J. Physiol. (1985), **363**, *pp.* 403–417
With 6 text-figures
Printed in Great Britain

DIFFERENT TYPES OF SLOWLY CONDUCTING AFFERENT UNITS IN CAT SKELETAL MUSCLE AND TENDON

BY SIEGFRIED MENSE* AND HANS MEYER

From the Physiologisches Institut der Universität Kiel, Olshausenstr. 40-60, D-2300 Kiel, F.R.G.

(*Received 17 October 1984*)

SUMMARY

1. In chloralose-anaesthetized cats, the impulse activity of single afferent units conducting at less than 30 m s^{-1} and having receptive fields in the triceps surae muscle or the calcaneal tendon, was recorded from thin filaments of the dorsal roots L7 and S1. The receptive fields of the units were tested with a variety of graded natural stimuli (local pressure, stretch, contractions, temperature changes). In addition, the algesic agent bradykinin was injected into the receptive fields, but the sensitivity of the receptors to this substance was not used for classification purposes.

2. Four types of receptors could be distinguished using the strongest response to innocuous natural stimulation as the criterion for characterizing a given ending: (a) nociceptors showing no response to innocuous forms of stimulation and requiring noxious (tissue-threatening) stimuli to be clearly activated; (b) low-threshold pressure-sensitive receptors responding to innocuous indentation of the tissue but being relatively insensitive to stretch and contractions; (c) contraction-sensitive receptors reaching high discharge frequencies during active contractions of moderate force and innocuous stretch, but being relatively insensitive to local pressure stimulation; (d) thermosensitive receptors responding strongly to small changes in temperature without reacting to innocuous mechanical stimulation.

3. The possible involvement of the different receptor types in central nervous functions (nociception, mechanoreception, ergoreception, thermoregulation) is discussed.

INTRODUCTION

Cutaneous receptors with small myelinated (group III) and non-myelinated (group IV) afferent fibres are known to be highly specialized in all the species studied so far. They fulfil mechanoreceptive, nociceptive and thermoreceptive functions and appear to be quite (but not totally) insensitive to stimuli belonging to a different modality (for a review, see Boivie & Perl, 1975).

The degree of specialization of group III and IV receptors in deep tissues (skeletal muscle, tendon, joint) is less well studied. The first investigations employing single

* To whom correspondence should be sent at the following address: Anatomisches Institut III der Universität Heidelberg, Im Neuenheimer Feld 307, D-6900 Heidelberg, F.R.G.

fibre recording techniques for studying such endings in skeletal muscle showed that great differences in response behaviour existed among these units. Thus, some group III receptors in the cat could only be activated by noxious stimuli while others responded to innocuous stretch and contractions (Paintal, 1960; Bessou & Laporte, 1961). Group IV receptors in muscle were likewise found to possess quite different response properties (Iggo, 1961). These findings were supported and extended by more recent work on muscle receptors with fine fibres of the cat's hind limb (Mense, 1977; Mense & Stahnke, 1983) and neck (Abrahams, Lynn & Richmond, 1984). A problem for the interpretation of the experimental data is the broad responsiveness of many of the units, especially if strong mechanical or chemical stimuli are employed (Kumazawa & Mizumura 1976, 1977; Kniffki, Mense & Schmidt, 1978). For this reason, the muscle group III and IV receptors in the dog were considered to be polymodal by some authors (Kumazawa & Mizumura, 1976, 1977).

It was felt that the controversy about the polymodality or specificity, respectively, of deep receptors with slowly conducting afferent fibres might at least partly be due to the fact that in most of the cited studies chemical stimuli were employed (e.g. strongly hypertonic saline, high concentrations of bradykinin) which are likely to activate not only nociceptors but also slowly adapting mechanoreceptors, as has been shown for cutaneous endings (Fjällbrant & Iggo, 1961; Beck & Handwerker, 1974). This does not mean that the mechanoreceptor is polymodal; in this case the stimulating effect of bradykinin has to be considered to be the result of an unspecific activation of a sensitive ending by a strong, inadequate stimulus. Chemical algesic stimuli have proved to be useful for producing a strong excitation of deep group III and IV receptors (cf. Mense, 1977) but it is doubtful whether they can be used to determine the receptive nature of a given unit (e.g. as nociceptive, non-nociceptive or polymodal).

The aim of the present investigation was to find out whether in cat muscle and tendon, different types of group III and IV receptors can be distinguished, if only such stimuli are used that are likely to occur in the natural environment of the animal. The observed differences in response behaviour between individual units were so great that the existence of different receptor types appears to be more likely than the assumption of a single population of polymodal receptors. Preliminary accounts of part of the data have been published (Mense & Meyer, 1983; Mense, Craig, Lehmann-Willenbrock & Meyer, 1985).

METHODS

The results were obtained from twenty-five cats of both sexes weighing 2·1–3·9 kg. They were anaesthetized with chloralose 60–70 mg kg^{-1} I.P. initially followed by single doses of the same anaesthetic (10 mg kg^{-1} I.P.) as required to maintain a deep level of anaesthesia, characterized by the absence of flexion reflexes and maximally constricted (slit-like) pupils. In five experiments, anaesthesia was induced with ketamine hydrochloride (Ketanest) 10–15 mg kg^{-1} I.M. followed by chloralose 40–60 mg kg^{-1} I.P. The animals breathed spontaneously. Blood pressure and body temperature were continuously monitored and kept at physiological levels.

