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FACILITATION AND DEPRESSION OF MUSCLE STRETCH RECEPTORS BY REPETITIVE ANTIDROMIC STIMULATION, ADRENALINE AND ASPHYXIA

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In the preceding paper (Paintal, 1959), it has been shown that it is possible to study certain local events in muscle stretch receptors, even though the action potentials are recorded at a distance, by applying brief pulls to the muscle and noting changes in the pull-impulse latency. Further, it was shown that, as in the Pacinian corpuscle (Diamond, Gray & Sato, 1956; Loewenstein, 1958), there was no detectable propagation of impulses in the non-myelinated ending. It was also suggested that one could study the effects of drugs on the recovery of excitability of the endings following an antidromic impulse. This was possible because of the reproducible and constant relation of the curves of pull-impulse latency and antidromically conditioned pull-impulse latency to each other under constant conditions, so that any change in this relation would reflect a change in recovery processes following an antidromic impulse. Using this approach the effects of three agents, repetitive antidromic stimulation, adrenaline, and asphyxia have been studied.

The term recovery or recovery processes has been used to designate all processes which raise the excitability of the ending from zero immediately after arrival of an antidromic impulse at the ending to maximum with a certain time course. If these processes are accelerated recovery is enhanced and vice versa. Accordingly, other things being the same, reduction of the antidromically conditioned pull-impulse latency will indicate enhancement of recovery.

The term post-tetanic antidromic depression used in this paper refers to the reduction or absence of the steady discharge for variable periods after a train of antidromic stimuli.

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METHODS

Experiments were done on lateral gastrocnemius-soleus endings as described in the preceding paper (Paintal, 1959); one experiment was done on a decerebrate cat.

RESULTS

Effect of antidromic stimuli

As was done by Matthews (1933) the effects of antidromic stimuli were observed exclusively on endings which, after adaptation, fired regularly so that the effects of one or more stimuli could be studied systematically in different parts of the impulse cycle, the cycle beginning immediately after an orthodromic impulse and ending just before the discharge of the next one.

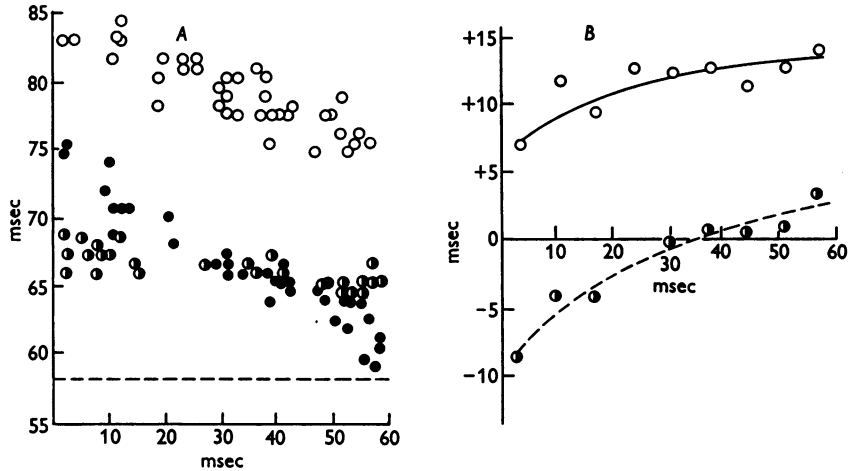

Fig. 1. Effects of one and two antidromic stimuli on recovery of a lateral gastrocnemius-soleus stretch receptor. In *A*, ● = responses, with one stimulus; ○ = with two simuli separated by 2·8 msec; ◑ with two stimuli separated by 48·3 msec. *B* shows the difference curves obtained by subtracting values obtained with one stimulus from those obtained with two stimuli in *A*. Interrupted line in *A* indicates normal impulse interval. Abscissa for ● in *A* = interval between preceding orthodromic impulse and antidromic stimulus; ordinate = interval between antidromic stimulus and next orthodromic impulse. Abscissa for ○ and ◑ = interval between preceding orthodromic impulse and first antidromic stimulus; ordinate = interval between 2nd antidromic stimulus and next orthodromic impulse.

The effect of antidromic stimuli depends on the number and on the frequency of stimuli applied. If one stimulus is applied early in the impulse cycle the interval between this stimulus and the next orthodromic impulse is appreciably longer than the normal impulse interval (filled circles, Fig. 1*A*). The relation between the position of the stimulus in the impulse cycle and the latency between the stimulus and the next orthodromic impulse is typically (filled circles, Fig. 1*A*) as described by Matthews (1933).

