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STRETCH SENSITIZATION OF HUMAN MUSCLE SPINDLES

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SUMMARY

1. Sixty-seven afferents from the finger extensor muscles were consecutively recorded by microneurography.

2. The units were classified as primary or secondary muscle spindle afferents or Golgi tendon organ afferents on the basis of their responses to ramp-and-hold stretches, sinusoidals superimposed on ramp-and-hold stretches, maximal twitch contractions and isometric contractions and relaxations.

3. The muscle was repeatedly stretched and then either kept short or long for a few seconds followed by a slow ramp stretch. The responses of the muscle afferents to the slow stretch were compared under the two conditions.

4. Thirty out of thirty-eight units classified as primary spindle afferents and four out of eleven units classified as secondary afferents showed an enhanced response to the slow ramp when the muscle had been kept short compared to the response when the muscle had been kept long.

5. None of the eighteen Golgi tendon organ afferents showed any difference in this respect.

6. It is concluded that stretch sensitization does occur in human muscle spindles and, when present, constitutes firm evidence of the afferent originating from a muscle spindle rather than a Golgi tendon organ. In addition, due to differences in the response characteristics of primaries and secondaries, the test may aid in separating muscle spindle primary afferents from secondary afferents.

INTRODUCTION

The afferent impulse rate from muscle spindles is a function not only of muscle length, movements and efferent fusimotor activity, but also a function of the intricate biophysical properties of the muscle spindles themselves.

One aspect of the complicated behaviour of muscle spindles which was originally demonstrated long ago is the 'after-effects' of fusimotor stimulation and repeated stretches (Hunt & Kuffler, 1951; Brown, Goodwin & Matthews, 1969; Proske, 1975). These after-effects, which have recently been studied by several groups, consist of an enhanced response to *subsequent* fusimotor stimulation or slow stretch. A supposedly kindred phenomenon has been described in the form of an increased muscle spindle responsiveness to slow stretches after prolonged periods of muscle rest (Morgan, Prochazka & Proske, 1984).

Several different explanations of the after-effects in muscle spindles have been suggested. Common to all is a postulated existence of long-lasting actomyosin cross-bridges in intrafusal muscle fibres. Stable attachments are presumed to be formed under the conditions mentioned above, i.e. following fusimotor stimulation (Brown *et al.* 1969), stretch-induced contraction of bag_1 fibres (Poppele & Quick, 1981; Emonet-Dénand, Hunt & Laporte, 1985*b*) or spontaneously (Morgan *et al.* 1984).

So far these phenomena have been shown in anaesthetized cats exclusively. A demonstration of sensitization under physiological conditions in attending human subjects constitutes an important basis for discussions of its functional significance.

In the present study, stretch sensitization was demonstrated in a majority of units classified as muscle spindle primary afferents and in a substantial proportion of the secondary afferents but not in any of the Golgi tendon organ afferents. A preliminary report of the study has been presented (Edin & Vallbo, 1986).

METHODS

Subjects

The experiments were performed on twenty-one volunteers, aged 20–30 years. All had given their informed consent prior to the experiment in accordance with the Declaration of Helsinki. The subjects were comfortably seated in a dentist's chair with the left arm resting on a supporting plate. The forearm was resting in a vacuum cast which enclosed the flexor side of the forearm while leaving the extensor muscles accessible for palpation. The hand, with the wrist joint in an intermediate position, was held by an adjustable clamp which permitted free finger movements.

Neurophysiological technique

The microneurographic technique developed by Vallbo and Hagbarth (Vallbo & Hagbarth, 1968; Vallbo, 1972), was used to record single-unit activity from the radial nerve in the upper arm. We only included slowly adapting afferents which showed an increased response to well-localized poking over the extensor digitorum communis or extensor indicis proprius muscles and, in addition, responded to passive flexion of at least one metacarpophalangeal (MCP) joint and/or isometric contractions of individual fingers. If the afferent responded to passive movements of more than one finger, the finger with the best response was selected for the test manipulations.