Two paraffin pools were formed by sewing skin flaps to metal rings: one was situated over the dorsal aspect of the left hind limb; this pool contained the gastrocnemius–soleus (g.s.) muscle together with stimulating electrodes for the g.s. nerve; all the other nerves to the lower hind limb were cut. The distal thirds of the medial gastrocnemius (m.g.) and lateral gastrocnemius–soleus

(l.g.s.) muscle were separated in order to allow the introduction of one tip of the stimulating forceps or one of the thermodes, respectively (see below). The leg was fixed to the animal frame with screws through the tibia; the calcaneal tendon was cut and connected to a strain gauge with a strong metal wire. Prior to the disconnexion of the tendon, the initial length of the muscle (with the paw hanging freely) was marked with a needle inserted transversely through the tendon. Length changes could be read from a ruler that was fixed to the frame in a position parallel to the tendon, the needle serving as a pointer. After cutting the tendon the muscle was readjusted to its initial length, with the wire running horizontally from the tendon over a rope-pulley to the strain gauge. Defined increases in muscle length could be obtained by pushing the wire downwards between rope-pulley and strain gauge with a metal bar. The metal bar was connected to a calibrated lever system so that the desired length changes could be pre-selected.

The second pool covered a laminectomy from vertebrae L1 to L7. Recordings of single fibre activity were made from thin filaments of the dorsal roots L7 and S1. Only units that could be activated by electrical stimulation of the g.s. nerve were studied. Fibres conducting at less than 2·5 m s^{-1} were classified as group IV, those having a conduction velocity of 2·5–30 m s^{-1} as group III.

Each unit was tested with the following stimuli: (1) local pressure graded in three steps: (a) touch; slightly touching or stroking the surface of the tissue with a fine painter's brush; this stimulus was repeated about once every second. (b) Moderate pressure; innocuous steady deformation of the tissue for 15 s using a forceps with broadened tips (diameter 1 cm); application of this stimulus to the experimenter's thenar muscle through the intact skin was not painful. (c) Noxious pressure; squeezing the tissue with the same forceps for 15 s; this stimulus was perceived as painful when applied to the human thenar muscle. (2) Muscle stretch graded in increments of 3 mm (3, 6, 9, 12 mm). Since the maximal increase in length of the g.s. muscle that could be attained by bending the paw was found to be 8–9 mm (starting from a position in which the paw was hanging freely with an angle of about 120 deg for the knee joint and 120 deg for the ankle joint), length increases of more than 8 mm were considered to be unphysiological. (3) Isometric rhythmic contractions induced by electrical stimulation of the muscle nerve. The intensity of the stimuli was graded so that the muscle reached maximal contraction force in two to four steps. The value for maximal contraction was determined at the beginning of each experiment; it ranged from 2·0 to 7·0 kP. The test periods lasted 30–60 s, with a tetanic contraction (50 Hz) of 500 ms duration being elicited every second. The voltage necessary for induction of muscular activity never exceeded the electrical thresholds for the afferent units under study. (4) Thermal stimulation with thermodes through which cold (mostly 26–28 °C) or warm (mostly 42–43 °C) water was circulated. The temperature of the paraffin pool containing the g.s. muscle was around 32 °C. The thermodes used each had a surface area of 12 × 75 mm; they were mounted as a pair at the end of large plastic forceps. The thermodes were placed from both sides on that part of the m.g. or l.g.s. muscle which contained the receptive ending under study. (5) Injection of a bradykinin solution into the mechanosensitive receptive field. Intramuscular injections were preferred over intra-arterial ones, as they ensured that the ending was actually reached by the stimulating substance. The injections consisted of 0·1–0·3 ml of a Tyrode solution containing 86 μg ml^{-1} bradykinin base. In earlier studies, this concentration had proved to be effective for stimulating group III and IV muscle receptors upon intra-arterial injection (Mense, 1977). If no response occurred to the injection, the area surrounding the receptive field was infiltrated with a larger volume of bradykinin solution (0·5 ml) in order to make sure that the ending had come into contact with the chemical stimulant. The responsiveness of a unit to bradykinin was not used for classification purposes. The tests with bradykinin were performed in order to see whether the response behaviour of a given unit was changed after topical application of the algesic agent (S. Mense & H. Meyer, in preparation).

For the designation of a given unit, e.g. as pressure sensitive or contraction sensitive, its best (strongest) response to innocuous stimulation was used. For instance, a receptor which reached a considerable proportion of its maximal discharge frequency during contraction of a force well below maximum, and which showed no or a distinctly smaller response upon stimulation with moderate pressure and innocuous temperature changes, was labelled contraction sensitive. Only if no clear-cut reaction occurred upon innocuous stimulation was the unit considered to be nociceptive. Group III fibres supplying muscle spindles (cf. Stacey, 1969) were excluded from the study.

The following precautions were taken in order to minimize the chance of recording from receptors which might have been sensitized by the unsterile surgical exposure of the muscle and tendon, or

by repeated mechanical and chemical testing of the tissue: (1) all animals received an intramuscular injection (into the contralateral hind limb) of a mixture of ampicillin and oxacillin (Totocillin; 0·1 g kg^{-1}) to prevent bacterial infections. (2) A maximal number of three units was studied per cat (one in the m.g. muscle, one in the l.g.s. muscle and a third one in the calcaneal tendon). In a few experiments, two units located in the same muscle were accepted for study if their receptive fields were clearly not overlapping.

