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Mechanisms of the Clasp-knife Reflex Studied in an Animal Model

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Summary. The mechanisms of the clasp-knife reflex were studied in the soleus muscle of an animal model, the decerebrate cat with a dorsal hemisection of the lower thoracic cord. The reflex is shown to be autogenetic, and to depend on muscle length in keeping with previous suggestions. However, the magnitude of the inhibition increases with increasing initial force, and the inhibition is mimicked by gentle manipulation of the muscle and tendon surface. Concurrent muscle afferent recordings showed that the electromyogram (emg) reduction was not a result of a decline in Ia afferent input and was not well related to secondary or tendon organ afferent discharge.

It is now known that many group III and some group IV muscle afferents are also activated by muscle stretch and contraction, and we here report limited stretch sensitivity in four non-spindle group II afferents. Since these fiber groups each include afferents that produce inhibition of extensor motoneurons, it is proposed that the clasp-knife reflex may result from the activation of these slowly conducting afferent fibers.

Key words: Clasp-knife reflex – Muscle afferents

The clasp-knife reflex is characterized by the abrupt decline in muscle force that occurs during rapid forcible movement of a spastic limb. This reflex has been attributed to the central inhibitory effects of Golgi tendon organ discharge (Ballif et al., 1925; Fulton and Pi-Suner, 1928), on the premise that tendon organs appeared to have high thresholds (Matthews, 1933) and were activated abruptly at high forces. However, it is now known that tendon organs are both extremely sensitive to active muscular contraction (Jansen and Rudjord, 1964; Houk and Henneman, 1967) and are active over most of the normal range of force gradation (Houk et al., in press). Furthermore, the pattern of clasp-knife

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inhibition is inconsistent with expected tendon organ behavior (Burke et al., 1970) in that the inhibitory effect far outlasts the decline in active muscle force, whereas tendon organ activity should decline in parallel with the reduction in muscle tension. Recently, Burke et al. (1970) have suggested that the secondary spindle ending is the receptor responsible for clasp-knife inhibition because of a clear dependence of quadriceps clasp-knife inhibition on joint angle (and therefore on muscle length) in both spastic human subjects and in a related animal model.

The arguments regarding the physiological basis of the clasp-knife response are presently incomplete for several reasons. First, the inhibition has not been shown unequivocally to originate directly from the stretched muscle, although this appears likely (Burke et al., 1970). Second, the basis for a discrete inhibitory threshold is unclear – secondary receptors would presumably be active throughout most of the range of muscle length change, unless fusimotor activity also proved to be ineffectual. Third, a decline in the emg could result from withdrawal of Ia excitation, arising in turn from fusimotor inhibition, rather than from direct motoneuronal inhibition. These issues could be resolved by direct observation of muscle afferent discharge and the emg of a separated muscle during the clasp-knife response, yet only one brief comment on this exists (Eldred et al., 1953).

We have investigated the mechanisms of the clasp-knife reflex in an animal preparation described previously, the decerebrate cat with dorsal hemisection of the spinal cord (Burke et al., 1972). The stretch responses of the functionally separated soleus were examined prior to and following cord hemisection. We also examined the response of soleus muscle afferents during clasp-knife behavior, using small filaments teased from otherwise intact dorsal roots.

Our results support an autogenetic contribution to the clasp-knife reflex but cast doubt upon both tendon organ and secondary spindle receptor afferents as the source of stretch-induced inhibition. As an alternative to these previous theories, we propose that the clasp-knife reflex may be mediated by the central inhibitory effects of groups III and IV (and perhaps non-spindle group II) muscle afferents possessing classical flexor reflex actions.