The effect of two stimuli depends, as expected, on the position of the stimuli in the impulse cycle and on the interval between the stimuli, the depression being greater if the interval between the stimuli is small (compare open circles and half-filled circles in Fig. 1). The actual contribution by the second of a pair of stimuli to the total depression of excitability may be obtained by subtracting the effects obtained with one stimulus (filled circles) from that obtained with two stimuli (open circles and half-filled circles). The result of this procedure, which is shown in Fig. 1*B*, reveals that the depression due to the second stimulus is greater if the pair of stimuli fall in the latter part of the cycle.

Increasing the number of stimuli at fixed frequency of stimulation increases the duration of depression represented by the interval between the last stimulus and the first orthodromic impulse. This agrees with Matthews (1933). But to study this relation between the number of stimuli and the duration of depression it is necessary to apply the train of stimuli at a fixed part of the impulse cycle, because of the contributory effects of the preceding orthodromic impulse which are noticeable even with a train of six stimuli.

In some receptors the relation between the number of stimuli (from 1 to 10) and the duration of depression is linear, but in some the curve flattens out with greater numbers of stimuli. The latter is somewhat deceptive because increasing the duration of repetitive stimulation further or increasing the frequency of stimulation invariably leads to prolonged depression. Perhaps such receptors encountered by Matthews (1933) in a preliminary investigation of repetitive antidromic stimulation led him to believe that increasing the number of stimuli beyond 10 had no additional effect on the latency of the first impulse.

With a fixed frequency of stimulation, increasing the duration of tetanic stimulation increases the duration of depression (Fig. 2). A similar observation on tongue thermoreceptors has been made by Dodt & Walther (1957). The duration of depression may last for several seconds. The effect of increasing duration of stimulation at different frequencies is shown in Fig. 2. This figure is typical of responses of the majority of receptors. Typically, the curves show two phases, an early one with a small slope and a later one with a steeper slope. Depression following tetanic stimulation with high frequencies is often profound; in a few instances, however, it lasted for barely a fraction of a second even with high frequency stimulation for several seconds. The period of depression represented by the interval before the appearance of the first impulse does not represent the total duration of depression, which may be several times greater because the initial frequency of discharge of the receptor may be attained only after relatively much longer periods. With fixed duration of tetanic stimulation, the duration of depression increases with the frequency of stimulation. This fact can be gauged from Fig. 2.

The steady discharge usually returns gradually after a prolonged period of

post-tetanic depression. In some instances the initial part of the discharge after depression was grossly irregular. The interval between the first and second impulses after post-tetanic depression may be normal if the interval between the end of the train of stimuli and the first impulse is not long; most often, however, the interval between the first and second impulse is greater than normal. The interval also tends to increase with the duration of the tetanus. Usually, the relation of the duration of the second interval to the duration of the tetanus is not consistent owing to the irregularity of the discharge at the beginning of activity after the depression.

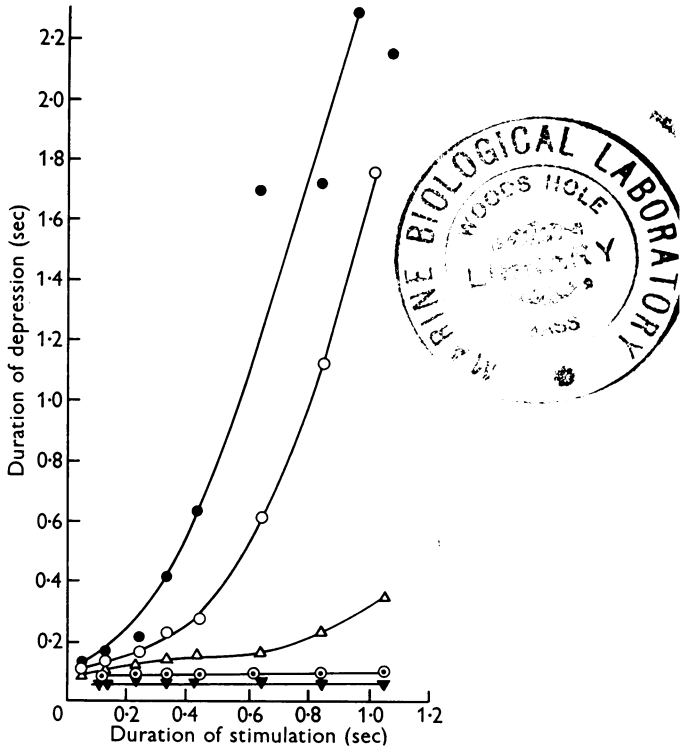

Fig. 2. Graphs showing that duration of depression of a lateral gastrocnemius-soleus stretch receptor varies with the duration of antidromic stimulation. Graph –●–●– = stimulation at frequency of 360/sec; –○–○– = at 260/sec; –△–△– at 180/sec; –⊙–⊙– = at 100/sec; –▼–▼– = at 60/sec.