Surface electrodes on the extensor and flexor side of the forearm were positioned to give an optimal electromyographic recording of the extensor digitorum and flexor digitorum muscles, respectively.

Actuator

An upgraded version of the servo device described elsewhere (Hulliger, Nordh & Vallbo, 1982) was used for finger manipulations. The finger controlled by the receptor-bearing portion of the extensor muscle was enclosed in a finger splint and connected to the actuator by a metal bar. The finger and the actuator arm together with the metal bar and a virtual line between the MCP joint and the servo axis formed a parallelogram. Simple vector analysis shows that the torque and the angle of the MCP joint were identical with the torque and angle measured at the servo axis, providing that such a parallelogram was formed by careful adjustments of the finger position (Edin & Vallbo, 1987).

Classification of afferents

The classification of units into Golgi tendon organs, primary and secondary muscle spindle afferents was based on a number of tests as follows.

Ramp-and-hold stretches. The presence of an initial burst, a deceleration response and prompt silencing at muscle shortening were all taken to indicate a primary muscle spindle afferent. No response at all of a unit, whether spontaneously active or not, was taken as support for the unit being a Golgi tendon organ afferent.

Sinusoidal stretches. Low-amplitude 20 and 50 Hz sinusoidal movements were superimposed on

ramp-and-hold stretches. Locking of the impulse discharge to the sinusoidal frequency was taken as speaking in favour of the afferent being a primary rather than a secondary spindle afferent.

Twitch contraction. Electrically induced maximal isometric twitch contractions were elicited transcutaneously and the classical signs of loading and unloading were noted (Edin & Vallbo, 1987).

Isometric contractions and relaxations. The subjects made a slowly increasing isometric contraction of the parent muscle portion followed by a sudden voluntary relaxation. A clear correlation to the torque output was taken as support for a tendon organ afferent rather than a muscle spindle afferent, whereas an increase during relaxation was taken as support for a spindle afferent.

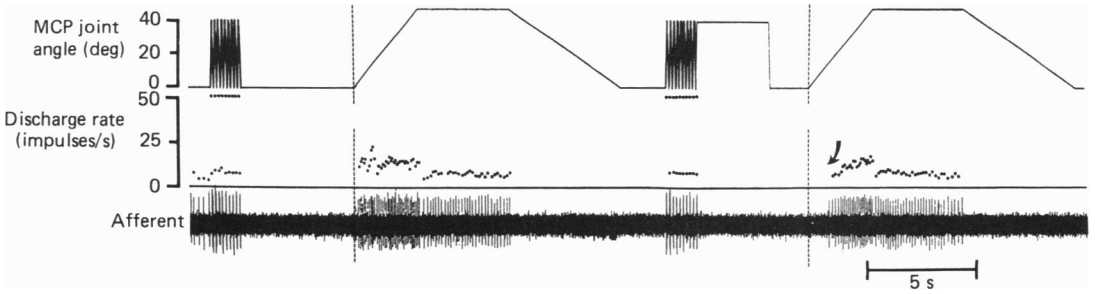

Fig. 1. Sample record to illustrate the test sequence. Continuous recording from a primary afferent from the extensor digitorum muscle. The sequence consisted of two test runs, both including a series of fast movements and a test ramp. In one of the runs the muscle was held short before the test ramp, while in the other it was held long for 3·2 s after the fast movements. From top to bottom are displayed the position at the metacarpophalangeal (MCP) joint, the instantaneous discharge rate and the original nerve signal. Zero angle represents full extension, but not overextension, at the MCP joint.

In forty-seven units, the identification procedure was run only once, whereas in the remaining twenty units it was repeated twice or several times.

The individual afferent was classified on the basis of the balance of evidence even when it did not exhibit all the characteristics of the unit type.

