J. Physiol. (1961), **156**, *pp.* 498–514
With 10 *text-figures*
Printed in Great Britain

PARTICIPATION BY PRESSURE-PAIN RECEPTORS OF MAMMALIAN MUSCLES IN THE FLEXION REFLEX

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(*Received* 21 *November* 1960)

It has been established in an earlier paper (Paintal, 1960) that there are a separate group of sensory endings in muscles that are stimulated by local pressure but not by external stretch. It was suggested that these receptors mediate some kinds of muscle pain; they were therefore termed pressure-pain receptors (Paintal, 1960). Most of these endings are connected to Group III afferent fibres of muscle nerves, some to Group II and a few to Group I fibres. It was also shown that the afferent fibres of Group III terminate mainly in pressure receptors, a few in stretch receptors and some in receptors that cannot be activated mechanically (Paintal, 1960). Like the Group I and Group II bands, therefore, the Group III fibres are a mixed group.

The reflex effects produced by natural stimulation of stretch receptors connected to Group I fibres are well known (Lloyd, 1943*b*; Granit, 1950, 1952; Granit & Ström, 1951; Hunt, 1952) and the results are in agreement with those obtained by stimulating Group I nerve fibres themselves. The effects of natural stimulation of stretch receptors with Group II fibres have been studied in isolation only recently by Laporte & Bessou (1959), who found that the endings of soleus and tibialis anterior respectively inhibit and excite their own motoneurones. So far it has not been possible to study the effects of stimulating endings connected to Group III fibres, since hitherto nothing was known about these endings. However, it is known that electrical stimulation of Group II or Group III fibres facilitates flexor reflexes (Lloyd, 1943*a*; Brock, Eccles & Rall, 1951; Eccles & Lundberg, 1959*a*; Kuno & Perl, 1960), in addition to influencing certain crossed reflexes (Perl, 1958). Since it is now known that the majority of Group III fibres terminate in pressure-pain receptors (Paintal, 1960) it is to be expected that the reflex effects of these endings will be essentially similar to the effects of stimulating Group III fibres—an expectation borne out by the results of the present investigation, which was aimed at determining the reflex effects of pressure-pain receptors of triceps surae and tibialis anterior.

METHODS

Adult cats were anaesthetized with ether and the spinal cord was cut at the level of the atlanto-occipital membrane. The brain was destroyed by pithing and the animal was put on artificial ventilation. The pelvis and the left hind limb were immobilized by transfixing them with pins, and muscular movements were prevented by injecting D-tubocurarine or gallamine (Flaxedil; May & Baker) intravenously. The sural and tibial nerves were always cut; the latter was cut distal to its branches to the triceps surae as far centrally as possible, to avoid stimulating its central end when the intact lateral gastrocnemius-soleus nerve was stimulated. Other nerves were cut according to the nature of the experiment.

In some experiments local pressure was applied to the triceps surae muscle by an electromechanical device (presser) powered by an audioamplifier into which square pulses of short duration were fed from a stimulator triggered by the sweep of the oscilloscope. In these experiments the flattened end of a wooden rod connected to the presser was applied to the ventral surface of the triceps surae, which was exposed by separating this part of the muscle from the underlying bone. The tendo Achillis was elevated after cutting the plantaris tendon and the muscle was sandwiched between the rod of the presser and a pressure gauge applied to its dorsal surface. The part so sandwiched consisted of the muscular part of the muscle, about 2–3 cm from the point of insertion of the tendon on the calcaneus. In these experiments the intensity and duration of the pressure pulses were kept constant. Usually about 0·5–1 kg pressure was applied and the duration of the pressure pulse was about 3·5 msec (Fig. 4). Often, as in Fig. 4*B*, there were some oscillations of low amplitude after the main pressure pulse. These should be kept in mind when considering the conditioning effects of pressure pulses applied at large intervals before the test stimulus. The pressure gauge was connected to a d.c. amplifier and led to one channel of the oscilloscope; it was calibrated by applying weights to its surface.

Monosynaptic reflexes were recorded monophasically from the cut central end of L 7 or S 1 ventral roots. These reflexes were elicited by stimulating the cut central ends of the following nerves: posterior biceps semitendinosus (BST), triceps surae, deep peroneal (DP) and tibialis anterior (TA). Occasionally an intact nerve was stimulated in order to avoid cutting off the sensory inflow from a particular muscle. The conduction time for the Group I volley from the stimulating electrodes on a peripheral muscle nerve to the spinal cord was determined at the end of an experiment by recording the arrival of the afferent volley monophasically from the peripheral end of a cut dorsal root near its entry into the spinal cord.

Whenever it was necessary to take many records of monosynaptic reflexes, the oscilloscope trace was masked except for the section occupied by the reflex (Figs. 2, 3 and 7). This procedure allowed continuous records to be taken over prolonged periods with considerable economy of recording paper.

RESULTS

Stimulation of pressure-pain receptors in lateral gastrocnemius and soleus (LGS)

Effects on posterior biceps and semitendinosus (BST) monosynaptic reflex. Since many pressure-pain receptors of lateral gastrocnemius and soleus are located near the junction between the muscle and the tendo Achillis (Paintal, 1960), this region was chosen exclusively for stimulating these receptors; it was usually situated about 2·5–3 cm central to the insertion of the tendon on the calcaneus. This was a fortunate choice, because it was found later that squeezing this part caused little stimulation of stretch

receptors, as revealed by recording impulses from the whole lateral gastrocnemius-soleus (LGS) nerve (Fig. 1).