The fact that the duration of depression increases with the number of stimuli implies that the depressant effects of antidromic impulses sum with each other. Each antidromic impulse produces some depression at the ending, which decays with a certain time course, and the effect of the subsequent one is added on to the depression that remains. A way in which this could be achieved was revealed by the effects of short trains of stimuli repeated at

suitable intervals. The amount of depression increased with each succeeding train and it was found that the amount of depression after any particular train was related to the residual depression remaining before this train, i.e. the duration of depression varied with the impulse duration immediately before the application of the train of stimuli. From direct observations on the sensory cell of the crayfish Eyzaguirre & Kuffler (1955) arrived at a similar conclusion.

That post-tetanic depression observed in these experiments was not due to electrotonic block of the afferent fibre at the stimulating electrodes was proved by noting during the period of depression the appearance of orthodromic impulses on pulling the muscle manually or briefly with a puller. In any case the likelihood of electrotonic block was remote, because stimuli of only 0·03 msec duration and usually less than 0·5 V intensity were used to stimulate the whole nerve trunk near the muscle.

Post-tetanic depression was not due to activation of inhibitory fibres such as occurs in the crayfish stretch receptor (Kuffler & Eyzaguirre, 1955) because depression only appeared at threshold for the afferent fibre concerned; reduction of stimulus strength below this level had no effect. If depression was produced by inhibitory fibres it would imply that their fibre characteristics were identical with those of the afferent fibres examined, and since the conduction velocities of the latter ranged from 30 to 115 m/sec the inhibitory fibres would form a large fraction of the efferent outflow; such a possibility is quite remote. Post-tetanic antidromic depression was not dependent on the anaesthetic used (chloralose) because an experiment on a decerebrate cat yielded identical results.

Effect on recovery of excitability after an antidromic impulse. In order to determine whether recovery processes were in any way influenced by tetanic stimulation, the relation between pull intensity and pull-impulse latency and antidromically conditioned pull-impulse latency, respectively, was first plotted (see Fig. 7*A* and related description in text; also discussion in Paintal, 1959). With the antidromic stimulus fixed in the same position the effect of repetitive stimulation on pull-impulse latency and antidromically conditioned pull-impulse latency was noted. If the intensity of the pull was large, repetitive stimulation which abolished the continuous discharge did not in some receptors affect the pull-impulse latency. In other receptors the pull-impulse latency was increased (Fig. 3*A*). With weak pulls repetitive stimulation was always followed by an increase of pull-impulse latency. Often the pull response was abolished and it returned gradually. The antidromically conditioned pull-impulse latency also increased after repetitive stimulation (Fig. 3*B*), the increase being greater if the antidromic stimulus was closer to the pull pulse. It was noted that the antidromically conditioned pull-impulse latency usually increased by an

amount expected from the relation of the graphs of pull-impulse latency and antidromically conditioned pull-impulse latency to each other. Post-tetanic depression could therefore be accounted for entirely by the change in the pull-impulse latency, and consequently recovery processes during antidromic post-tetanic depression were unchanged, or if they were the change was too small to be detected. In occasional experiments the antidromically conditioned pull-impulse latency fell after tetanic stimulation, suggesting enhanced recovery. Eventually, this was found to be due to incomplete neuromuscular block. The muscle spindle was unloaded with each stimulus, thus increasing the antidromically conditioned pull-impulse latency above normal, an effect abolished by tetanic stimulation so that the latency fell.

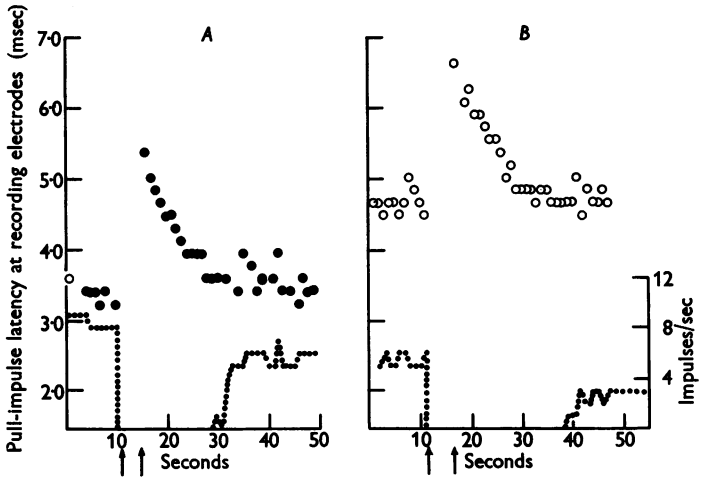

Fig. 3. Effect of repetitive antidromic stimulation on pull-impulse latency (*A*) and antidromically conditioned pull-impulse latency (*B*) of a lateral gastrocnemius-soleus stretch receptor. The nerve was stimulated at 300/sec between the arrows. Dotted curve in both *A* and *B* represents frequency of steady discharge.