Test procedure

The movement parameters used for the stretch sensitization test (Fig. 1) were scaled versions of the parameters used in the cat experiments performed by Morgan *et al.* (1984). The scalings were based on the assumption that the MCP joint radius is 7 mm and the length of the muscular portion of the extensor muscles is 120 mm. The conditioning rapid stretches were performed with a velocity of 700 deg/s and an amplitude of 41 deg (corresponds to about 5 mm in the cat soleus). The position called 'short muscle length' below corresponds approximately to a fully extended MCP joint while 'long muscle length' corresponds to a 41 deg flexion in the MCP joint (6 mm in cat soleus). The slow ramp was performed with 18 deg/s (2·2 mm/s in cat soleus), reaching an amplitude of 49 deg. The angular stretch amplitudes and velocities were identical in all experiments.

With all units the first run consisted of a sequence when the muscle had been kept short for 5 s before the slow test ramp. In the second run the muscle was kept long for 3·2 s and then short for 1·8 s before the slow ramp (Fig. 1). In twenty-seven units, including twenty-one muscle spindle afferents, the two runs were repeated in the reverse order.

Data analysis

The electromyographic signals and the nerve signal, as well as the position and torque signals, were stored on analogue tape (Philips Analog 714) for later off-line analysis. Using a microprocessor-based device which was constructed in the laboratory, all triggered nerve spike events were checked

by visual inspection on an expanded time scale which displayed the details of the impulse shape before they were accepted.

Signs of unintentional contractions of the parent muscle were carefully checked for in the EMG and torque records. If muscular contractions were present in the periods when it was essential that the subject remained relaxed, the record was discarded.

RESULTS

Of the sixty-seven units analysed, thirty-eight (57%) were classified as primary muscle spindles, eleven (16%) as secondary muscle spindles and eighteen (27%) as Golgi tendon organs.

Thirty out of the thirty-eight primaries (79%) showed signs of stretch sensitization, i.e. the discharge was stronger at the commencement of the slow ramp stretch when the muscle had been kept short during the previous 5 s, and it was weaker when the muscle had been kept long (Figs 1 and 2*A*). In the vast majority of primary afferents the enhanced response was present in the first 10–15 deg of the test ramp mainly as an initial burst which was lacking in the desensitized state; after the initial part of the ramp stretch the instantaneous frequency plots of the two tests usually coalesced.

Quantification of the difference in afferent discharge seemed unnecessary because the sensitization effect was very prominent, when it was present at all. The average of several test responses did not differ significantly from single trials, i.e. if signs of sensitization were not obvious in a single trial, it could not be demonstrated in the averaged response either.

When stretch sensitization was found with a unit, it was not only present when the test was repeated, but also when the order of the two test runs was reversed (Fig. 3).

The lack of sensitization with some primaries might have been due to an insufficient amplitude of relative stretch. It appeared as though many of the non-sensitized primaries were subjected to a smaller relative stretch than the sensitized ones, as suggested by their response during the slow ramp stretch. Most of the non-sensitized primaries (seven out of eight) but very few of the sensitized ones (three out of thirty) failed to respond at the foot of the test ramp but impulse acceleration was delayed, as if some slack was taken up by the first part of the ramp. When we became aware of this effect, the initial position of the finger was slightly adjusted to provide a more stretched muscle to start with. As a consequence the proportion of sensitized primaries increased from eleven out of eighteen to nineteen out of twenty in the following experiments.

Only four out of eleven secondary afferents (36%) displayed signs of sensitization (Fig. 2*B*). None of these secondaries showed the characteristic initial burst of sensitized primary afferents. With three of these secondaries the sensitization appeared as simply an earlier onset of the discharge during the test ramp. The fourth secondary, in addition to the earlier onset of discharge, showed a small but unusually prolonged initial increase of its discharge (Fig. 2*B*, bottom). Although some of the remaining seven secondaries were active from the start of the slow ramp, no clear difference was evident between the two test ramps with different immediate prehistories.