Squeezing the muscle either between finger and thumb or between the jaws of dissecting forceps always increased the BST monosynaptic reflex (Fig. 2). This response survived the cutting of all nerves to the hind limb with the exception of the nerve to the lateral gastrocnemius and soleus. To distinguish the action of pressure-pain receptors from those of stretch

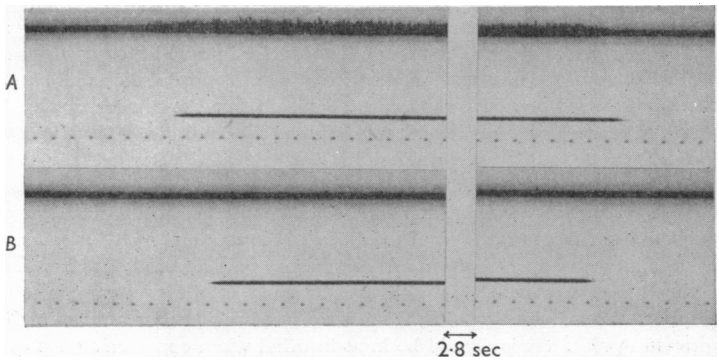

Fig. 1. Records of impulse activity in peripheral end of cut lateral gastrocnemius-soleus nerve, *A* while stretching the muscle, and *B* while squeezing the musculo-tendinous region, during signals. From above downwards in each record, impulse activity, signal and 1/10 sec time marks.

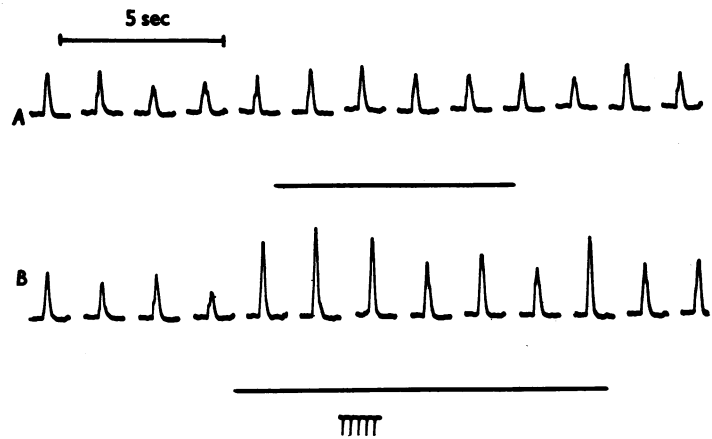

Fig. 2. Segments of sweeps showing biceps-semitendinosus (BST) monosynaptic responses. The sweeps recur at intervals of 1·6 sec and were taken on moving recording paper. During signal in *A* the triceps surae was pulled, and in *B* it was squeezed between finger and thumb. Medial gastrocnemius nerve was intact. Note increase in monosynaptic response while muscle was squeezed. Time marker, msec.

receptors, which, as mentioned above, can also be stimulated a little by squeezing the muscle, the effects of local pressure were compared with those of stretching the muscle. Since it is known that Group I fibres (Eccles, Eccles & Lundberg, 1957) and Group II fibres (Kuno & Perl, 1960) of triceps surae facilitate BST motoneurones, it was not surprising to find that stretching the muscle to about 700 g often facilitated these motoneurones. However, this facilitation was very often much less than that produced by squeezing the muscle. Typical responses are shown in Fig. 2. When these are considered in relation to the impulses produced by stretching and squeezing the muscle (Fig. 1) it may be concluded that squeezing the muscle facilitates the reflex primarily by stimulating endings other than stretch receptors, probably pressure-pain receptors (Paintal, 1960).

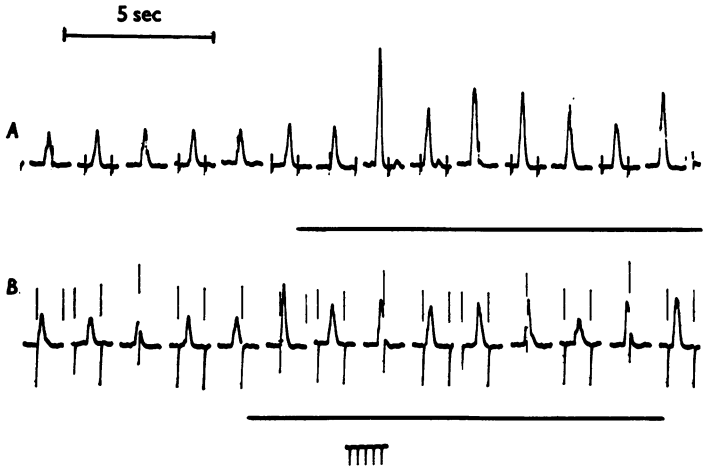

Fig. 3. BST monosynaptic responses. Record *A* was taken while the LGS nerve was stimulated repetitively at 270/sec with stimuli 10 times threshold for Group I. In *B* the strength of the stimuli was 66 times threshold. In both *A* and *B* the triceps surae was squeezed during signals. Note that the effect of pressure is not blocked by 10 times threshold stimuli in *A*. The sweeps recur every 1·6 sec. Time marker, msec.