Figure 3 shows that the steady discharge returned gradually and concurrently with the return of the pull-impulse latency and antidromically conditioned pull-impulse latency to initial levels. The return to normality of both types of events was almost invariably concurrent. The actual relation of the two curves of course varied with the strength of the pull, so that with weak pulls the steady discharge sometimes returned before the pull responses appeared, but the return to normality was always signalled by the simultaneous return of the normal response to pull and the return of the steady discharge to the initial frequency.

Effects of adrenaline

In some preliminary experiments it was found that adrenaline (adrenaline chloride containing $<0{\cdot}1\%$ sodium bisulphite as preservative) when injected

intravenously abolished the steady discharge. This substance has no known action on intrafusal muscle fibres and so it is suitable for studying the effects of drugs on the endings.

The initial action of adrenaline, which set in about 30–150 sec after injection, was of two types. In some receptors the first effect was an increase in the frequency of discharge to less than twice the initial frequency. The frequency then either fell gradually until the discharge was abolished or it merged into the phase of greatly increased activity (Figs. 4, 5). In the second type of response the discharge was gradually abolished without any preliminary increase. With 100–200 μg of adrenaline the discharge returned gradually after a few seconds of silence and soon reached normal levels. With larger doses of 300–500 μg the silence lasted several minutes until it was interrupted by a gradually increasing discharge which attained a relatively high frequency of about 80–300 impulses/sec, after which the discharge became irregular and then ceased. This cycle could be repeated one or more times. Eventually, the discharge returned gradually after several minutes of silence until the original frequency of discharge was attained. This behaviour recalled to mind the response of muscle stretch receptors to occlusion of the circulation (Matthews, 1933). Indeed, some of the effects of adrenaline were probably due to asphyxia because with the large doses used blood flow to the muscle must have been stopped. This was confirmed in one experiment on a 12 kg dog, in which 1 mg adrenaline stopped, for several minutes, the blood flow to the hind limb, measured with a flowmeter.

Effect on recovery of excitability after an antidromic impulse. The above changes in the steady discharge were recorded simultaneously with changes in pull-impulse latency and antidromically conditioned pull-impulse latency. The results of a typical experiment are shown in Fig. 4. The first change was a moderate increase of the steady discharge leading to a considerable acceleration a few seconds later. During the period of marked acceleration, the pull-impulse latency remained almost unchanged but the antidromically conditioned pull-impulse latency fell appreciably. This suggests that recovery processes were enhanced at this time. The steady discharge fell to about 16 impulses/sec about 100 sec after the injection of adrenaline and after this the pull-impulse latency began to rise with an almost parallel change in the antidromically conditioned pull-impulse latency. At this time (105–110 sec) the difference between the pull-impulse latencies and the antidromically conditioned pull-impulse latencies was considerably smaller than that which existed before adrenaline was given (Fig. 4). This is strong evidence of enhanced recovery, especially since there is an indication of rising pull-impulse latency at this time. It is important to keep this reasoning in mind, because in curves relating pull-intensity to pull-impulse latency and antidromically conditioned pull-impulse latency (e.g. Fig. 7*A*),

if the slope of the former is less than that of the latter at a particular setting of pull intensity, then a small change in the pull-impulse latency can account for a large change in the antidromically conditioned response.

At about 130 sec after injecting adrenaline in Fig. 4 the steady discharge rose to about 90/sec in spite of raised pull-impulse latency. At this time recovery still seems to have been enhanced because of the low difference between pull-impulse latency and antidromically conditioned pull-impulse latency. 140 sec after adrenaline had been given the antidromically conditioned responses ceased, not as a result of reduced recovery but probably owing to increased pull-impulse latency which continued to rise until it reached its maximum at about 200 sec after the injection of adrenaline. Thereafter the pull-impulse latency