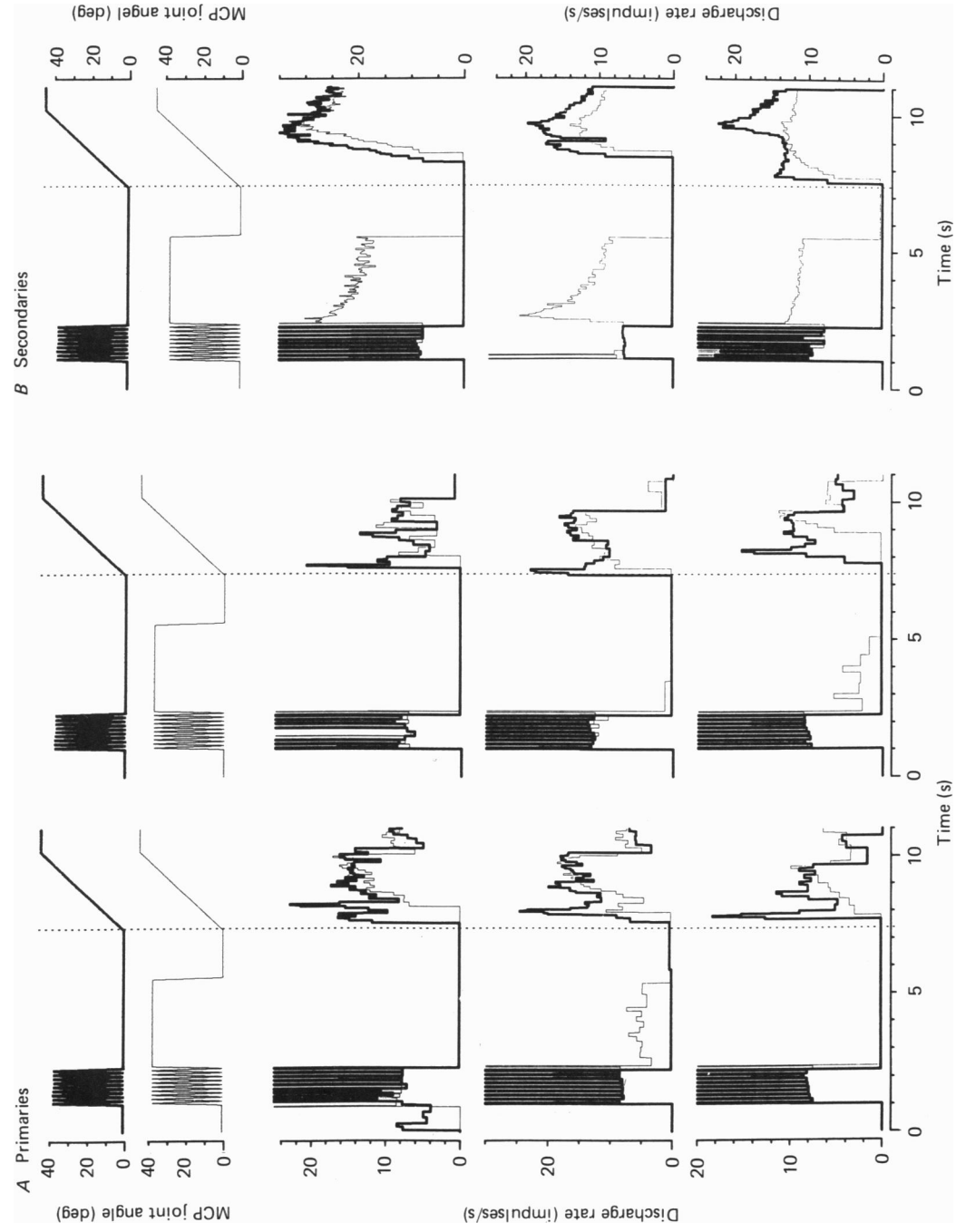

Fig. 2. Examples of sensitization in muscle spindle afferents. *A*, sample runs with instantaneous impulse rates from six different primary afferents. Thick and thin lines represent data from the two types of test runs as shown in Fig. 1, i.e. thick lines indicate runs when muscle was held short between fast movements and test ramp, and thin lines indicate runs with long muscle after the fast movements. The difference in discharge rate is particularly evident during the first 15–20 deg of stretch. *B*, sample runs from three secondary afferents. In contrast to the primaries, an initial burst was usually lacking in the secondaries but a sensitization was manifest as an earlier onset of the discharge.