In order to show that pressure-pain endings with Group III fibres (or smaller) facilitate the reflex, the receptors connected to Group I and Group II fibres were depressed antidromically by repetitive stimulation at a frequency ranging from 200 to 460/sec. Since Eccles & Lundberg (1959*b*) have shown that all Group II fibres should be stimulated by stimuli 8–10 times the threshold for Group I, stimuli of at least this strength were used to stimulate the intact LGS nerve. However, in most experiments stimuli of about 16 times threshold were used, to allow for any relative refractoriness in the nerve fibres at high frequencies of stimulation. These stimulus

strengths have been used throughout this investigation to stimulate Group I and Group II fibres. It is to be expected from the observations of Eccles & Lundberg (1959*b*) and Kuno & Perl (1960) that at this stimulus strength some Group III fibres will also be excited. This does not vitiate the results, since the main purpose of these experiments was to determine the reflex effects of endings connected to Group III fibres only.

As had been expected, tetanic stimulation by itself enhanced the BST monosynaptic responses initially but the responses soon stabilized themselves (see Eccles & Rall, 1951). While the nerve was thus tetanized it was found that facilitation of BST monosynaptic reflex by squeezing the muscle was not obviously reduced (Fig. 3*A*), thus showing that endings with fibres smaller than Group II facilitate the reflex by pressure. No conclusion can, however, be drawn about the role of Group I and Group II fibres from this observation, because of unknown central effects of tetanic stimulation. For instance, one cannot conclude that endings with Group I and Group II fibres did not contribute to the facilitation on the basis that facilitation was not reduced during tetanization as in Fig. 3*A*.

Although the above experiment indicated that endings with fibres smaller than Group II facilitate the BST monosynaptic reflex, it was still not certain whether facilitation by squeezing the muscle was due to stimulation of pressure receptors connected to Group III fibres or to endings connected to non-myelinated fibres, especially since Voorhoeve, Laporte & Bessou (1958) have demonstrated facilitation of flexor reflexes by non-myelinated fibres. The stimulus strength of repetitive stimulation was therefore increased to about 70 times threshold in order to block nearly all endings connected to Group III fibres. As expected, this sometimes facilitated the monosynaptic responses considerably, but after they had become stabilized it was found that facilitation by squeezing the muscle was much reduced (Fig. 3*B*), although it was still present in some experiments; this was presumably due to endings connected to non-myelinated fibres. No definite conclusion concerning the relative contribution by pressure-pain endings with Group III fibres can be drawn from this experiment, because the reduced facilitation during tetanization, shown in Fig. 3*B*, may have been due entirely to the central effects of tetanic stimulation.

Evidence that pressure-pain receptors connected to Group III fibres facilitate the BST monosynaptic reflex was obtained by applying pressure pulses to the triceps surae with the presser as described in methods. This procedure itself yielded a reflex discharge in ventral roots with a latency ranging from 15 to 28 msec (Fig. 4*B*), but since the destination of the motoneurones stimulated could not be ascertained this aspect of the response was not pursued further.

As shown in Fig. 4*B*, the facilitation of the BST monosynaptic response by pressure pulses was marked, being sometimes three times greater than the control responses. The interval between the pressure pulse and the BST test stimulus at which facilitation by the pressure pulses appeared varied from 12 to 18 msec. Maximum facilitation appeared at about 26–30 msec. Since the central delay associated with the facilitation of the reflex by the larger LGS afferent fibres is small (see Kuno & Perl, 1960), these long latencies suggest that slowly conducting myelinated fibres were responsible for the facilitation, assuming that the excitation time of the endings by the pressure pulses did not take more than 1–3 msec. However, participation by pressure-pain and stretch receptors connected to Group I and Group II fibres could not be ruled out in such an experiment and the

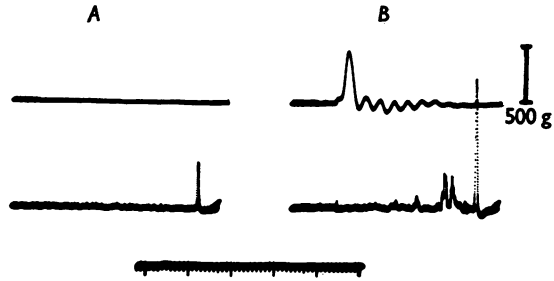

Fig. 4. Effect of pressure pulses to triceps surae on BST monosynaptic responses. The lower traces in *A* and *B* show the monosynaptic response. *B* shows that application of a pressure pulse (upper trace) greatly increases the monosynaptic response. The pressure also yields a reflex response in some unidentified motoneurones before the flexor monosynaptic reflex in *B*. Time marker, msec and 10 msec.

LGS nerve was therefore tetanized as described earlier, in order to depress antidromically all endings connected to these larger fibres. While the nerve was thus tetanized the effect of pressure was examined and it was found that facilitation by the pressure pulses though reduced was still prominent (Fig. 6). These results therefore prove that pressure receptors connected to Group III fibres facilitate the BST monosynaptic reflex.