Methods

Ten cats weighing from 2.5–3.5 kg were used. Anesthesia was induced with a mixture of fluothane, nitrous oxide, and oxygen, following which decerebration was performed by inter-collicular section and aspiration of rostral brain tissue. A limited laminectomy, confined to the L6 segment was then performed, exposing portions of the L7 and S1 dorsal roots. The left soleus muscle and its innervation were separated from surrounding structures and the remaining nerve supply to the leg, cutaneous and muscular, was sacrificed. The maximum physiological length was measured by forcible ankle dorsiflexion with the achilles tendon intact, and the distal attachment of the soleus was severed so as to include a small calcaneal bone chip, facilitating secure attachment of the muscle to the muscle stretcher. The animal was supported in a spinal frame by a head holder and a vertebral clamp attached to the dorsal spines of the lower thoracic vertebrae; no hip pins were used. The left leg was held firmly by concave cups clamping the knee at the tibial tuberosities and at the medial and lateral malleoli. Skin flaps were used to fashion oil pools about the laminectomy and leg dissections. Animal core temperature was measured via a rectal thermometer and maintained by a ventral heating pad. Limb oil pool temperature was controlled at 35°.

Spinal Section

This procedure was performed after the recording of a detailed series of control observations in the unanesthetized decerebrate. Local anesthesia of the cord was provided by procaine soaked cotton pellets applied to the dorsal columns, and light general anesthesia was also reinduced (as described above). Dorsal hemisection of the cord was then performed at the T11–T12 level using blunt dissection with Dumont No. 5 forceps – – – cord dissection was extended ventrally until the denticulate ligaments were visualized. At the end of six experiments, the lesioned cord segment was excised and fixed in saline-formaldehyde for later study of serial sections.

Muscle Stretch

Muscle stretch was provided by a translational table, which was capable of generating controlled constant velocity stretch of specified amplitude. The stretcher was of a ball screw design, configured as a velocity servo. Muscle length was calculated from the position of the translational table which was specified digitally by counting pulses from an optically encoded disk attached to the motor shaft. Measurement resolution was 25 μ and velocities ranged from 0.2–200 mm/s.

Muscle force was measured by a strain gauge cantilever beam myograph, placed at the site of tendon attachment to the translational table. The stiffness of the myograph was 160 N/mm; the stiffness of the translational table was about 40 times greater.

The muscle emg was measured as a quantitative index of reflex response. The tips of two stainless steel wires (type 302), 0.002 in in diameter and isonel insulated, were bared for some 3 mm and the wires were then inserted into the soleus. The emg potentials were recorded differentially using a peripheral amplifier, then fed to a central processor for further amplification, full wave rectification and appropriate low-pass filtering.

Muscle Afferent Recordings

In six of the spinal-lesioned animals, muscle afferent fibers were isolated from fine filaments teased from a small natural dorsal root fasciculus. The remaining dorsal roots were left intact in order to facilitate reflex transmission. We used a 'spray' of small separately insulated platinum electrodes to record from as many as 3 afferent fibers simultaneously. These electrodes were attached via flexible shafts to a metal block, which was in turn screwed to the 7th lumbar vertebral spine. Neuronal activity was recorded on a monopolar electrode with the lumbar skin flap acting as the indifferent. Amplification was provided by low noise differential amplifiers, placed close to the animal.

The identification of muscle spindle receptors and Golgi tendon organs followed standard criteria (Hunt and Kuffler, 1951). In cases where the distinction between tendon organs and spindle receptor afferents remained in doubt, a compliant connection between the tendon and the myograph was helpful (Houk et al., 1971). Our sample consisted of 33 primary endings, 17 tendon organs, and 24 group II afferents. Afferent conduction velocity was calculated from the latency of response to muscle nerve stimulation, using the length of the nerve measured by dissection at the completion of the experiment.

Data Collection and Processing

Spike discharge on each filament was processed to provide single units using a spike height discriminator system. Each spike recognition triggered the emission of a standard pulse, which served to activate the computer based interval measurement system. The discharge of each afferent was stored as a series of inter-spike intervals.

Muscle force, length, and the emg were transmitted to the computer following analog to digital conversion. Sampling was under computer control and the various signals were stored digitally for later analysis. In each case, the signals were filtered prior to sampling by a low pass filter whose frequency response was 3 dB down at half the sampling frequency; this precaution was taken to reduce aliasing.