Sensitization was not present in any of the eighteen Golgi tendon organ afferents. Most of them did not respond at all to the test ramps, whereas two presented one or two impulses at the foot of the ramp. Five tendon organ afferents which were spontaneously discharging did not change their impulse rate at all. One of them is illustrated in Fig. 4, together with examples of two non-sensitized muscle spindle afferents.

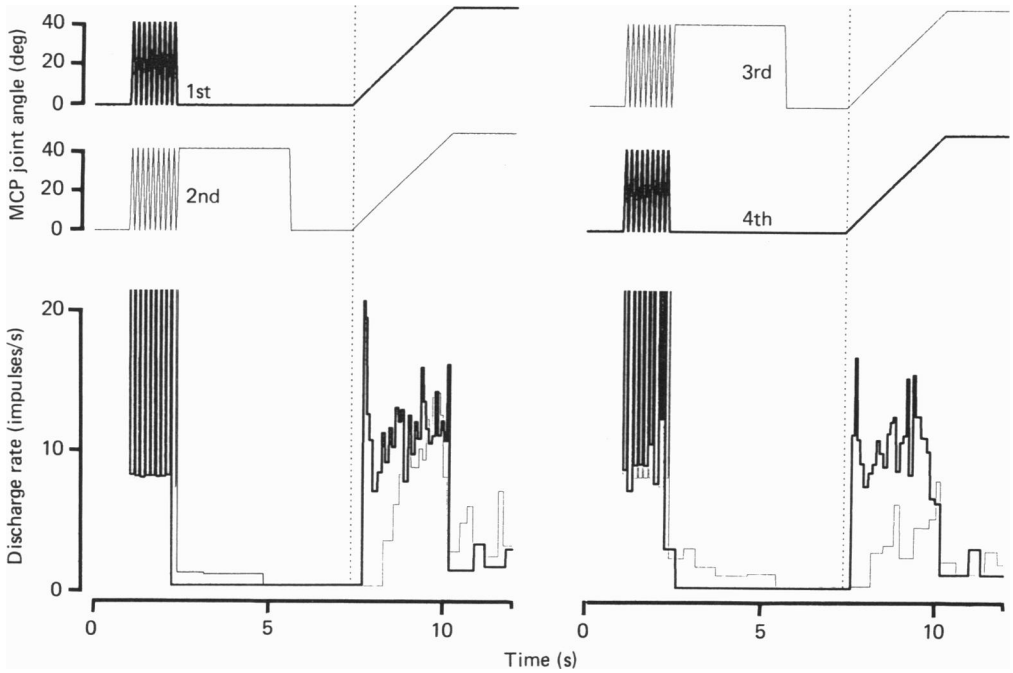

Fig. 3. Independence of test order. Four sequential runs showing instantaneous impulse rate of a primary afferent to demonstrate that sensitization and desensitization were independent of the previous history of individual test runs.

DISCUSSION

Stretch sensitization was found in many of the spindle afferents whereas it was not seen in any of the tendon organ afferents. Differences were also present between the groups of units classified as primary and secondary spindle afferents. However, the findings in this respect should be regarded as provisional with regard to details, because the separation of units in spindle primary and secondary afferents was based on receptor properties exclusively and not on conduction velocity which may provide a more solid classification, particularly when borderline units are excluded.

Primary muscle spindle afferents

Stretch sensitization could be demonstrated in 80% of primary afferents from muscle spindles. It is not clear from the literature if this proportion is representative also for the cat because the relative numbers of non-sensitized primaries are not reported.