The contribution through the larger fibres was excluded also by applying single volleys of about ten times threshold simultaneously with the pressure pulse. It was confirmed by recording impulses from the cut peripheral end of the whole LGS nerve that this single volley considerably reduced the observable discharge in large fibres. As is shown in Fig. 5*D*, this produced no change or only slight reduction in the facilitation produced by the pressure pulse. This shows that considerable reduction of the afferent input through the larger fibres had no effect on the facilitation by pressure pulses. In this experiment it was necessary to ensure that the

interval between the LGS stimulus and the test BST stimulus was such that the first stimulus did not itself alter the response. To be on the safe side, the moment of its application (and therefore also that of the pressure pulse) was so adjusted that it tended to reduce the monosynaptic reflex (compare Fig. 5*A* with 5*B*). The unobservable central effects of the LGS stimulus must be kept in mind when interpreting the changes quantitatively, and since these effects are unknown no attempt has been made to evaluate the relative contribution by the large fibres to the total facilitation shown in Fig. 5*C*.

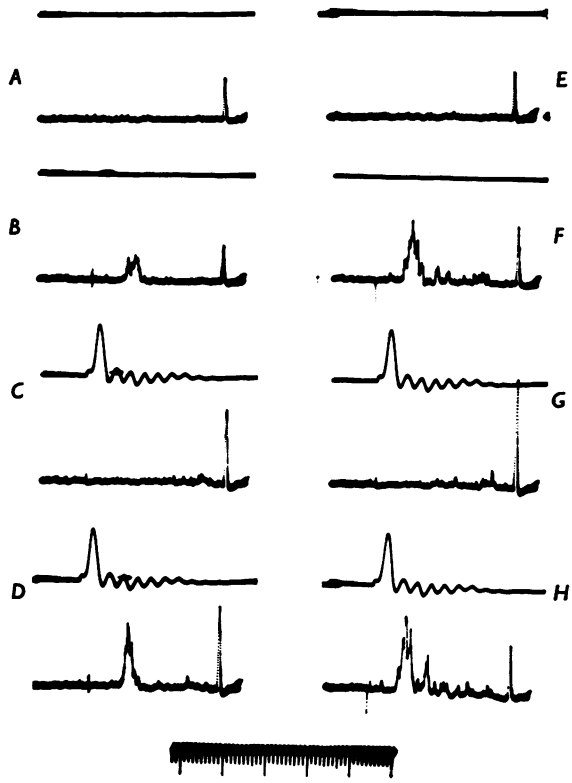

Fig. 5. BST monosynaptic reflex. *A* and *E* show the size of the control response (lower traces). *C* and *G* show the effect of pressure pulses on this response. In *B* a 10-times-threshold stimulus to the intact LGS nerve was applied before the flexor stimulus at such an interval that it did not increase the response. In *D* the stimulus and pressure were applied together; the undiminished response, compared to those in *C* and *G*, shows that the 10-times-threshold stimulus did not block the facilitating effect of the pressure pulse. In *F* the stimulus was 49 times threshold, i.e. sufficient to stimulate most Group III fibres. Application of this stimulus and the pressure pulse together in *H* prevented the facilitatory effect of the pulse. Time marker, msec and 10 msec.

It was thought that if the strength of the LGS stimulus was increased to about sixty times threshold, impulses from endings from Group III fibres would also be blocked. This was done, as shown in Fig. 5*F*, *G* and *H* and it was found that facilitation by the pressure pulses was prevented (Fig. 5*H*). This was interpreted to mean that the strong stimulus prevented BST facilitation by depressing the endings of Group III fibres peripherally, because care was taken to ensure that the stimulus did not itself reduce the monosynaptic reflex by adjusting its position and therefore also that of the pressure pulse so that the LGS stimulus in fact facilitated the monosynaptic response a little (compare Fig. 5*E* and *F*). However, this interpretation is not unequivocal, because it is possible that the central effects of the LGS stimulus itself may have been responsible for preventing the facilitation. A second possibility, that the strong LGS stimulus stimulated the same BST motoneurones that would have been facilitated by the pressure pulse, has to be kept in mind. However, the reflex discharge produced by the stronger stimulus itself was often not much greater than that produced by the weaker one (compare Fig 5*D* with 5*H*).

The interval between the pressure pulse and the flexor volley was varied and the effect of this on the monosynaptic responses was noted. At each interval ten conditioned responses were compared with twenty test responses (ten before and ten after) and the conditioned responses were expressed as a percentage of the test responses. As expected the facilitation varied with the interval between the pulse and the flexor volley (Fig. 6). Figure 6 shows that, apart from the reduction in the facilitation, there is not much difference in the curves obtained with and without tetanization of the LGS nerve. Since the minimum latency for facilitation is also the same, this indicates that in this particular experiment, endings connected to Group I and Group II fibres did not contribute significantly to the facilitation by pressure in the absence of tetanic stimulation. The reduced facilitation during tetanic stimulation could be due to the central effects of tetanic stimulation or to the antidromic stimulation of some Group III fibres. Since for facilitation to occur the minimum interval between the initiation of impulses by the pressure pulse (allowing about 3 msec for initiation time at the endings) and the arrival of the flexor volley at the spinal cord is about 15 msec, and since the conduction distance from the point of application of pressure to the spinal cord was about 220 mm, it follows that the volley of impulses were conducted over fibres with conduction velocity of at least 15 m/sec. As the interval was increased, impulses over more slowly conducting fibres could also exert their effects and thus add to the facilitation as shown in Fig. 6.

