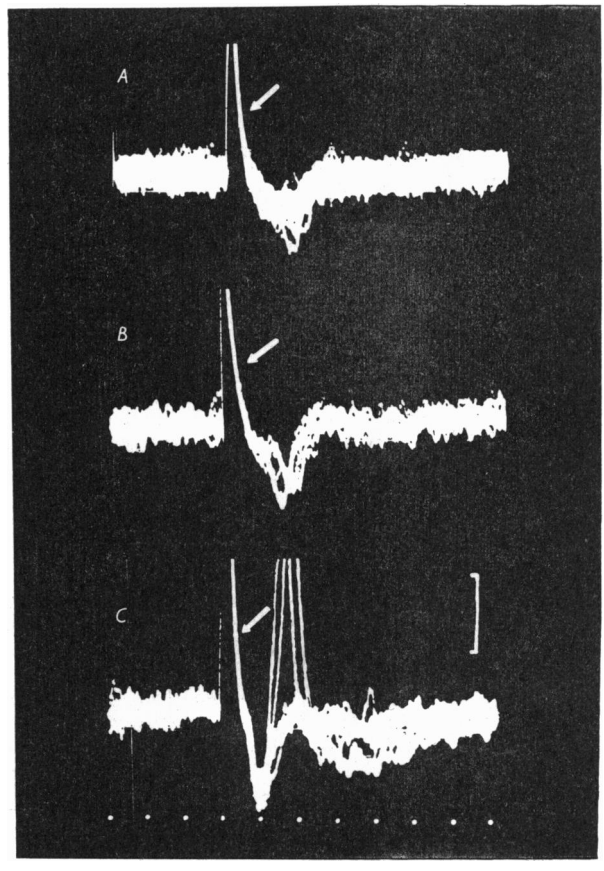

Fig. 12. Responses to mechanical stimulation following application of procaine. Strength of mechanical pulse increased from *A* to *B* and from *B* to *C*. Arrow shows artifact from onset of mechanical pulse which lasted for remainder of sweep. Vertical calibration adjoining *C*, 20 μV. Roving electrode at central end of inner core. Stylus, 0·5 mm from distal end. Inner core length 0·9 mm. Time, 1 msec. Spikes in *C* retouched.

accompanying generator action so that the spike-like process in the non-myelinated axon was able to excite an impulse.

In most preparations in the absence of procaine no detectable generator potential could be seen when recording as above. This is presumably due

to the low current density produced along the external longitudinal resistance by normally subthreshold mechanical pulses. However, in the presence of procaine the threshold for the initiation of the spike-like positive response appears to be raised, allowing the generator amplitude to

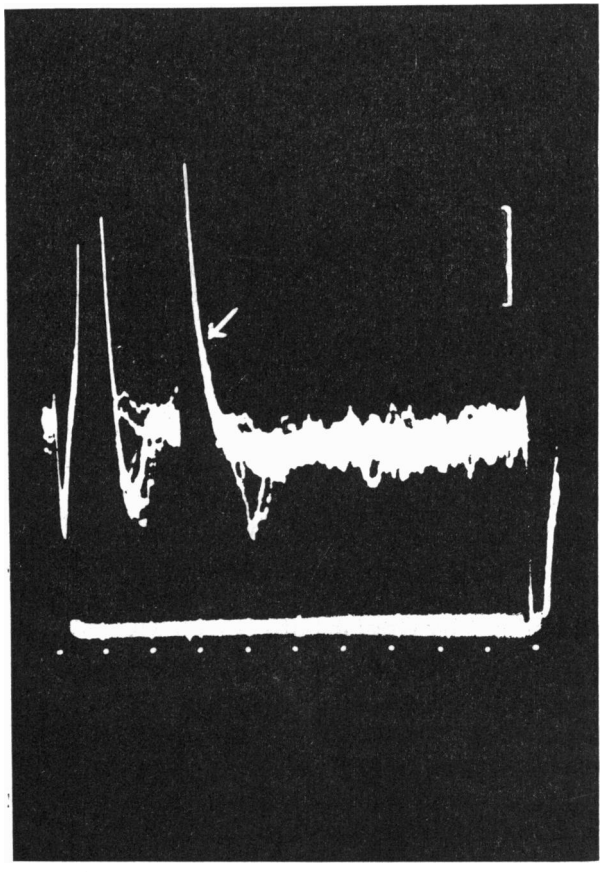

Fig. 13. Positive deflexion of antidromic and orthodromic responses. Antidromic response failed to show positive phase on two traces, following which mechanical stimulus evoked positive deflexion. Time 1 msec intervals. Vertical calibration 20 μV. Recording and stimulating conditions as in Fig. 12. Arrow shows artifact from onset of mechanical pulse.