For data processing, conventional electronic equipment was used (pre-amplifier, filter, window discriminator). The peristimulus time histograms shown in the Figures were constructed by a laboratory computer with 1024 addresses. In one half of the addresses the fibre activity was stored, the other half was used for simultaneous recording of the output of the strain gauge.

RESULTS

Successful recordings were obtained from fifty-six units (thirty group III and twenty-six group IV). Of these, sixteen receptors (ten group III and six group IV) had receptive fields including the calcaneal tendon. The receptor types observed in the muscle were present also in the tendon; therefore, the afferent units from both tissues will be described together. With the stimuli used, four different receptor types with group III and IV afferent fibres could be distinguished. One of these types exhibited all signs of a nociceptor, the other three responded clearly to everyday stimuli and were therefore considered as not fulfilling nociceptive functions.

Nociceptive units. This type was not or was only liminally activated by innocuous local pressure, physiological stretch, active contractions of moderate force and innocuous temperature changes, but gave clear responses to tissue-threatening or damaging stimuli such as noxious local pressure, unphysiological stretch and intramuscular injections of bradykinin (Fig. 1). Out of nineteen nociceptive units tested with noxious pressure and bradykinin, eleven (58%) responded to both forms of stimulation. The remaining six could be activated by noxious pressure but not by bradykinin, even though a large portion of the muscle containing the receptive ending was infiltrated with the algesic solution. In these cases it was unknown whether the receptors constituted specialized mechano-nociceptors or possessed an additional chemosensitivity to substances other than bradykinin. All nociceptive receptors reached their maximal discharge frequency upon noxious pressure stimulation, i.e. no unit was found that gave maximal responses to unphysiological stretch (exceeding 8 mm). A remarkable feature of the nociceptive units was that their response properties could be changed by injection of the receptive field with bradykinin. More than half of them (53%) showed signs of a sensitization with lowering of the mechanical threshold into the innocuous range (S. Mense & H. Meyer, in preparation).

Low-threshold pressure-sensitive (l.t.p.) units. Most of these units (ten out of eighteen) responded to touching the receptive field with a soft painter's brush or a blunt glass rod; they increased their discharge rate upon stimulation with moderate and noxious pressure (Fig. 2). Eight of the l.t.p. units required moderate pressure to be activated; in these cases it was assumed that the mechanosensitive endings were situated more deeply inside the muscle. An observation supporting this assumption was that they did not respond to compression of superficial layers of the muscle with forceps. L.t.p. receptors were relatively insensitive to stretch and contraction; they responded best to forces acting in a direction perpendicular to the long axis of the

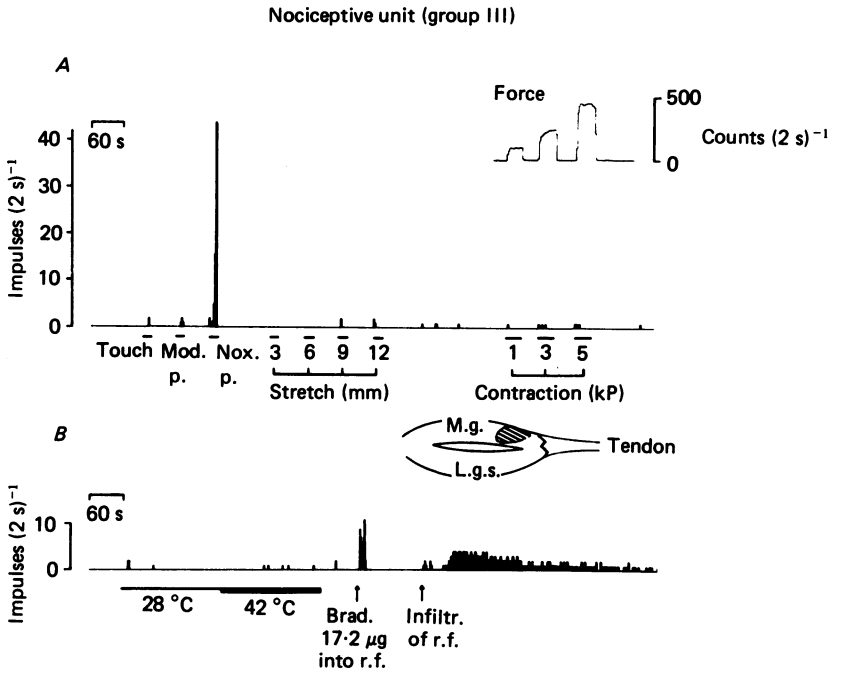

Fig. 1. Nociceptive unit with group III afferent fibre, conduction velocity 12 m s^{-1}. The receptive field is marked by the hatched area on the medial gastrocnemius (m.g.) muscle. Bin width of peristimulus time histogram of the fibre's activity: 2 s. The duration of the stimuli used is indicated by the length of the bars underneath the histogram. *A*, mod. p., moderate pressure; nox. p., noxious pressure. The scale of the force registration above the histogram is given in arbitrary units (counts $(2\ s)^{-1}$). Because of the long bin width, the force registration during the exercise period remains elevated even though the contractions were intermittent. *B*, values of cold and warm stimulation indicate temperature of water circulating through thermodes in contact with the receptive field. Arrows: single injection of bradykinin (brad.) into or infiltration (infiltr.) of the receptive field (r.f.) with the algesic agent.

muscle. Probably, this was due to the fact that many of these receptors were situated in the connective tissue surrounding the tendon and muscle which is not strongly affected by forces building up inside the muscle. (Because of the poor sensitivity of these receptors to the mechanical forces of muscle stretch and contractions, they were not labelled low-threshold mechanosensitive but l.t.p.)