In the experiment from which the graph of Fig. 6 was plotted it was found that ten-times-threshold conditioning volleys (adequate to stimulate

all Group II fibres (Eccles & Lundberg, 1959*b*)) did not facilitate the BST monosynaptic reflex, whereas there was obvious facilitation with stimuli of greater intensity. This was not the common type of response, but it provides evidence to show why receptors connected to larger fibres did not contribute to the facilitation by pressure pulses in this experiment. In most of the experiments, however, there was obvious facilitation of BST monosynaptic reflex with stimuli less than twice threshold. Indeed the

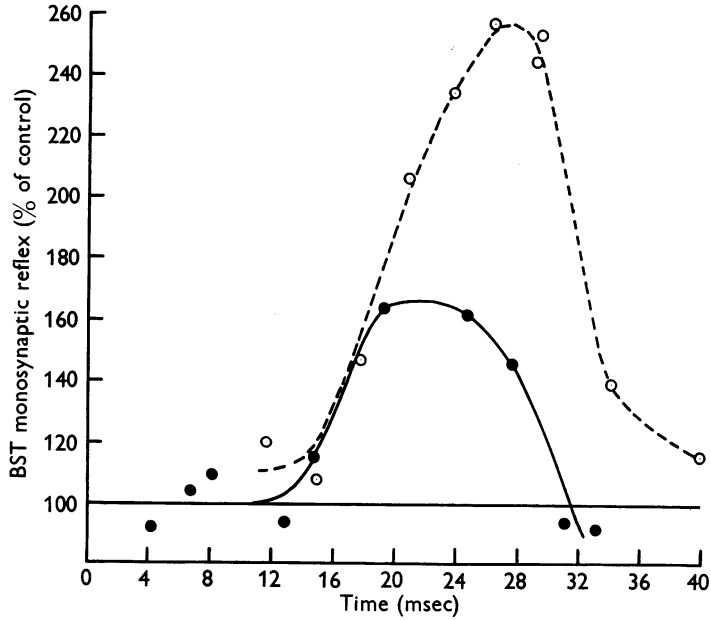

Fig. 6. Conditioning effect of pressure pulses to triceps surae on BST monosynaptic reflex (ordinate). The abscissa represents the interval between the application of the pressure pulse and the time of arrival of the flexor Group I volley at the spinal cord. The ordinates indicate the size of the monosynaptic response expressed as a percentage of the control response. Graph - -○- -○- - shows responses without tetanization of LGS nerve; graph —●—●— shows responses while the nerve was tetanized continuously at 460/sec with stimuli 13 times threshold for Group I.

curves showing the conditioning effect of LGS volleys on BST monosynaptic responses were similar to those obtained by Kuno & Perl (1960) and to those obtained by Eccles & Lundberg by applying conditioning stimuli to the plantaris nerve in the spinal preparation (Eccles & Lundberg, 1959*a*). In such experiments, unlike that shown in Fig. 6, the latency at which facilitation by pressure set in while the LGS nerve was tetanized was clearly greater than when the nerve was not tetanized. For example, in one experiment without tetanization the latency was 12 msec

and with tetanization 20 msec. This suggests that endings connected to larger fibres, probably those of Group II, were responsible for the earlier facilitation. This is understandable, because stretch receptors with Group II fibres may be stimulated by the pressure pulse and there are significant numbers of pressure-pain receptors connected to Group II fibres (Paintal, 1960).

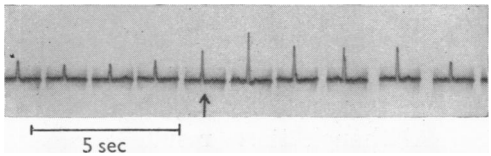

Fig. 7. Record to show the effect on BST monosynaptic reflex of introducing a hypodermic needle at arrow into triceps surae near tendo Achillis. The sweeps recur every 1·6 sec.

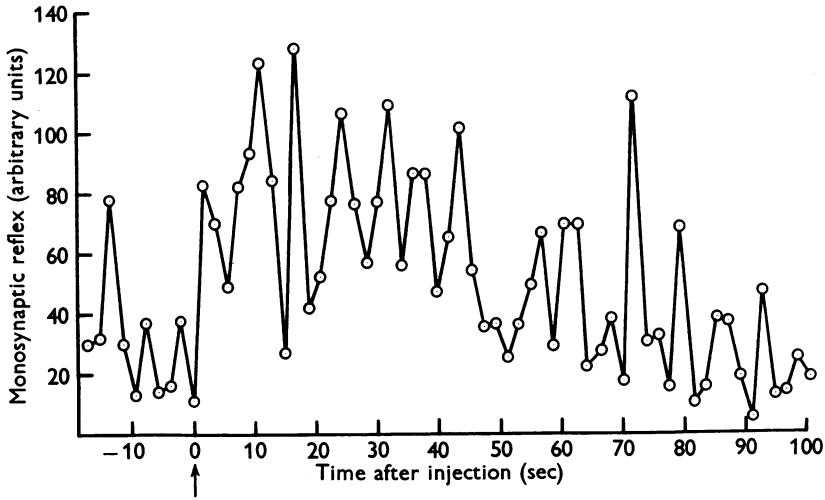

Fig. 8. Graph to show the effect on the BST monosynaptic reflex of injecting 0·5 ml. 6 % NaCl into the triceps surae at arrow.