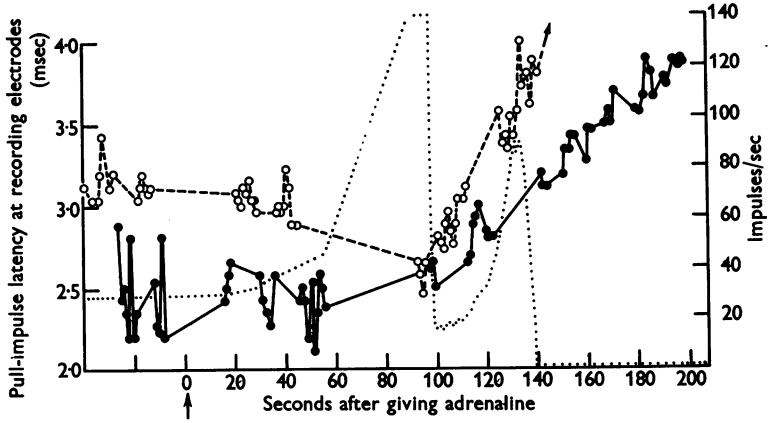

Fig. 4. Effect of 500 μg adrenaline injected at arrow on the steady discharge, · · · · ·, pull-impulse latency, —●—●—, and antidromically conditioned pull-impulse latency, –○– –○– of a gastrocnemius-soleus stretch receptor obtained in a decerebrate cat.

remained at this level till about 13 min after injecting adrenaline when it began to fall gradually. This phase was characterized by periodic oscillations of the pull-impulse latency in the absence of any steady discharge. By 24 min the pull-impulse latency had reached normal values but there were now no antidromically conditioned responses. Recovery of excitability after an antidromic impulse was therefore greatly depressed at this time, as it had probably been for several minutes past. The steady discharge appeared at about 24 min and it increased gradually to attain a frequency of about 20/sec at about 26 min after adrenaline had been administered. The antidromically conditioned pull-impulse latency did not return to normal values till about 70 min after giving adrenaline. Adrenaline therefore depressed recovery for a long period in this receptor (probably owing to asphyxia) after a short period of enhanced activity soon after injection. These observations show that the return of the steady discharge to near normal values is not a satisfactory index of the condition of the ending, as the steady

discharge had approached normal values at about 26 min after adrenaline had been given, at which time recovery was greatly depressed.

The enhancement of recovery during the early phase of action of adrenaline was seen in a number of other receptors, e.g. that shown in Fig. 5 which was obtained from a fibre in the same nerve filament as that of Fig. 4. In this case, with the position of the antidromic stimulus used, there were no antidromically conditioned pull responses before the injection of adrenaline. However, at about 125 sec after adrenaline had been given antidromically conditioned pull responses suddenly appeared and their latency fell rapidly to reach the lowest value at 150 sec after which they rose once again. These changes in the

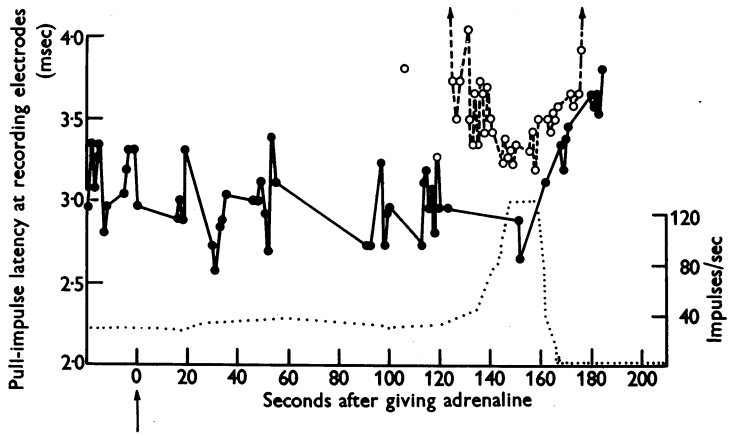

Fig. 5. Graphs showing increased recovery of a stretch receptor after injection of 500 μg adrenaline at arrow. Curve ·····, steady discharge, curve –●—●–, pull-impulse latency and curve –○– –○–, antidromically conditioned pull-impulse latency; obtained from another fibre present in the same filament from which results of Fig. 4 were obtained.

antidromically conditioned responses occurred concurrently with a considerable increase in the frequency of the steady discharge. When the discharge fell the antidromically conditioned pull-impulse latency rose. At this time Fig. 5 shows that the pull-impulse latency also began to rise, but the small difference between this and the antidromically conditioned latency at about 170 sec shows clearly that recovery was enhanced greatly. The rise in the antidromically conditioned pull-impulse latency after 160 sec was therefore due entirely to a rise in the pull-impulse latency. The enhancement of recovery is attributable to adrenaline itself, because no initial enhancement of recovery was seen after asphyxia (see below).

In a few receptors the increase in the antidromically conditioned pull-impulse latency paralleled that of pull-impulse latency through the various changes in the steady discharge. In these instances the increase in the antidromically conditioned pull-impulse latency could be explained as being due to an increase in the pull-impulse latency without any change in recovery.