Out of seventeen l.t.p. units tested with injections of bradykinin, fifteen (88 %) gave a clear response. Whether the responsiveness to bradykinin really reflects a chemosensitivity of the l.t.p. units is not known. An alternative explanation would be that the excitation was due to the mechanical disturbance of the tissue caused by the pressure of the injection and/or the oedematous swelling following the application of bradykinin. In the histogram of the impulse activity of l.t.p. units, the magnitude of the response to bradykinin did not exceed that of the response to innocuous pressure stimulation (cf. Fig. 2), i.e. these units reacted to an innocuous mechanical stimulus with a degree of excitation similar to that elicited by a painful chemical stimulus.

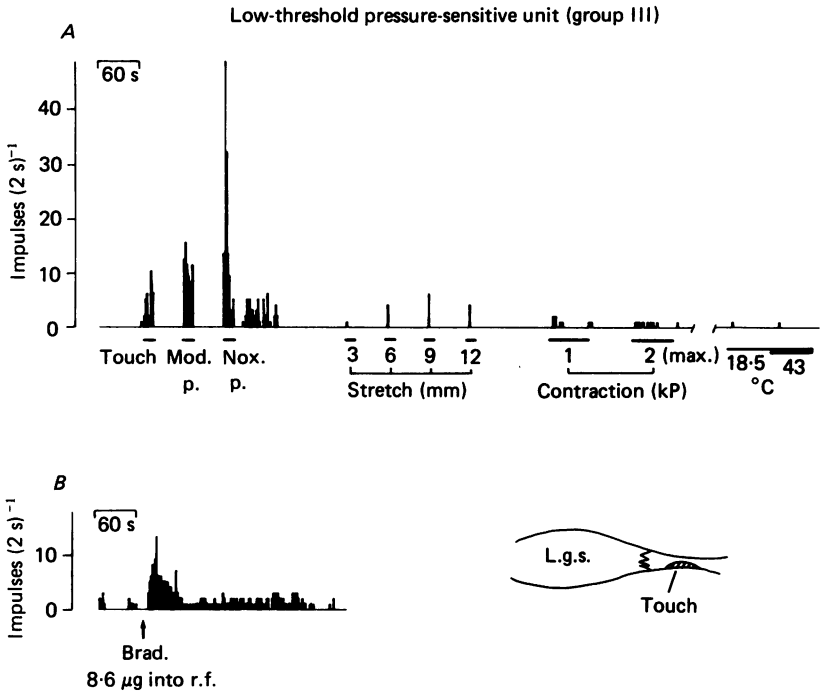

Fig. 2. Low-threshold pressure-sensitive unit with group III afferent fibre, conduction velocity 9 m s^{-1}. Labelling of receptive field and stimulation procedures as in Fig. 1. In this case, a contraction force of 2 kP was maximal.

In contrast to the nociceptive units, the l.t.p. units usually showed no decrease in mechanical threshold after injection of their receptive field with bradykinin; they rather exhibited a reduced responsiveness to all forms of mechanical stimulation. Of nine l.t.p. units, only one appeared to be sensitized by bradykinin towards mechanical stimuli.

Contraction-sensitive (c.s.) units. The best physiological stimuli for this receptor type were active contractions. The responses to contractions of increasing force were well graded, relatively strong activation occurring far below the maximal force of contraction (Fig. 3*A*). Six of the twelve c.s. units found were also sensitive to passive stretch in the physiological range (up to about 8 mm, see Methods), but showed no or only small responses to local pressure of innocuous intensity. Thus, the c.s. receptors responded best to forces acting in parallel to the long axis of the muscle. They appeared to be identical to the probably mechanically activated $c.s._m$ units described in an earlier study (Mense & Stahnke, 1983). Units sensitive to innocuous stretch but not to contractions were not found, but half of the contraction-sensitive endings did not respond to stretch (see above). During contractions some of the latter showed responses with a longer latency and a slow decline after the end of the exercise period. These receptors probably correspond to the contraction-sensitive units with a non-mechanical mechanism of activation, which were labelled $c.s._x$ in the publication cited above. Bradykinin was also an effective stimulant for the c.s. receptors: out of eight units tested, six were activated by injections of the substance into their