All the foregoing experiments have shown that pressure-pain receptors of LGS facilitate BST monosynaptic reflex. Since these receptors are stimulated by introducing a hypodermic needle into the muscle or by injecting 6 % NaCl solution locally (Paintal, 1960), it is expected that these procedures will also facilitate BST motoneurones, which in fact they most often did. The facilitation produced by introducing a needle was usually short-lasting (Fig. 7). This is to be expected, because this procedure only yields a short train of impulses from pressure-pain receptors (Paintal, 1960). The facilitation following local injection of 0·5 ml. 6 % NaCl set in

within a few seconds and it often persisted for 2–3 min (Fig. 8). This is to be expected from the effects of 6% NaCl on pressure-pain receptors. The contribution by endings connected to larger fibres may be ignored, because local injection of 6% NaCl at the peripheral site chosen for injection (i.e. near the musculo-tendinous junction) usually has no noticeable effect on stretch receptors (Paintal, 1960). However, rarely a massive discharge in the larger fibres may be produced by 6% NaCl, so that facilitation of the BST monosynaptic reflex through Group I and Group II fibres had to be ruled out. This was done by tetanic stimulation, as described earlier, and it was found that the facilitatory effect of 6% NaCl persisted while the LGS nerve was tetanized. Although these results once again indicate that pressure-pain receptors with Group III fibres facilitate the BST monosynaptic reflex, the possible contribution by endings connected to non-myelinated fibres must be kept in mind.

Effects on triceps surae motoneurones. It has been confirmed that strongly stretching triceps surae can inhibit the triceps surae or LGS monosynaptic reflex, presumably owing to stimulation of tendon organs (Granit, 1950; Hunt, 1952), although in the initial phase there may be some facilitation, as would be expected from the observations of Lloyd (1943*b*), Granit (1950) and Hunt (1952). On the other hand, squeezing the muscle inhibited the motoneurones to a much greater extent than that produced by stretching the muscle. This was presumably due to stimulation of pressure-pain receptors, a conclusion strengthened by the fact that inserting a hypodermic needle and injecting 6% NaCl locally also inhibited the triceps surae monosynaptic reflex; the latency and duration of inhibition followed the same time course as the facilitation of the BST monosynaptic reflex.

Application of local pressure pulses yielded similar results, i.e. there was inhibition of triceps surae monosynaptic reflex. This inhibition set in after a latency of about 20 msec in one experiment (Fig. 9), a fact suggestive of action mediated by slowly conducting myelinated fibres. In the experiment illustrated in Fig. 9 the inhibition became so pronounced that at an interval greater than 29 msec the monosynaptic reflex was completely inhibited by the pressure pulse. In these experiments the LGS nerve was intact and test stimuli were applied either to this nerve alone or to both this and the central end of the cut medial gastrocnemius nerve.

Effects on tibialis anterior (TA) or deep peroneal (DP) monosynaptic reflex. Stretching triceps surae always inhibited TA or DP monosynaptic responses, as would be expected from the observations of Granit (1952). On the other hand squeezing triceps surae occasionally either slightly facilitated these motoneurones or was without effect. In these cases conditioning stimuli of Group III strength to LGS nerve clearly facilitated the

DP monosynaptic reflex. This is in agreement with some of the observations of Eccles & Lundberg (1959*b*). More frequently, however, squeezing triceps surae inhibited the DP monosynaptic reflex markedly (Fig. 10) and correspondingly, Group III strength conditioning volleys to cut LGS nerve produced pronounced inhibition. This inhibition by squeezing triceps surae is surprising, because pretibial muscles are flexors and Group III fibres

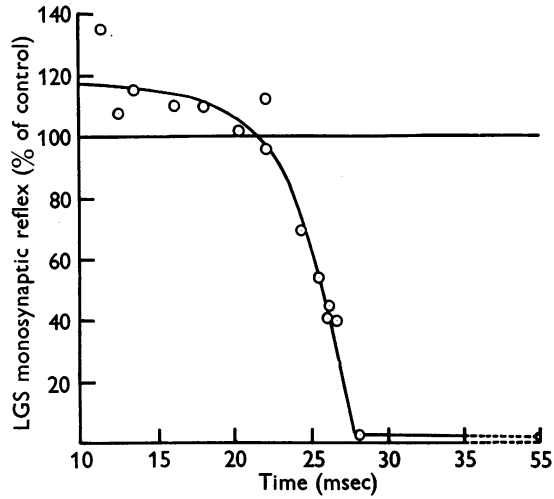

Fig. 9. Graph showing conditioning effect of pressure pulses applied to triceps surae on LGS monosynaptic reflex. Abscissa indicates interval between the application of pressure pulse and arrival of Group I LGS volley at spinal cord. Ordinate represents size of monosynaptic response expressed as percentage of control response.