Experiments were carried out under the control of the digital computer (PDP 11/20); both the stretcher movement and the collection of analog and event data were specified by a data collection program. Data were usually collected as distinct 'trials' in which various signals were recorded prior to and following the application of a controlled muscle stretch. Individual trial records were written onto digital disks, (RK05) and later onto magnetic tape (Dectape) allowing delayed examination of results. Individual trials were displayed and reproduced graphically, or used to assemble ensemble averages. Other analysis programs allowed measurement of the average values within specified regions of the response (pre- and post-ramp comparisons for example) and enabled appropriate statistical computations.

EMG Quantification

The filtered rectified emg output was usually calibrated in equivalent force units – (newtons (N)) by measuring average force and emg levels over the isometric pre-ramp interval (1 s) in a sequence of trials. Measurements were made in the decerebrate state at a constant muscle length and the crossed extensor reflex was used to induce force and emg variations. Although the force-emg calibration was derived from the decerebrate preparation, and only at one muscle length, use of the same emg units was continued in the spinalized animal at a variety of different static and dynamic lengths. This represented an attempt to provide a more useful measure of emg activity, allowing comparison between the decerebrate and spinal-lesioned state.

Results

Part I: Characteristic Features of the State Produced by Spinal Hemisection

The effects of dorsal hemisection of the spinal cord are probably caused by interruption of descending inhibitory reticulospinal projections to flexor reflex pathways (Engberg et al., 1968). These descending pathways traverse the dorsolateral funiculus (Engberg et al., 1968); their interruption in the decerebrate cat has been shown to lower the threshold of flexor reflexes evoked by stimulation of high threshold afferents, and to decrease the stiffness of stretch reflexes in extensor muscles (Grillner, 1970). More directly, Burke et al. (1970) showed that the dorsal hemisection produced behavior analogous to the spastic state in that the classical clinical signs of the clasp-knife response were evoked by rotation of joints in undissected legs of decerebrate cats.

Autogenetic Basis of the Clasp-knife Reaction

We examined the stretch response of the functionally isolated soleus muscle in 10 decerebrate animals prior to and following spinal hemisection. Each animal showed a classic stretch reflex prior to the lesion, as evidenced by a sustained increase in muscle force and emg activity (Fig. 1, left).

Following the dorsal quadrant lesions, there remained a transient stretch-induced increase in these parameters, but this increase was followed by a steep decline culminating in virtual emg silence. The responses following hemisection typify the classic clasp-knife pattern – – – an early rise in tension curtailed by an abrupt decline when the stretch exceeds a certain point.