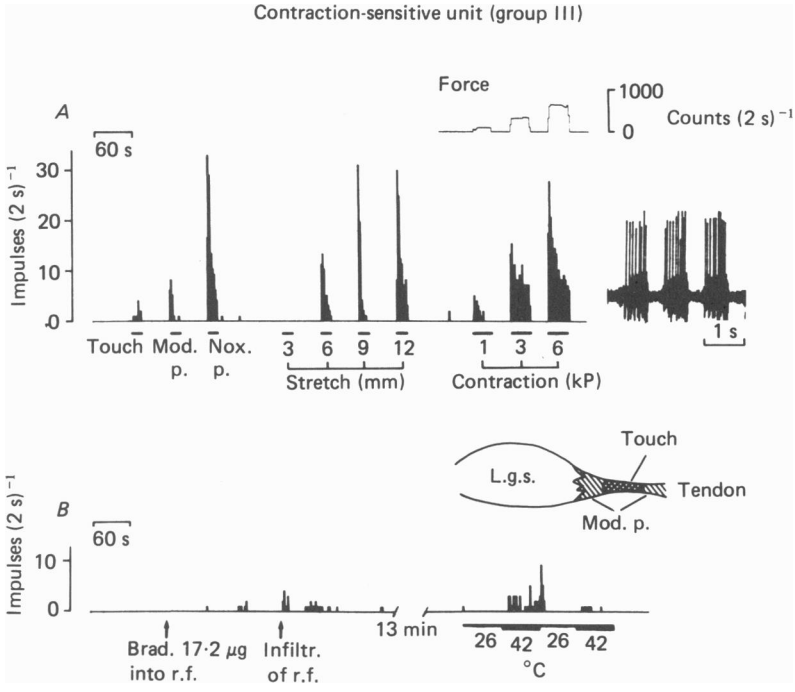

Fig. 3. Contraction-sensitive unit with group III afferent fibre, conduction velocity 26 m s^{-1}. Labelling of receptive field and stimuli as in Fig. 1. The original registration at the right end of *A* shows the fibre's activity during rhythmic contractions with a force of 6 kP. The small response to warming in *B* was not reproducible and, therefore, not considered to indicate thermoreceptive properties of the unit.

receptive fields. Again, the responses to a high dose of bradykinin were not of greater magnitude than those to contractions of moderate force (e.g. 50% of maximal contraction). Like the l.t.p. units, the c.s. units were usually not sensitized following intramuscular injections of bradykinin. Of seven units tested, none showed a lowered mechanical threshold after application of the algesic substance.

Thermosensitive units. Receptors of this type gave graded responses to temperature stimuli in the physiological range. Three cold- and two warm-sensitive endings were found. The warm-sensitive unit shown in Fig. 4 had a background activity of a few impulses per minute at the starting pool temperature of 32 °C. A temperature rise to 35 °C was sufficient for eliciting a clear response (Fig. 4*B*); stronger warming stimuli evoked an increase in discharge frequency that showed a dynamic and static component. Cold-sensitive units were activated by a drop in temperature of a few degrees centigrade, they fell silent or reduced their discharge frequency upon warming the receptive field (Fig. 5). The thermosensitive receptors were usually totally insensitive to innocuous pressure, passive stretch and active contractions. The only exception was a warm-sensitive unit which was activated during contractions with a time course indicating a thermally mediated effect, probably due to the temperature increase in the working muscle. The slight reduction in discharge frequency of the cold-sensitive ending during and after the exercise periods in Fig. 5*B* most likely has

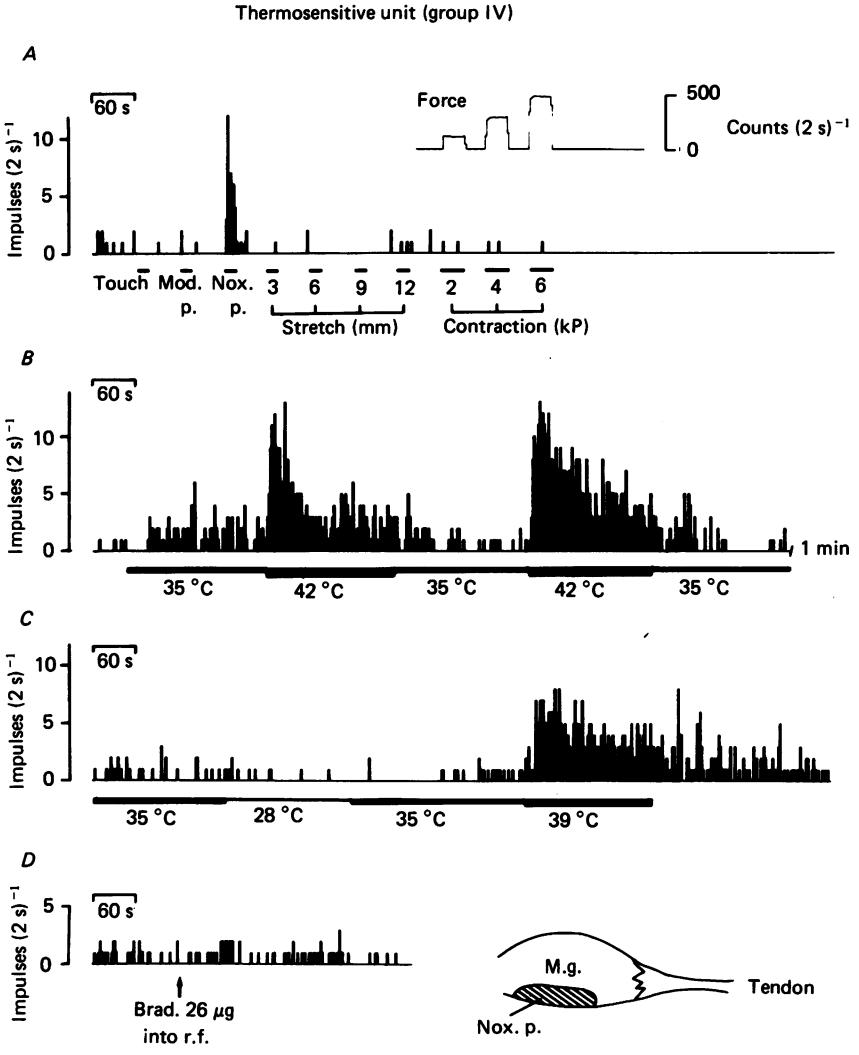

Fig. 4. Warm-sensitive unit with group IV afferent fibre, conduction velocity 1·1 m s^{-1}. Labelling of receptive field and stimuli as in Fig. 1. Starting temperature of the pool containing the muscle was 32 °C.

the same cause. High rates of background discharge, such as that shown in Fig. 5, were observed in thermosensitive units only.