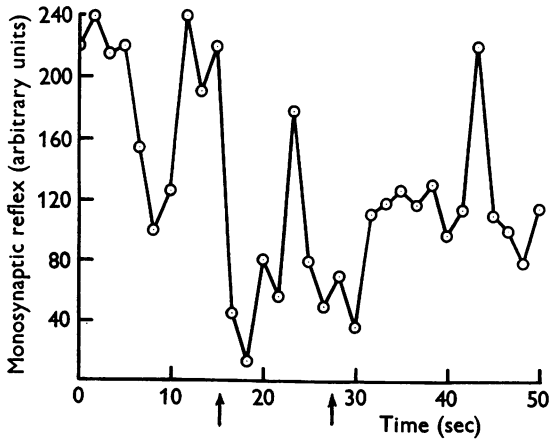

Fig. 10. Graph showing inhibitory effect of squeezing triceps surae, between arrows, on deep peroneal monosynaptic reflex, expressed in arbitrary units.

(which end predominantly in pressure-pain receptors (Paintal, 1960) of muscle nerves are known to facilitate the flexion reflex (Lloyd, 1943*a*; Eccles & Lundberg, 1959*a*, *b*). The evidence that this inhibition is caused by pressure-pain receptors is very strong, because stimulation of tendon organs (which are more likely to be stimulated than muscle spindles by squeezing the musculo-tendinous junction of triceps surae) of LGS or their nerve fibres facilitates DP monosynaptic reflexes (Laporte & Lloyd, 1952; Granit, 1952; Hunt, 1952; Eccles *et al.* 1957). The fact that these effects were not mediated by Group I or Group II fibres was established, as already described, by carrying out the above manoeuvres while the LGS nerve was stimulated repetitively to block impulse activity in Group I and Group II fibres. As expected, the inhibition of DP monosynaptic reflex by squeezing triceps surae was not much altered. However, the possible effects of endings connected to unmyelinated fibres must be kept in mind, because these experiments have not excluded their effects. In agreement with the effects of squeezing triceps surae, it was noted that local injection of 6 % NaCl also inhibited the DP monosynaptic reflex.

Effects of pressure-pain receptors in tibialis anterior

In order to stimulate pressure-pain receptors, the tibialis anterior muscle was squeezed about 1–2 cm distal to the entry of the nerve into the muscle, because many pressure-pain receptors are located in this region (Paintal, 1960). This produced much less facilitation of BST monosynaptic reflexes than that produced by squeezing triceps surae; sometimes there was no facilitation at all. In view of the current belief that Group III fibres of muscles facilitate flexor reflexes, this behaviour was quite unexpected, because there are apparently more pressure-pain receptors in TA than there are in LGS (Paintal, 1960). Stretching TA also facilitated the BST monosynaptic reflex and this facilitation was either equal to or little less than that produced by squeezing the muscle. These effects, although reduced, survived during repetitive stimulation designed to block endings connected to Group I and Group II fibres. This indicates that Group III fibres are probably involved in addition to any other concerned.

Stretching or squeezing TA reduced or abolished triceps surae monosynaptic responses. In this instance the effect of pressure was clearly more marked than that of stretch, suggesting that the effect of pressure was mediated through pressure-pain endings.

Whereas stretching TA inhibited the DP monosynaptic responses, squeezing the muscle facilitated them. This is in agreement with the known effects of stimulating Group III fibres of flexor muscles (Brock *et al.* 1951). Sometimes squeezing the muscle inhibited DP motoneurones, an effect presumably attributable to the stretch receptors because squeezing TA,

unlike squeezing triceps surae, yields an appreciable discharge in stretch receptors.

Stretching or squeezing extensor digitorum longus muscle about its middle produced effects similar to those obtained from TA. Since there are certain similarities in the shape and size of these two muscles it is probable from these results that there are many pressure-pain receptors located somewhere near the middle of this muscle also.

DISCUSSION

The main conclusions to be drawn from these results are that impulses from pressure-pain receptors connected to Group III fibres of LGS facilitate the BST monosynaptic reflex and inhibit their own, and although they sometimes facilitate those of pretibial muscles they more often inhibit them; pressure-pain receptors of TA (and probably also those of extensor digitorum longus) facilitate their own motoneurones and those of BST and they inhibit those of triceps surae. With the exception of one observation all the others are in conformity with the known effects of stimulating Group III fibres, i.e. they facilitate flexor muscles and inhibit extensors in accordance with the pattern of the flexion reflex (Lloyd, 1943*a*; Eccles & Lundberg, 1959*a*; Kuno & Perl, 1960). However, pressure-pain receptors of different muscles are not equally effective in facilitating the flexion reflex, because facilitation of BST monosynaptic responses by LGS pressure-pain receptors is sometimes several times greater than that produced by TA receptors in the same experiment, in spite of the fact that there are apparently more pressure-pain receptors in TA than in LGS (Paintal, 1960). The results also fit in with those of Brock *et al.* (1951), because the pressure-pain receptors of extensors (triceps surae) inhibit their own, and those of flexors facilitate their own, motoneurones. This is what Brock *et al.* referred to as autogenetic inhibition and facilitation by Group III fibres.