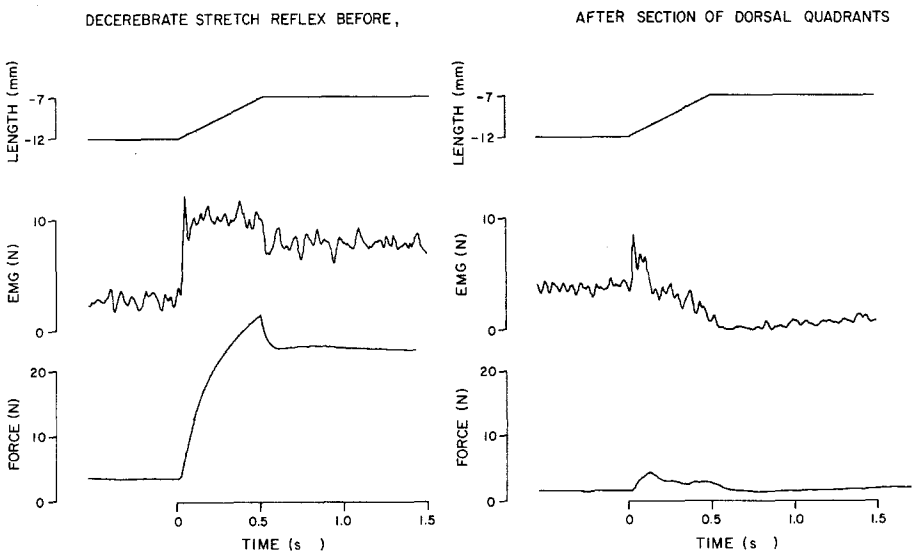

Fig. 1. Demonstration of autogenetic origin of the clasp-knife reaction. Traces on the left illustrate the stretch reflex obtained from a functionally isolated soleus muscle in a decerebrate cat prior to any spinal lesion. The records represent ensemble averages of seven trials, each recorded with 12 ms sample intervals; the electromyogram (emg) was full wave rectified and lightly filtered prior to averaging. Traces on the right illustrate the conversion to an inhibitory stretch response (clasp-knife) that resulted from dorsal hemisection of the spinal cord at T-12. The emg is calibrated in force units that are derived from a pre-lesion emg-force relation. Note that a greater initial emg in the post-lesioned case produced much less force, a modification attributable to low discharge rates of motor units. Loss of emg efficacy is also evident during stretch, because the steep decline in emg during the ramp is accompanied by relatively little force decrement; the residual force is largely passive. The associated increase in emg variability is not evident here, since the traces represent ensemble averages of a large number of trials (n = 19)

In three of the animals the stretch induced inhibition was less than that illustrated and was sometimes simply a decreased stiffness of the stretch reflex. Histological examination of the spinal cord in two of these animals (the third was not examined) revealed that the lesions did not extend all the way to the denticulate ligaments, whereas in the other four animals examined the lesions were substantially complete. The persistence of the response when the muscle is functionally isolated demonstrates that it can be mediated by autogenetic reflex pathways. Furthermore, the fact that the emg usually declines below its initial level is evidence against Herman's (1970) contention that the clasp-knife reaction is simply an expression of stretch reflex adaptation. It is clear that an active inhibitory process is involved.

Dependence of Inhibition on Muscle Length and Motor Output

The finding of a stretch-induced inhibition at the longest muscle lengths, and its absence at the shortest lengths (Burke et al., 1970) suggests that there could be

a specific threshold for the inhibitory process, which might be difficult to measure precisely using manually delivered movements (Burke et al., 1970). Our observations with functionally isolated muscles show that there is a clear threshold, and define the different parameters upon which the threshold depends.

The response to a small stretch, initiated at some intermediate length was often purely excitatory (Fig. 2b), whereas large amplitudes would provoke a pattern of excitation followed by inhibition (Fig. 2a).

The procedure used to measure this effect was to subtract the time average of the emg calculated over the initial isometric interval from that measured over a specific interval during application of a stretch – – – typically during the last half of the dynamic phase of stretch (i.e., the ramp), or at the new maintained length (i.e., the plateau). The first half of the ramp was not used, for the consistent excitatory response in this phase appeared quite independent of the inhibitory process. Figure 2c shows an example of the relation of the emg increment to stretch amplitude. The relation has a positive initial slope that reverses to a negative one (i.e., a decrement) with large amplitudes of stretch. The point of reversal denotes the onset of the clasp-knife response.

The demonstration that stretch induces an active inhibition required that there be an initial level of emg activity, which was sometimes spontaneously present, although it was more usually generated by crossed extensor reflex activation. We observed that both the degree of inhibition, and the threshold point are related to the initial level of motor output, as measured by the initial emg. In fact, this effect proved to be the origin of a portion of the inter-trial variability that is evident from the standard deviation bars in Fig. 2c. Graphs in which the measured emg increments (or decrements) were plotted as a function of the initial emg showed greater decrements when the level of initial emg was higher (as in Fig. 2d). This dependence on motor output was documented extensively in seven preparations, and in two of these the emg level at which inhibition became apparent was very sharply defined.

Presumably the latter relation represents a dependence on muscle force, although a dependence on some more central mechanism is also tenable. For example, the crossed extensor reflex could induce a change in the spinal response to a given autogenetic inhibitory input. Against this possibility, the magnitude of the reflex evoked during crossed extensor activation was comparable to that observed when motor output varied in the course of spontaneous changes in central excitability. An apparent dependence on force could also arise from certain types of nonlinear input-output relations, although our studies of stretch responses (Fig. 2 – 1 and 2 mm stretches; Fig. 3), provide no evidence for this mechanism. However, a central nonlinearity remains a viable possibility.