Loewenstein & Altamirano-Orrego (1956) noted reduction of threshold of the Pacinian corpuscle following administration of adrenaline. Clear evidence of this was not obtained in the present investigation. However, the possibility of reduction of threshold is not ruled out, because the experiments were not especially designed to elucidate this point.

Effects of asphyxia

The characteristic responses of muscle stretch receptors after local ischaemia have been described in detail by Matthews (1933). Similar effects have been obtained in the present investigation after asphyxia. Figure 6 shows a typical series of events before and after shutting off the respiratory pump in a fully curarized cat. In this receptor the first change was a reduction of the steady discharge at about 110 sec after begining asphyxia; this fell to zero at 126 sec.

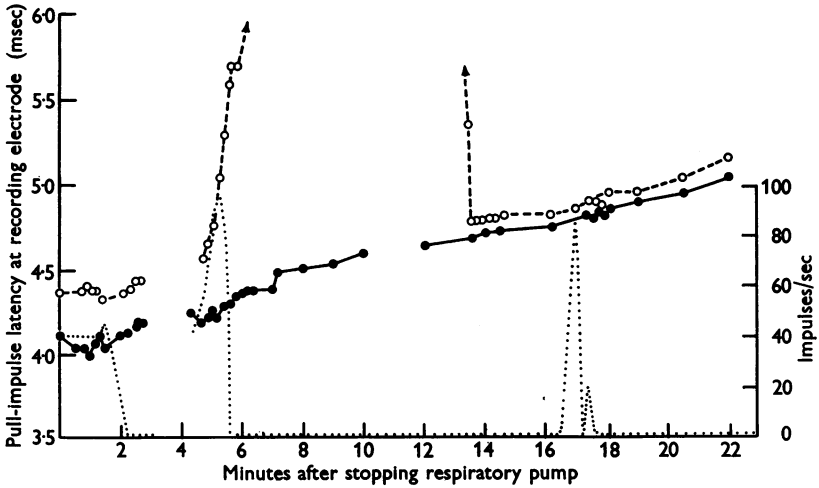

Fig. 6. Effect of asphyxia on a lateral gastrocnemius-soleus stretch receptor. Curve ·····, steady discharge; curve —●—●—, pull-impulse latency which increased steadily; curve –○– –○–, antidromically conditioned pull-impulse latency. Note marked depression of recovery shortly after 4 min, associated with increase of steady discharge.

The pull-impulse latency and the antidromically conditioned pull-impulse latency began to increase soon after asphyxia began and the former continued to rise steadily till the very end when all responses to pull disappeared at about 24 min of asphyxia. The antidromically conditioned pull-impulse latency on the other hand showed a much steeper rise beginning at about 4·5 min after starting asphyxia and this continued until 6 min when antidromically conditioned pull responses disappeared till 12 min. The steep rise in the antidromically conditioned pull-impulse latency was coincident with a considerably increased frequency of the steady discharge which rose to about 95 impulses/sec and then fell rapidly to zero. This phase of increase in the

steady discharge therefore occurred simultaneously with considerably reduced recovery of the ending.

The antidromically conditioned responses returned at about 13·3 min (Fig. 6) and the latency fell rapidly to attain a very low level when compared to the pull-impulse latency, particularly when reckoned in the light of the relation of the two responses respectively to pull intensity. At this time therefore there was an apparent increase in the recovery processes which was maintained till the end as shown in Fig. 6. Similar apparent increase of recovery of excitability after an antidromic impulse was observed in other receptors.

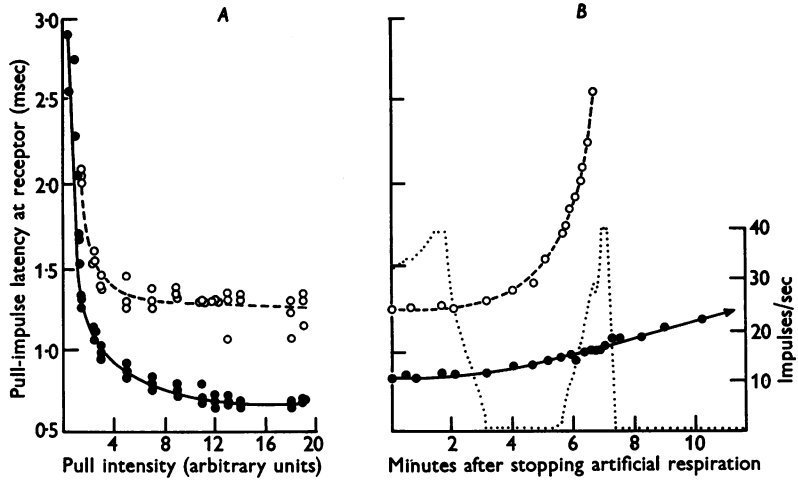

Fig. 7. Graphs showing how a change in the antidromically conditioned pull-impulse latency was interpreted. For explanation, see text. *A* shows the relation of pull-impulse latency –●—● and antidromically conditioned pull-impulse latency –○--○– to pull intensity before asphyxia. *B* shows the steady discharge ·····, pull-impulse latency and antidromically conditioned pull-impulse latency after asphyxia.