The only observation that does not fit into the general scheme is the inhibition of TA or DP monosynaptic reflexes by pressure-pain receptors of LGS or by conditioning stimuli of Group III strength to the nerves of triceps surae. At first this was somewhat perplexing, but when the observations of Eccles & Lundberg (1959*b*) were published the reason for this behaviour became understandable. Eccles & Lundberg have shown that volleys to Group III fibres of LGS can produce both excitatory and inhibitory post-synaptic potentials in DP motoneurones and that mixed effects are often in evidence in the same motoneurone. This they explained by suggesting that there are two pathways from high-threshold afferent fibres to flexor motoneurones—the excitatory one open normally in spinal

cats and the inhibitory one functioning when the excitatory one is suppressed, e.g. by low blood pressure (Eccles & Lundberg, 1959*b*) or by suitable accessory stimulation (Kuno & Perl, 1960). However, this state of affairs applies to only certain muscles, because there are other muscles, e.g. BST which are not inhibited by pressure-pain receptors—this being in agreement with the observations of Eccles & Lundberg (1959*b*).

Tibialis anterior is probably an exceptional flexor in that it is made up of a mixture of slow and fast fibres, the latter occupying the more superficial part of the muscle (Gordon & Phillips, 1953). These subdivisions also differ in their reflex responses because Gordon & Phillips (1953) noted that the deeper motor units had a lower reflex threshold in response to pinching the toes and the superficial ones a higher maximal frequency of firing in flexion reflexes. These differences must be kept in mind when interpreting reflex changes in the monosynaptic reflex of TA in response to stimulation of pressure-pain receptors.

If the DP motoneurones were the only flexor motoneurones that yield mixed responses to stimulation of pressure-pain receptors or their Group III fibres, one could, for the time being, ignore this solitary evidence that does not fit into the pattern of the flexion reflex. However, some other observations of Eccles & Lundberg (1959*a*) indicate that this is not the only exception, because Group III fibres of quadriceps can also inhibit semitendinosus motoneurones. This inhibition, which apparently appears at higher stimulus strengths, is not due to Renshaw inhibition (Eccles & Lundberg, 1959*a*). The authors suggested once again that this could be due to the existence of two pathways by which impulses in high-threshold muscle afferent fibres could act on flexor motoneurones.

The reflex effects of pressure-pain receptors connected to Group II fibres have not been studied in detail because it was not possible to block all fibres other than those of Group II. On the other hand, while studying the effects of Group III pressure-pain receptors it was possible to block by repetitive antidromic stimulation all the endings connected to Group I and Group II fibres. An important shortcoming of this method of blocking conduction of impulses in selected fibres is that the central effects of repetitive stimulation may be considerable in magnitude, and are largely unknown. This criticism must be kept in mind even though in this investigation the nerve used for eliciting the monosynaptic reflex was not tetanized and the reflex effects of natural stimuli were examined only after the monosynaptic responses had become stabilized following the onset of tetanic stimulation (see Fig. 3). However, in spite of its limitations it can provide valuable information if the results are interpreted conservatively, as has been done in this investigation. Besides, no other method (e.g. pressure, temperature, electrotonic block or local anaesthesia)

offers as precise a means of producing a graded and relatively constant block of impulses from sensory endings for prolonged periods.

Although the results of the present investigation have provided good agreement between the effects of natural stimulation and the effects of nerve volleys, it must be pointed out that the interpretation of the effects of the latter have become complicated, since it is now known that Group II fibres innervate a heterogeneous group of stretch and pressure-pain receptors (Paintal, 1960). In addition, some pressure-pain receptors are also connected to Group I fibres so that there are functionally three kinds of fibres in Group I. As was pointed out by Lloyd (1957), the effects of Group II fibres connected to stretch receptors cannot be regarded as nociceptive and therefore the customary practice of lumping together the reflex effects of Group II and Group III fibres, the latter being mostly connected to pressure-pain receptors, should perhaps be abandoned.

SUMMARY

1. The posterior biceps semitendinosus (BST) monosynaptic reflex was conditioned by natural stimulation of sensory receptors of muscles and it was shown that squeezing the triceps surae near the tendo Achillis or the tibialis anterior facilitated this reflex in spinal cats.

2. By applying pressure pulses locally and by blocking the endings of selected afferent fibres by stimulating them either tetanically or by single volleys, it was established that pressure-pain receptors connected to Group III afferent fibres facilitate the BST monosynaptic reflex. There was suggestive evidence that this reflex was also facilitated by endings connected to non-myelinated fibres.

3. Stimulating pressure-pain receptors of LGS inhibited triceps surae monosynaptic reflex and it sometimes facilitated DP monosynaptic reflex in accordance with the pattern of the flexion reflex. More frequently, however, it inhibited DP or TA monosynaptic reflexes markedly. This peculiarity has been discussed in relation to the findings of previous investigators.

4. The results obtained show that stimulation of pressure-pain receptors connected to Group III fibres facilitates the flexion reflex and are in conformity with those obtained by stimulating the afferent fibres themselves.

I am indebted to Professor C. C. Hunt, Dr E. R. Perl and Professor A. Lundberg for valuable criticisms.

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