Four of the five thermosensitive receptors encountered in this study could also be activated by noxious pressure (cf. Fig. 4*A*). In fact, if only the data presented in part *A* of Fig. 4 are considered, the receptor might be mistaken as a nociceptor (cf. Fig. 1*A*), although the responses of thermosensitive units to noxious pressure were of smaller magnitude.

The thermosensitive receptors appeared to be less sensitive to the injection of bradykinin than the other types. Of four units tested with the algesic agent, only one, a cold-sensitive receptor, responded with an increase in discharge frequency. It is not

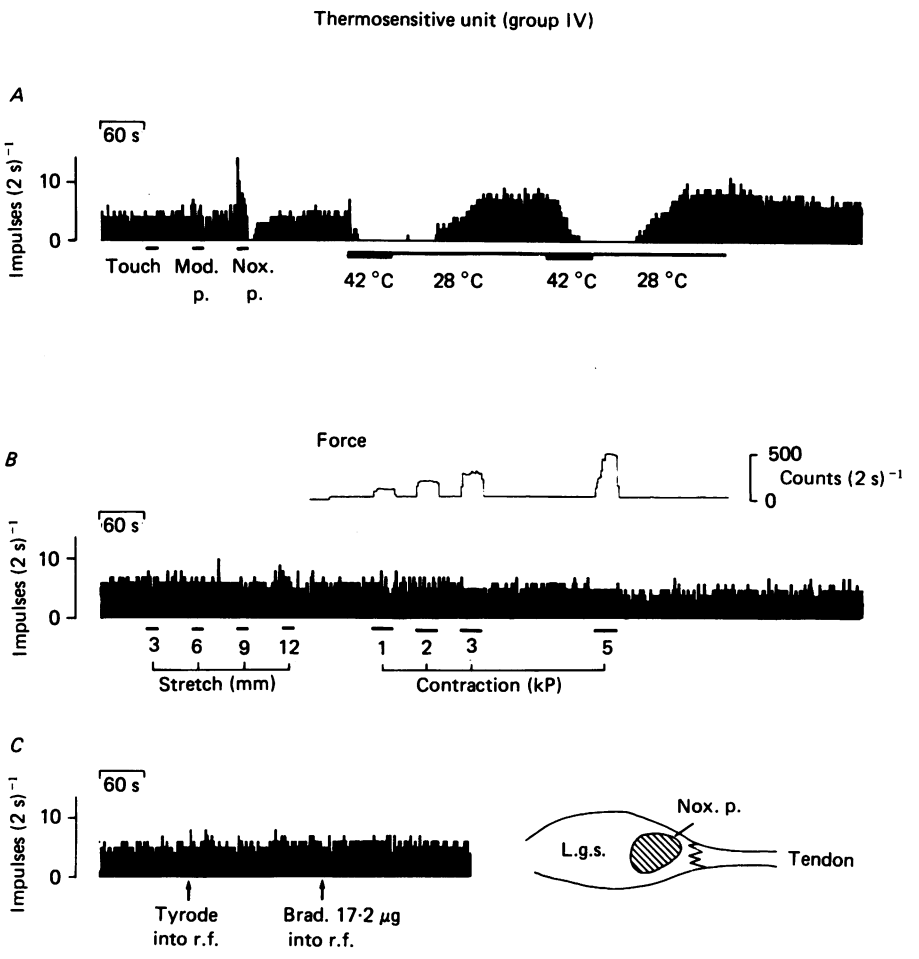

Fig. 5. Cold-sensitive unit with group IV afferent fibre, conduction velocity 0·75 m s^{-1}. Labelling of receptive field and stimuli as in Fig. 1. Starting temperature of the pool containing the muscle was 31 °C. In *B*, the histogram during contractions of 3 and 5 kP was smoothed by hand in order to remove movement artifacts.

clear whether the temperature of the bradykinin solution (24 °C) might have contributed to the effect. Attempts to reproduce the response with further injections of bradykinin and of cold Tyrode solution failed.

Distribution of response types among group III and IV units. The most frequent type found among group III receptors was the l.t.p. unit (44 %), followed by nociceptive (33 %) and contraction-sensitive endings (23 %), respectively (Fig. 6). Thermosensitive receptors with group III afferent fibres were not observed. Taken together, the presumably non-nociceptive units (l.t.p. and c.s.) made up the majority of the group III receptors. Among the endings with group IV afferent fibres, the nociceptive type was the most prominent (43 %), the other three types each occurred with the same frequency of 19 %. In the right-hand panel of Fig. 6, the data from group III and IV endings are pooled. It is apparent that among these receptors, units probably not

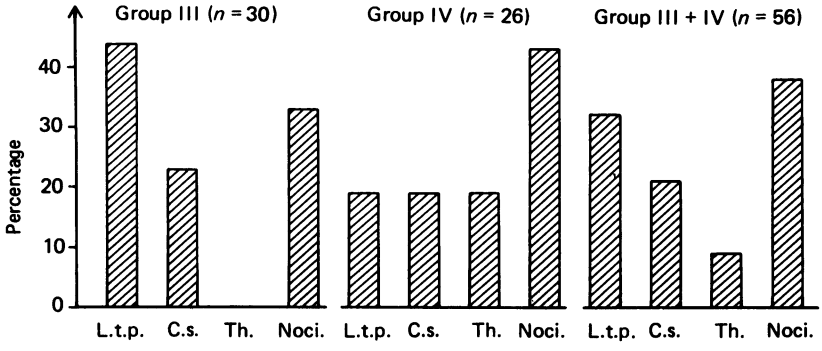

Fig. 6. Distribution of receptor types among group III and IV afferent units. L.t.p., low-threshold pressure-sensitive units; c.s., contraction-sensitive units; th., thermosensitive units; noci., nociceptive units.

fulfilling a nociceptive function (l.t.p., c.s. and thermosensitive units) by far outnumber the nociceptive ones (62 *vs.* 38 %).