be increased sufficiently to become evident. It is of interest that the effect of procaine on this preparation was nearly immediate, suggesting that substances may diffuse to the region of the axon very rapidly after the outer lamellae have been removed.

Figure 13 shows superimposed responses of a preparation, treated with procaine ($< 0{\cdot}05\,\%$), in which the antidromic response was followed by a

mechanical pulse. The roving electrode was located near the central end of the inner core, the stationary electrode at the distal end. On most of the traces the antidromic impulse showed a positive phase after the principal negative deflexion. In such cases, the mechanical pulse failed to evoke a positive deflexion. However, in two traces the positive phase of the antidromic response failed to appear and in both cases the subsequent mechanical stimulus produced a spike-like positive response. When the antidromic response was not accompanied by a positive phase, mechanical stimuli following at very short intervals evoked this type response, with no apparent refractory period following the antidromic response. These findings suggest that under some circumstances the antidromic impulse may not invade the non-myelinated axon. However, when the non-myelinated axon appeared to be invaded, as was usually the case, this region was refractory for a period of time to the initiation of orthodromic impulses even by strong generator action.

DISCUSSION

The generation of impulses by mechanical stimulation of the Pacinian corpuscle has been studied by several investigators. Alvarez-Buylla & Ramirez de Arellano (1953) recorded local responses in such corpuscles, which appeared to play a role in the initiation of impulses by this sense organ. A detailed study of the potential changes recorded across an air gap, between the axon as it emerged from the corpuscle and a point more central, was carried out by Gray & Sato (1953). The potential recorded in response to mechanical stimuli could be separated into three phases: The first phase was graded in amplitude and rate of rise by varying the size of the mechanical stimulus, was not abolished by procaine, and showed summation when two successive stimuli were delivered. When the first phase reached a critical level a second phase of the response, of the same polarity, arose abruptly and had an essentially all-or-none character. The first phase was considered a graded depolarization of the nerve terminal, the second an impulsive event within the corpuscle. A third phase of opposite polarity followed the second and could be abolished by procaine in the central pool. It was considered to result from activity central to the air gap. At that time the location of the first node was not known. On the assumption that it was extracorpuscular, Gray & Sato attributed the first and second phases to the non-myelinated ending. A subsequent study by Quilliam & Sato (1955) showed that the first node was intracorpuscular, the second usually lying just outside the corpuscle. Thus the records obtained by Gray & Sato (1953) were probably taken across the region of axon between the second and third nodes. The second phase in their recordings must have represented impulse activity at the first two nodes

but their findings did not exclude the possibility of impulse activity in the unmyelinated ending.

Diamond *et al.* (1956) studied the responses recorded across an air gap between the 2nd and 3rd nodes of the Pacinian corpuscle when polarizing currents were passed across the gap. By passing inward currents through the corpuscle, together with its associated first and second nodes, they were able to show only two distinct potential steps arising from the receptor potential in response to suprathreshold mechanical pulses. These were attributed to the activity of the first and second nodes and it was concluded that the non-myelinated axon showed no evidence of a conducted response. It is difficult to reconcile their results with the findings of the present study. However, there are several possible explanations for their not finding evidence of a response attributable to impulse activity in the non-myelinated axon: Current flow could have been distributed, by virtue of the lamellar structure, in such a way as to block the non-myelinated axon and first node at nearly the same level of anodal polarization. Also, the discontinuity between impulse initiation in the non-myelinated axon and first node may have been undetectable under the recording conditions used.