A sudden reappearance of the steady discharge with a peak frequency of 85 impulses/sec for a short while at about 16·6 min had no effect on the pull responses or antidromically conditioned pull responses (Fig. 6) thus indicating that the steady discharge need have no influence on the responses to transient pulls. This was noted repeatedly.

The initial depression of recovery processes (Figs. 6, 7*B*) was observed in every ending investigated. Proof of actual depression was obtained by interpreting the results in conjunction with the graphs relating pull intensity and the two latencies, respectively. Since this procedure has been used throughout this investigation an example will be described in detail (Fig. 7). Before asphyxia began the pull-impluse latency in Fig. 7*B* was about 0·83 msec and the antidromically conditioned pull-impulse latency was about 1·24 msec.

This was a normal response, because Fig. 7*A* shows that the antidromically conditioned pull-impulse latency at a pull-impulse latency of 0·83 msec should have been about this much. About 6·3 min after stopping the respiratory pump the pull-impulse latency had increased to 1·00 msec. Figure 7*A* shows that at this level with recovery unchanged the antidromically conditioned pull-impulse latency should have been about 1·45 msec. Instead, it was about 2·55 msec (Fig. 7*B*), which shows clearly that recovery of excitability following an antidromic impulse was greatly depressed. At about this time the steady discharge reappeared and lasted for about 1 min. This ending therefore provides another example of increase in steady discharge during depressed recovery.

In every receptor examined there was a steady rise in the pull-impulse latency, as is shown in Fig. 6. There is no doubt that this was associated with a raised threshold to pull, because if the pull-impulse latency was increased at a particular setting of pull intensity (near maximum) then reduction of the pull would inevitably abolish the response, as did happen in some receptors. Simultaneous changes in threshold could not be determined in the above experiments owing to technical difficulties. Besides, it was not particularly advantageous to determine it, because the responses normally varied considerably in latency at threshold, so that evaluation of changes in responses would be difficult. This difficulty could have been overcome by taking the mean of several responses, but this would not have permitted recognition of rapid changes in the response of the ending. However, in two receptors only changes in threshold after asphyxia were studied. In both the threshold rose gradually in a manner expected from the curves of pull-impulse latency obtained from several receptors.

Responses to transient pulls survived in different receptors for as long as 25 to over 60 min after asphyxia. At this time conduction in the afferent fibres themselves was satisfactory and the conduction velocity of the fibres was hardly altered.

DISCUSSION

Post-tetanic antidromic depression of sensory receptors is not unusual. In the frog it was first elegantly demonstrated by Cattell & Hoagland (1931) who showed that orthodromic impulses generated in one ending of a cutaneous afferent fibre and travelling antidromically to another ending of the same fibre depressed the responses of the latter. It has also been demonstrated in the sensory cell of the crayfish (Eyzaguirre & Kuffler, 1955). Recently Dodt & Walther (1957) showed that antidromic stimulation of the lingual nerve depresses thermoreceptors in the tongue, which they felt was due to positive after-potentials. Matthews (1933) did not observe any prolonged antidromic depression in muscle stretch receptors of the cat. In the frog (Matthews, 1931) he noted acceleration of the discharge which was presumably due to stimulation of intrafusal muscle fibres (cf. Eyzaguirre, 1958).

The marked post-tetanic antidromic depression is of physiological significance in the case of two or more sensory endings connected to the same afferent fibre because activity in one ending will depress the responses in the others, particularly if high-frequency discharges are produced by the first one. Since the effects of orthodromic impulses are similar to those of antidromic ones (Paintal, 1959), it follows that orthodromically generated high-frequency discharges in an ending will depress the responses of that ending. It is therefore possible that this type of depression may form an important component of 'off effect' phenomenon in sensory endings. Indeed, Eyzaguirre (1958) has already given some indication of this in muscle spindles of frogs.

The discussion that follows is based on the fact that the terminals of muscle stretch afferent fibres are non-myelinated (Barker, 1948) and that since there is no detectable non-myelinated propagation of the impulse (Paintal, 1959), this part of the fibre is the site of production of non-propagated receptor potentials which initiate propagated impulses at the first node of Ranvier of the afferent fibre as in the Pacinian corpuscle (Diamond *et al.* 1956).