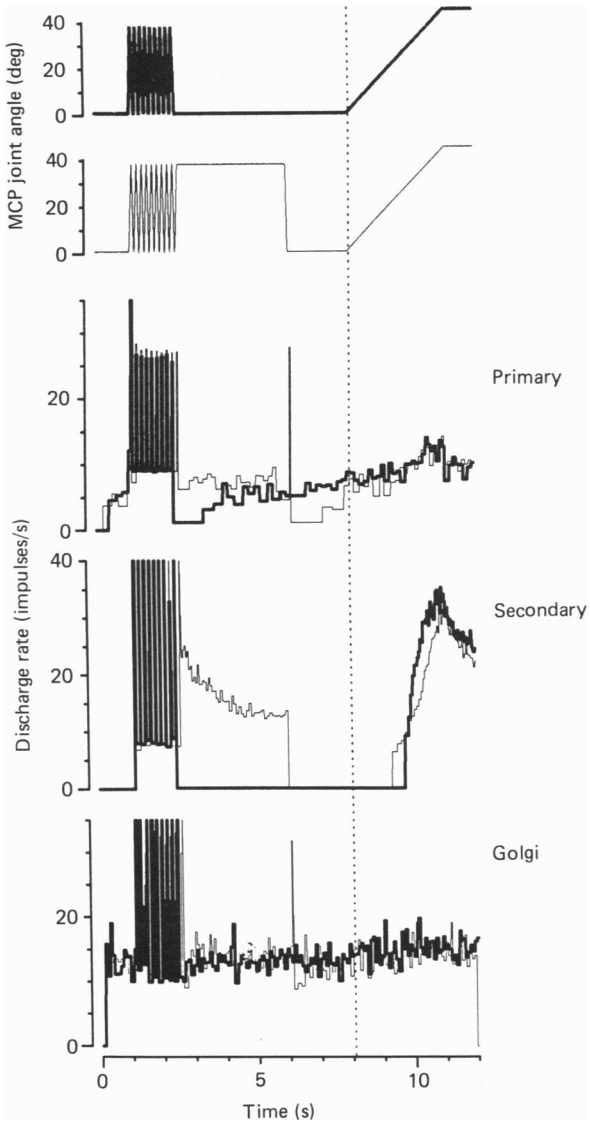

Fig. 4. Muscle afferents lacking sensitization. Sample records of the instantaneous impulse rates from a primary spindle afferent, a secondary afferent and a tendon organ afferent. The primary afferent, which in this test responded rather sluggishly, displayed a more typical response when the muscle was more stretched, i.e. a high-frequency initial burst, a deceleration response and a prompt silencing at muscle shortening during a ramp-and-hold stretch commencing at a 30 deg more flexed joint position. Furthermore, its discharge was locked at the frequency of a 50 Hz sinusoidal superimposed on a ramp-and-hold stretch and showed a clear pause followed by an intense burst during a maximal twitch contraction. The thick and thin lines have the same significance as in Fig. 2.

The lack of sensitization in some of our primaries might be due to particular factors in the present study. One is that the range of muscle length might have been inadequate in the test. If the muscle was so short that the spindle remained slack during a substantial part of the imposed movement, the total length changes produced by the conditioning rapid stretches might not have been sufficient to activate the bag_1 fibre and/or to break the 'stuck' bonds of its actomyosin filaments. In fact, the response profiles of the sensitized and the non-sensitized primaries were different and suggested that this factor might have accounted for the lack of sensitization in some units.

Another possibility is that a continuous and low-level dynamic fusimotor activity was present in some subjects. This would probably put the bag_1 fibre in the same functional state in the two test ramps regardless of previous stretch. On the other hand, the fact that most primaries exhibited sensitization supports the interpretation that dynamic fusimotor drive is largely lacking in relaxed human muscles.

Secondary muscle spindle afferents

The general features of the after-effects in the units classified as secondaries were identical to those reported by Proske & Morgan (1985), i.e. the units, when sensitized, either simply began to fire earlier during the ramp or, with one secondary afferent, displayed a small but prolonged increased discharge during the first part of the test ramp stretch. Again, information about the proportion of cat secondaries which demonstrated the phenomenon is lacking in Proske & Morgan's report (1985), whereas we saw it in about a third of the secondaries.