In five animals we studied the dependence on muscle length over a wider range, by imposing constant velocity length changes starting from several different muscle lengths. Figure 3 a and b shows the responses to "triangular" stimuli beginning from two different initial lengths. There is a striking difference in the slopes of the emg responses during the constant velocity stretch at the two lengths. The effect is better illustrated when the emg response is plotted against

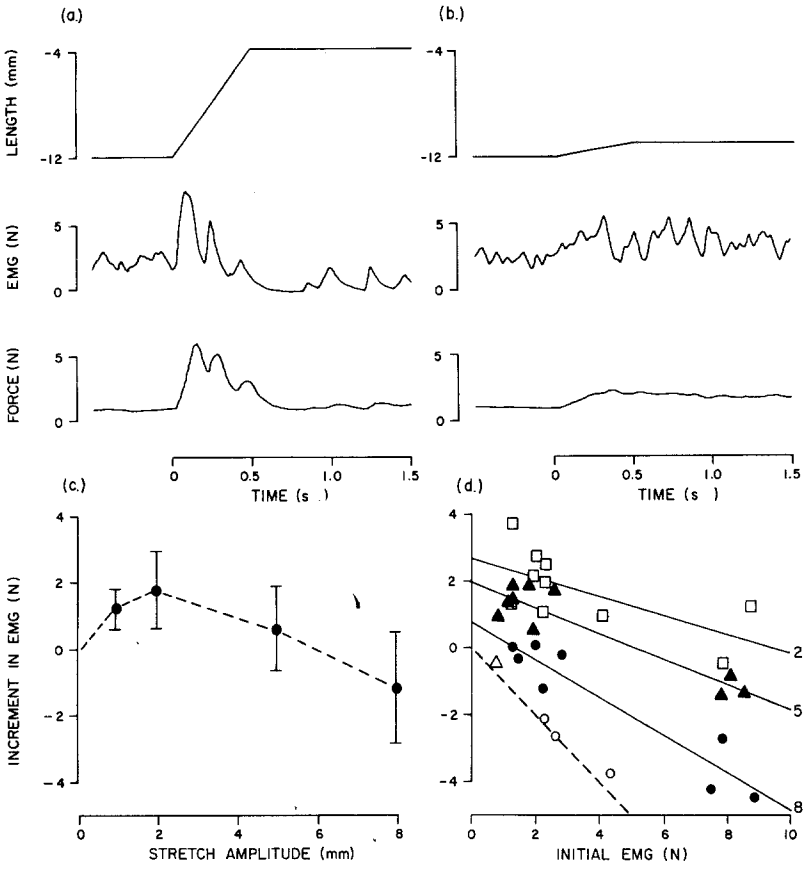

Fig. 2. The dependence of clasp-knife inhibition on stretch amplitude and motor output. Panels a and b contrast the force and emg responses to a large (8 mm) and small (1 mm) stretch. Both panels are single trials in which data is sampled at 6 ms intervals and smoothed with a low pass filter, time constant 60 ms. Panel a shows that the large stretch produces an initial excitation followed by a marked inhibition of force and emg, whereas a small stretch (panel b) produces excitation alone. Panel c shows that the emg increases for 1 and 2 mm stretch but declines at larger stretch amplitudes. The emg increment is measured as the difference between the time average during the last half of the ramp and the average pre-ramp level. 1 and 2 mm points were each calculated from 10 trials, 5 and 8 mm points from 11 trials, with standard deviation indicated in each case. Panel d demonstrates that inhibition increases with increasing initial emg, for three different stretch amplitudes. The emg change is measured exactly as in panel c. Each regression line, which is fitted to the set of responses collected for a particular stretch amplitude, has a negative slope and highly significant correlation – – – 2 mm, open squares (R = –0.66); 5 mm closed triangles (R = –0.80); 8 mm, closed circles (R = –0.82). The dashed line, with a slope of –1 denotes complete inhibition of the emg. Those responses specified by open triangle and open circles fall on or adjacent to the dashed line, and are not included in the regression calculation, thus the dependence on initial emg is not a saturation artifact