Location of receptive fields. As stated above, the receptor types encountered in the muscle were also present in the calcaneal tendon. The group III afferent units from the tendon showed a distribution of response types similar to that of muscle units (five l.t.p., three nociceptive, two c.s., no thermosensitive units). Only six group IV afferents with receptive fields in the tendon were studied; among these, no unit with nociceptive properties was found. Three receptors were low-threshold pressure sensitive, two contraction sensitive and one thermosensitive.

No differences in the location of the receptive fields were detected for c.s., nociceptive and thermosensitive units, i.e. similar proportions of these types were present in the various locations of the tissues studied (proximal, middle, distal third of g.s. muscle; calcaneal tendon). L.t.p. units differed from the other types in that their receptive fields were more often located in the calcaneal tendon (44 % against 16 % for nociceptive units). Another feature of l.t.p. units was that they often possessed two receptive fields. In most cases a receptive field with a low mechanical threshold in the distal parts of the muscle or in the tendon was associated with a second receptive field in the proximal or middle third of the muscle, the latter requiring moderate pressure for activation. Out of eighteen l.t.p. units, six (33 %) had double receptive fields. Among nineteen nociceptors, a double receptive field was present only in one unit; all c.s. units had single mechanosensitive receptive fields.

The sizes and shapes of the receptive fields varied greatly. The exact dimensions could be determined only for those receptors which responded to touching the surface of the tissue with a painter's brush. The smallest size observed measured about 2 × 2 mm, but sometimes the receptive field extended over more than 1 cm. The larger fields often had an oval shape with the greater diameter parallel to the long axis of the muscle.

DISCUSSION

The characterization of different receptor types attempted in this study was based solely on the effects of stimuli which are likely to occur in the natural environment of the experimental animal, such as local pressure, muscle stretch, active contractions and temperature changes. Although bradykinin was applied as an additional stimulus, the chemically evoked responses were not used for identifying a given unit, since it is known that the algesic substance activates not only nociceptors but also slowly adapting cutaneous mechanoreceptors (Fjällbrant & Iggo, 1961; Beck & Handwerker, 1974). Thus, the effects of bradykinin might blur existing differences between nociceptive and non-nociceptive receptors.

The fact that most receptors showed maximal response magnitudes upon stimulation with noxious pressure was not considered to indicate a nociceptive nature of these units (cf. Perl, 1984), since tendon organs and muscle spindles were also found to behave this way.

The assumption was made that a receptor which reaches a considerable percentage (20–40 %) of its maximal discharge frequency upon innocuous stimulation was not a nociceptor, even though it required noxious pressure to be maximally activated. As the non-nociceptive receptor types described in this report responded in a graded fashion to increasing intensities of stimulation within the physiological range, they were considered to be capable of signalling the presence of a physiological stimulus.

Most of the nociceptive endings had a response behaviour similar to that of cutaneous polymodal nociceptors, in that they responded to both noxious pressure and chemical algesic stimulation. Some of these units could also be activated by temperatures above 43 °C (H.-C. Hertel, B. Howaldt & S. Mense, unpublished results). Most probably, the group IV receptors which are excited during ischaemic contractions (cf. Mense & Stahnke, 1983) also belong to the nociceptive type. A possible function for the nociceptive units would be to mediate painful sensations from muscle and tendon (Lewis, 1942) and to evoke the nociceptive flexion reflex (Sherrington, 1910).

The physiological significance of the l.t.p. units is not clear. Judging from their response behaviour they would be suited to signal innocuous deformation of muscle and tendon. The endings requiring moderate pressure to be activated resembled the cutaneous 'moderate pressure receptors' (Burgess & Perl, 1967) which likewise were characterized by a mechanical threshold in the innocuous range and a maximal response to noxious intensities of stimulation. In the older literature, there are some reports suggesting the existence of a deep pressure sense in man (Head, Rivers & Sherren, 1905; Lewis & Pochin, 1938; Kellgren & McGowan, 1948), but whether the deep pressure sensations are due to activation of slowly conducting afferent fibres is unknown at present. From the histological point of view, the presence of sensitive mechanoreceptors with fine afferent fibres in muscle and tendon had to be expected, since paciniform corpuscles supplied by group III fibres have been shown to exist in these tissues (Stacey, 1969). It is questionable, however, whether paciniform corpuscles are contained in the l.t.p. type, since, in the few cases tested, no response to vibratory stimuli could be obtained.

The c.s. units of this report showed two subtypes, one with a sudden onset of the

response and a sensitivity to muscle stretch (probably mechanically activated), and another one with a delayed response to contractions and without a sensitivity to stretch (probably activated by mechanisms other than mechanical) (cf. Mense & Stahnke, 1983). The probably mechanically activated units exhibited a response behaviour similar to that of tendon organs. However, it is unlikely that tendon organs are included in this population, because the c.s. units required much more tension to be activated than the tendon organs recorded from in the same experiments. In addition, there is no evidence indicating that tendon organs are supplied by slowly conducting afferent fibres (cf. Houk & Henneman, 1967).