Further evidence as to the site of impulse initiation in the Pacinian corpuscle was advanced by Loewenstein & Rathkamp (1958). These authors found that the removal of the outer lamellae did not prevent the response of the corpuscle to mechanical stimulation. They showed, in addition, that localized pressure on the non-myelinated ending prevented the response to mechanical stimuli distal to the point of pressure. However, if a sufficient length of the non-myelinated ending was central to such a block, mechanical stimulation of this segment still evoked responses. Pressure to the first intracorpuscular node blocked impulse activity as recorded between the point of emergence of the axon from the corpuscle and a more central point on the axon, but a generator or receptor potential persisted in response to mechanical stimuli. They interpreted these results to indicate that the impulse was initiated at the first node and that the non-myelinated terminal was incapable of impulse activity. However, the possibility that pressure to the first node may also produce changes in the adjacent non-myelinated axon must be considered. Blocking pressure to the first node can be expected to produce a strong depolarization which would certainly be expected to spread into the nearby non-myelinated region, thereby preventing impulse conduction. Also, even apparently small injury during removal of lamellae is likely to block impulse conduction in the non-myelinated axon. Preparations showing a rise in mechanical threshold rather than the expected fall following dissection probably have suffered some injury to the non-myelinated axon (Hunt & Takeuchi, unpublished). In some preparations in which the threshold to mechanical stimulation has

risen considerably, strong stimuli evoke responses only when applied to the nerve ending just distal to the first node. The impulse is probably initiated at the first node in such preparations but this cannot be considered to be the normal course of events.

The present experiments provide several types of evidence indicating that the non-myelinated axon is capable of conducting impulses: (1) The response to an antidromic impulse appears to be conducted along the non-myelinated axon at a velocity of about 9 m/sec. The amplitude and time course of the antidromic potential recorded at various distances along the inner core are compatible with this being a propagated response. (ii) When recording with the roving electrode near the central end of the inner core, the negative deflexion of the antidromic impulse is usually followed by a positive deflexion of spike-like duration which is all-or-none in appearance. This indicates that the non-myelinated ending can produce a current sink with spike characteristics. (iii) When recording in a similar manner, the orthodromic impulse, evoked in response to a mechanical stimulus, shows an initial positive deflexion which is normally followed by a negative deflexion. At critical intervals after an antidromic impulse, or in the presence of procaine, this positive deflexion alone may be recorded. In these circumstances, it may be shown to have spike-like duration and to appear in an all-or-none fashion. This again indicates the existence of a current sink with the characteristics of an impulse in the non-myelinated axon. (iv) If the antidromic impulse invades the non-myelinated ending, the latter is refractory for an interval to the initiation of a spike-like current sink. When the antidromic impulse shows evidence of failing to invade the terminal, no such refractoriness is observed.

In recent years the idea has been advanced that the same region of nerve membrane cannot respond by eliciting both graded local potentials such as a generator potential and impulse activity (Grundfest, 1959). The crustacean stretch receptor cell has been cited as an example (Łowenstein & Rathkamp, 1958). In this cell the generator potential occurs in the mechanically sensitive dendritic terminals and by electrotonic extension depolarizes a region of the cell more centrally where an impulse is initiated. According to Edwards & Ottoson (1958), the impulse is set up in the axon at some distance from the cell body. The impulse invades the cell body and to some extent the dendrites, but the generator potential is not completely abolished (Eyzaguirre & Kuffler, 1955). One interpretation of these results is that the mechano-receptive region of the neurone cannot conduct impulses. However, this might not apply to all other mechano-receptors. The crustacean stretch receptor differs from many receptors in having the cell body with its dendrites located peripherally. The lack of invasion of the mechano-receptive region may be generally representative of a property

of the terminal portion of dendrites rather than of sensory endings in general which produce generator potentials. Conduction into dendrites of other cells may be limited (see Bishop, 1956). While there may be complete separation of areas of nerve membrane into those giving only generator responses and those producing impulses, this might be true of only small areas of the non-myelinated axon of the Pacinian corpuscle. Certainly the non-myelinated region taken as a whole appears capable of giving both types of response.