Gasser & Grundfest (1936) showed that considerable depression of excitability of mammalian A nerve fibres occurred after tetanic stimulation at high frequency; this depression could last for a few minutes and it was associated with pronounced positive after-potentials. Such depression associated with positive after-potentials must also occur in the region of the first node. This depression would inevitably raise the threshold of excitability of the first node relative to the receptor potential and would thus reduce or abolish the steady discharge and increase the pull-impulse latency as observed in these experiments. The increased threshold of the ending after tetanization would also fit into this scheme. An additional factor could be the depression of the static and dynamic receptor potentials electrotonically by the positive after-potentials (Diamond *et al.* 1956). These conclusions can be confirmed by noting the effect of tetanic stimulation on receptor potentials of muscle stretch receptors. This appears to be possible in the tenuissimus under favourable experimental conditions (Eyzaguirre, personal communication).

As has already been shown, post-tetanic antidromic depression is not due to reduced recovery processes. The experiments with adrenaline and asphyxia have shown that changes in the steady discharge may run parallel with or opposite to changes in recovery or pull responses. Thus an increased steady discharge may be associated with increased (Figs. 4, 5) or depressed recovery (Fig. 6) or with reduced or increased responses to pull. Reduction of the steady discharge was never coincident with increased recovery of the ending. Absence of the steady discharge was not due to depolarization block, because pull responses persisted often unchanged at this time. This view is supported by the frequent observation that the steady discharge was abolished in many endings with little or no prior increase.

The increase in the pull-impulse latency following adrenaline and asphyxia could be due to reduction of the dynamic receptor potential, to raised threshold of the first node of Ranvier, or to increased time constant of the non-myelinated membrane. Increased accommodation cannot explain the results because of the rapid rate of rise of the pull pulse used in these experiments. The fact that the threshold increased at the same time suggests that there was either a reduction in the dynamic receptor potential or an increase in the threshold of the first node.

The results have shown that certain recovery processes following an antidromic impulse are enhanced (attributable to adrenaline) and subsequently depressed after injection of adrenaline. Return of normal recovery may be delayed for 10–70 min—long after return of normal pull responses and steady discharge. The first action of asphyxia is to depress recovery. This depression may last for several minutes and after this time an apparent enhancement of recovery follows in some endings. It is possible that this apparent enhancement may be a genuine enhancement, but it is more likely that it is due to block of the antidromic impulse at some point which results in less depression of the receptor potential. If it is assumed that the block also blocks orthodromic impulses then it follows that the block cannot be in the first node of Ranvier or more centrally, because this would have to be associated with a corresponding increase in the pull-impulse latency owing to the necessity of initiating the impulse ahead of the block. Such increase was never seen (Fig. 6). According to this assumption, therefore, the site of the hypothetical block must be in the non-myelinated segment. This implies that antidromic impulses normally invade the non-myelinated segment, which contradicts Diamond, Gray & Inman (1958). However, a more plausible explanation suggested by Dr B. Katz (personal communication) is that the antidromic impulse (but not the orthodromic) is blocked at one of the points of subdivision of the myelinated afferent fibre owing to a low safety factor of conduction here. This would reduce the depressant effect of the antidromic impulse on the receptor potential. The orthodromic impulse is not blocked probably because, owing to the rapid pull, the impulses from the branches arrive synchronously at the point of subdivision and are thus able to sum, leaving the pull-impulse latency unaffected. Subdivision of the afferent fibre has been seen invariably in the muscle spindle by Dr Sybil Cooper (personal communication).

The choice of adrenaline was unfortunate because of secondary asphyxial effects arising from vasoconstriction, a point stressed by Bülbring & Whitteridge (1941) in connexion with lowered threshold of nerve fibres after administration of 5–25 μg of the drug. However, it is highly probable that the initial enhancement of recovery was due to the drug itself.

SUMMARY

1. Changes in recovery of excitability of an ending following an antidromic impulse were studied by evaluating a change in the antidromically conditioned pull-impulse latency with reference to pull-impulse latency in muscle stretch receptors of cats.

2. Tetanic antidromic stimulation reduced or abolished the steady discharge from stretch receptors. The duration of depression varied with the duration and frequency of antidromic stimulation. This depression was not due to reduced recovery of the ending. It is probably due to raised threshold of the first node of Ranvier of the afferent fibre owing to positive after-potentials produced in this region by antidromic impulses.

3. Adrenaline initially enhanced recovery of some endings, but eventually it always depressed it for prolonged periods. The latter effect was probably secondary to asphyxia accompanying strong local vasoconstriction.

4. Asphyxia depressed recovery of the ending from the start. In some cases this was followed by an apparent enhancement of recovery, which was probably due to block of the antidromic impulse. Possible sites of the block are discussed.

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