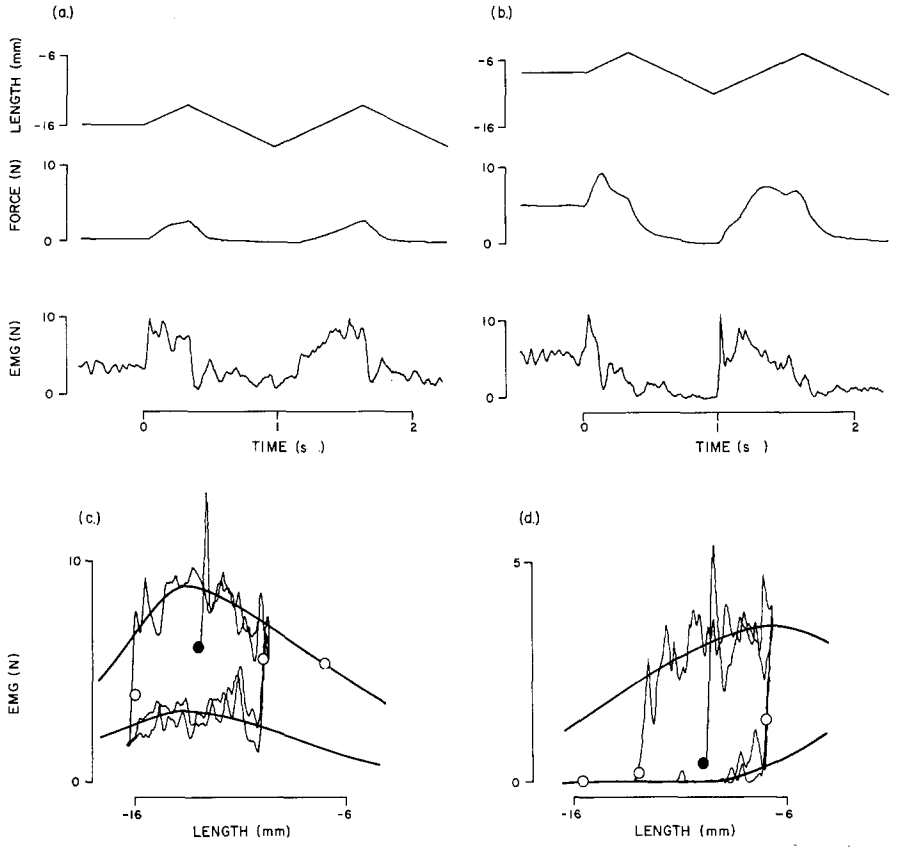

Fig. 3. Dependence of the clasp-knife reflex on initial muscle length. 'Triangular' stretches of ± 3 mm were initiated at –16 mm in part a and at –8 mm in part b, with velocity of 10 mm/s. Part a shows a predominant emg excitation during stretch, whereas in part b excitation is terminated abruptly, and is followed by a progressive decline in emg for most of the stretched cycle. All records (in part a–d) are ensemble averages, based on 8 trials with 14 ms sample periods. In parts c and d the thin irregular lines are trajectories of emg vs. length, derived from ensemble averages of emg and length in like trials, in both the decerebrate (part d), and the spinal lesioned animal (part c). Pre-stretch emg levels are represented by circles – – – the closed circles represent the initial emg for the illustrated trajectories. The smooth lines depict the emg envelope summarizing the response trajectory over all lengths; the change from a positive to negative slope at –12 mm in part c represents the clasp-knife threshold. Note that the emg response increases in proportion to stretch amplitude at shorter muscle lengths (part c), supporting a linear relation between afferent input and emg in this region. There is also a modest decline in the slope of the emg envelope near maximum length in the decerebrate preparation

muscle length, as in Fig. 3c which shows the emg-length trajectory averaged over all trials initiated at –12 mm (irregular trace), superimposed upon the response envelope obtained by pooling the results of all trials at all initial lengths. There is a clearly defined length, located at about –13 mm at which the slopes of the trajectories always change from positive to negative values. The