Certain aspects of the impulse in the non-myelinated axon of the Pacinian corpuscle are of interest. The apparent duration of the spike process is similar to that in its parent myelinated axon and therefore resembles that in myelinated *A* fibres rather than non-myelinated (*C*) fibres. In the latter the impulse duration is much longer, being about 2 msec (Gasser, 1950). Estimates of conduction velocity in the non-myelinated axon can only be considered as approximate but appear to be considerably less (about 9 m/sec) than in the myelinated fibre. If the latter has an external diameter of 8–10 μ (Glees, Mohiuddin & Smith, 1949) the velocity calculated on the basis of direct proportionality (conduction velocity = $6 \times$ diam., Hursh, 1939), would be 48–60 m/sec. Assuming a conduction velocity of 9 m/sec and a duration of 0·6 msec for the impulse in the non-myelinated axon, the wave-length would be 5·4 mm. This is more than five times the length of the non-myelinated ending. Along the length of axon occupied by the impulse differences in potential will exist but the short length of the non-myelinated axon relative to the wave-length of the impulse would be expected to produce relatively small current flows along the external resistance between electrodes on the inner core. This factor, as well as the amount of external shunting, and remaining barriers to current flow, are probably responsible for the small amplitude of the potentials recorded. As an antidromic impulse invades the nerve terminal, one might expect a relatively low safety factor at the junction between the non-myelinated and myelinated regions. There is considerable increase in the area of membrane that must be depolarized as the impulse propagates from the myelinated to the non-myelinated portions. This may explain the block of antidromic impulse conduction into the non-myelinated ending that was observed in some preparations. Such a block may develop from a rise in threshold, as a consequence of ageing, or deterioration. The facilitation of invasion by depolarizing the ending with a subthreshold mechanical pulse would be in keeping with this interpretation. In contrast, conduction from non-myelinated to myelinated axon might be expected to have a considerable margin of safety. Evidence of block of conduction centrally at this junction could only be obtained when the excitability of the first node was reduced (see Results).

Whether or not impulse conduction occurs generally in the non-myelinated terminals of vertebrate nerve fibres, both sensory and motor, remains to be determined. On recording from the sensory terminal of single muscle spindle afferent fibres in frogs, Katz (1950) noted small all-or-none potentials of several distinct amplitudes. These at times failed to initiate an impulse in the parent axon. At other times they summed and evoked a propagated impulse in the main axon. The intramuscular branches of the sensory axon to the muscle spindle are for a distance myelinated (Gray, 1957) and the small-amplitude impulses probably represent activity in these myelinated branches. The presence or absence of impulse conduction in the terminal non-myelinated ramifications of the muscle spindle receptor remains a question as it does in the case of most vertebrate receptors. However, the presence of impulse conduction in the non-myelinated ending of the Pacinian corpuscle suggests that the possibility of impulse conduction in other non-myelinated endings must be considered seriously.

SUMMARY

Potentials were recorded externally from Pacinian corpuscles in which outer lamellae had been removed to the inner core. One (stationary) recording electrode was placed at the distal end and the other (roving) recording electrode at various positions along the inner core. The principal findings were as follows:

1. An antidromic impulse, elicited by stimulation of the parent myelinated fibre, produces a spike-like negative deflexion at the roving electrode located at the central end of the inner core. This was usually followed by a smaller positive deflexion of similar duration. The latter, in certain circumstances, could be shown to occur in an all-or-none manner. As the roving electrode was moved toward the stationary electrode, the negative deflexion fell in amplitude, showed a measurable increase in latency of onset, but did not change in duration.

2. Mechanical stimulation by a stylus applied towards the distal end of the inner core produced a positive-negative potential change at the roving electrode located near the central end of the inner core. The initial positive deflexion, which indicates current flow into the non-myelinated axon, was all-or-none in character.

3. After a previous antidromic impulse, or under the influence of procaine, mechanical stimulation could elicit the positive component of the orthodromic response in isolation. In the presence of procaine a graded generator potential could be seen from which the positive orthodromic response originated.

4. The negative deflexion of the orthodromic response was smaller in amplitude than the antidromic response, apparently owing to depolarization

of the non-myelinated axon region by the mechanical stimulus. The antidromic response was also reduced in amplitude by a preceding mechanical pulse.

5. The above findings are interpreted as indicating that the non-myelinated axon of the Pacinian corpuscle can conduct impulses.

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