Since the c.s. units started to respond during weak contractions and reacted in a graded fashion up to the maximal force of contraction, they could signal the amount of work performed by the muscle. Thus, they might function as the hypothetical 'ergoreceptors' postulated by Kao (1963) which are thought to mediate cardiopulmonary reflexes during exercise. Evidence showing that such reflexes are elicited by slowly conducting muscle afferents has been obtained by McCloskey & Mitchell (1972).

Both l.t.p. and c.s. units might also be involved in non-nociceptive motor reflexes. Ellaway, Murphy & Tripathi (1982) have shown that low-threshold mechanosensitive group III muscle afferents exert an excitatory influence on γ-motoneurones. This reflex might heighten muscle spindle activity shortly after the onset of contraction. The group III-induced excitation was observed in γ-motoneurones to the l.g.s. muscle, an extensor, and thus does not fit into the 'flexor reflex pattern' concept of Eccles & Lundberg (1959) which postulates an excitatory action of group III muscle afferents predominantly on flexor motoneurones.

The proportion of thermosensitive units found in the present study is small in comparison with the great number of thermally induced effects in group III and IV muscle receptors observed in an earlier report (Hertel, Howaldt & Mense, 1976). In that study, mechanical stimulation could not be performed because the muscle was covered by large thermodes. Therefore, no distinction could be made between putative thermoreceptors and mechanoreceptors showing transient and ill-reproducible reactions to thermal stimulation (cf. Fig. 3*B*). The present results show that receptors behaving in a fashion similar to specific thermoreceptors of the skin (cf. Hensel, 1973) are actually present in skeletal muscle and tendon, but their number is small. It is unlikely that the thermosensitive endings of this report represent spurious thermoreceptors as described by Iggo (1969) in the skin of the rat, dog and monkey, since the spurious thermoreceptors were shown to possess a high mechanosensitivity and faster conducting afferent fibres (30–80 m s^{-1}). To the authors' knowledge, there is no evidence in the literature suggesting that subjective sensations of warmth or cold can be elicited from deep tissues. The only function of the thermosensitive units which could be speculated upon is a participation in thermoregulation. Jessen, Feistkorn & Nagel (1983) have provided experimental data showing that thermoregulatory responses can be evoked in the goat if the bone marrow space is cooled with implanted thermodes. Thus, thermosensitive receptors in deep tissues might form an additional input channel to thermoregulatory centres. However, evidence pointing to an involvement of slowly conducting afferent units in this function is still lacking.

A problem concerning the interpretation of the present results is the possible sensitization of nociceptive units by the unsterile surgical exposure of the deep tissues. This could lead to a lowering of mechanical thresholds into the innocuous range (Perl, Kumazawa, Lynn & Kenins, 1976) and consequently to a misinterpretation of nociceptors as l.t.p. units. Although precautions were taken to avoid recording from sensitized receptors (see Methods), it is difficult to rule out a sensitization in the case of a particular unit having a low threshold. It appears unlikely, though, that substantial proportions of the l.t.p. and c.s. units might consist of sensitized nociceptors for the following reasons: (1) the background activity in these units was less than that in nociceptive units; this was true for the proportion of units showing a background discharge as well as for the mean discharge frequency. If l.t.p. and c.s. units were sensitized nociceptors, it would be expected that the former should have a higher level of background discharge (cf. Perl *et al.* 1976). (2) In contrast to the nociceptive units, the l.t.p. and c.s. endings could usually not be sensitized by injections of bradykinin. If it is assumed that the latter types are sensitized nociceptors, the additional (but improbable) assumption has to be made that the sensitization had taken place in all or nothing fashion resulting in a maximal sensitization of all the units, so that no further sensitization could be obtained. (3) In another series of experiments (Mense *et al.* 1985), the impulse activity of single group III afferent fibres from deep tissues was recorded from the dorsal root entry zone without opening the skin overlying the deep tissues. Again, a similar proportion (37 %, excluding spindle group III afferents) could be activated by weak mechanical stimulation.

Thus it appears that in the skeletal muscle and tendon of the cat different types of group III and IV receptors exist, which might fulfil different functions. These types are so characteristic in their response behaviour that the alternative assumption, namely that they form a single population of polymodal receptors (Kumazawa & Mizumura, 1977) seems to be far less probable.

Additional evidence supporting the existence of different types of group III and IV receptors stems from morphological studies. In a combined light and electron microscopical investigation of these endings in the calcaneal tendon of the cat, von Düring, Andres & Schmidt (1984) found that group III fibres form six, and group IV fibres two different types of endings which could be distinguished by the shape of the terminals and/or by the location of the ending (adventitia of blood vessels, peritenoneum, connective tissue). The spinal projections of nociceptive and low-threshold mechanosensitive group III afferent units from the deep tissue of the cat hind limb were likewise found to differ in their spinal course and area of termination in the dorsal horn (Mense *et al.* 1985). These findings lend further support to the idea that slowly conducting afferent units from deep tissues are functionally diverse and show a relatively high degree of specialization.

The authors wish to thank Frau B. Howaldt for excellent technical assistance and Professor W. Jänig for helpful criticism of the manuscript. This work was supported by the Deutsche Forschungsgemeinschaft (Forschergruppe Nociception).

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