Golgi tendon organ afferents

Stretch sensitization was not found in any of the Golgi tendon organ afferents. It is not clear from previous studies if Golgis may exhibit sensitization at all. It is certainly not to be expected in the units which did not respond at all to the test stretch. Tendon organs are, with few exceptions (Barker, 1948; Marchand, Bridgman, Shumpert & Eldred, 1971), connected in series with the extrafusal fibres exclusively and not with the intrafusal fibres. However, it is well known that 'stuck' actomyosin bonds are also formed in extrafusal fibres and account for the short-range elastic component of the main muscle (Hill, 1968), which might influence the tendon organ response. Although it has been demonstrated in animal experiments that some tendon organs may respond with an initial burst suggesting an effect of 'stuck' actomyosin bonds (Proske & Gregory, 1977), it remains to be shown whether after-effects as studied in the present investigation ever occur in Golgi tendon organs or not.

Significance

Classification of muscle afferents. Although the sensitization test alone did not discriminate absolutely between the three types of afferent units, the test seems to be of considerable interest as a complement to other identification tests; in an unselected material of human muscle afferents about 60% of the afferents could be classified as muscle spindle afferents using this single criterion. In addition, the characteristics of the sensitization response which, in accordance with Proske &

Morgan's (1985) study on the cat, was found to be different in primaries and secondaries, is a further aid to differentiation between these two types of afferents. Stretch sensitization was very obvious and consistent in the units which exhibited the phenomenon at all (Fig. 3). Moreover, the test takes only 30 s to perform, and these two factors make it very valuable as an identification procedure.

Sensitization under normal conditions. It seems reasonable to raise the question of the extent to which the much debated differences between behaving animals and human subjects with regard to spindle response and fusimotor activation during self-generated movements (Taylor & Prochazka, 1981) may be related to after-effects, as suggested in previous reports (Vallbo, 1981; Hagbarth, Hägglund, Nordin & Wallin, 1985). Most of the data from behaving animals have been collected from hindlimb muscles during step cycles. The relatively fast movements, as well as alterations between stretch, shortening contraction and relaxation in the cyclic movements, may promote after-effects on dynamic sensitivity of spindle primaries, although it is difficult to predict the exact effect (Emonet-Dénand *et al.* 1985*a*, *b*). In most studies of voluntary contractions in human subjects, on the other hand, fairly slow and singular movements have been analysed. Moreover, the subjects are usually requested to relax their muscles between successive contractions in order to provide a long and stable control period for the following active movement. It is likely that after-effects of previous stretch and fusimotor activation may be quite different in the two types of movements (Emonet-Dénand *et al.* 1985*a*, *b*). Anyway, it seems that after-effects may be a serious complication when inference is made, on the basis of spindle afferent discharge, of the amount and type of fusimotor activation during self-generated movement.

The present study was not designed to discriminate between the two hypotheses regarding which mechanisms account for stretch sensitization of the primaries, i.e. whether it is due to stretch activation of the bag_1 fibre (Emonet-Dénand *et al.* 1985*b*) or to spontaneous formation of actomyosin cross-bridges in the bag_1 fibre when muscle length is kept constant (Morgan *et al.* 1984; Gregory, Morgan & Proske, 1986*b*). However, the demonstration of after-effects as a relatively regular phenomenon in human subjects invites further investigations. Particularly it seems of interest to define the natural conditions when after-effects do give rise to significant modifications of spindle discharge. It has been suggested that alternating movements in, for instance, locomotion, as well as the onset of muscular activity after a period of rest, are associated with prominent after-effects (Gregory, Prochazka & Proske, 1977; Emonet-Dénand *et al.* 1985*a*, *b*; Gregory *et al.* 1986*b*). Although it is tempting to speculate about the role of stretch sensitization in motor control, it seems more fruitful to postpone discussions of this matter until the phenomenon really has been demonstrated in natural movements and its size has been assessed.

Selective interference with muscle spindle afferents. The test used in the present study may be employed to explore the contribution of muscle spindles to motor control and kinaesthesia (Gregory *et al.* 1986*a*). The role of spindle afferents in the process of design and the execution of movements may be discerned by comparing the performance of a subject when the muscle spindles have been sensitized or desensitized just prior to voluntary movements. Similarly, the role of spindle afferents in perception of imposed movements may be analysed. The sensitization

procedure has the advantage of being selective towards muscle spindles, in contrast to other measures previously employed to modify spindle afferent input in human subjects during psychophysical and psychomotor tests.

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