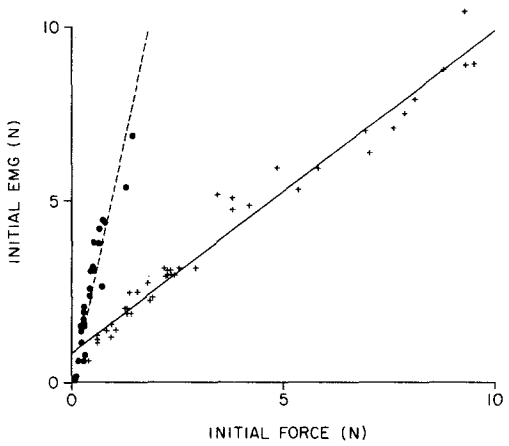

Fig. 4. Alteration of isometric emg-force relations following spinal hemisection. As in previous examples, emg is calibrated from isometric emg-force relations established in the decerebrate state prior to spinal section. Note that the slope of the emg-force relation increases approximately four-fold between the decerebrate (+) and the spinal-lesioned state (●), indicating a decline in the effectiveness of force production. This alteration, which is also evident in Fig. 1b, is probably a result of a reduction in average motoneuronal discharge rate

relation between initial (preramp) emg, and initial isometric length (circles) showed evidence of a similar length-dependent inhibition in the steady state.

For purposes of comparison, the same experiments had been performed in this animal prior to the dorsal quadrant lesion, and the results of the analysis are shown in part d of Fig. 3. Although there was some decline in emg, it was much less pronounced than that obtained after the lesion, and it occurred at a longer muscle length, one near the limit of the physiological range. This seems to be in accord with Matthews' (1959) comment that a proportion of decerebrate preparations demonstrate a decline in reflex force at longer muscle lengths.

The length at which the clasp-knife threshold was reached ranged from –13 mm in the case illustrated in Fig. 3 to –4 mm in one preparation (in which the clasp-knife response was evident only at high force levels). Other preparations had thresholds of –10, –12, –11, and –8 mm, when examined with stretches applied at 5 mm/s, and at comparable force levels.

Abnormal Features of Spontaneous Motor Control

The emg's recorded following hemisection consistently showed two alterations that may derive from a common pathological mechanism. The first is the emg pattern, which was consistently much more variable in amplitude after the lesion; the range of peak to peak variation in the rectified electromyogram was typically twice as large as before the spinal section. The second alteration is a four to seven-fold increase in the slope of the relation between emg and force in the steady state (as in Fig. 4), which means that, at any given level of mean emg, much less force was produced after the lesion. For example, Fig. 1 (right) shows that, following the spinal hemisection, pre-ramp emg has increased substantially above the pre-lesioned level, yet the initial force generated is much lower. This alteration in emg-force relation was not caused by fatigue or any other change in the contractile process, since force development, as tested by direct stimulation

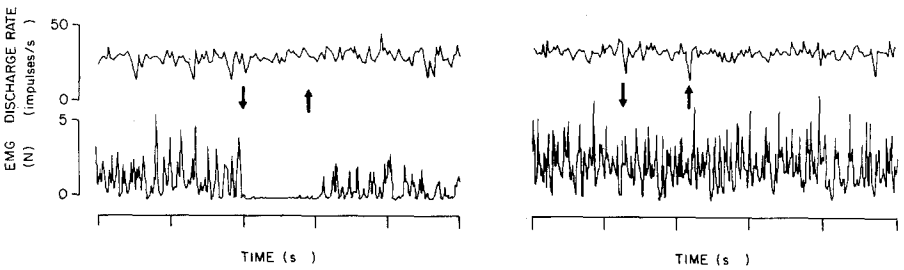

Fig. 5. Hypersensitivity to tendon manipulation, released by the spinal lesion. Gentle forceps pressure, applied over the interval specified by the arrows, produces profound reflex inhibition (left emg) that was blocked (right emg) by the application of dilute aqueous procaine solution to the tendon. The illustrated records are from single trials, in which emg was sampled every 16 ms. The discharge of a secondary ending (derived from an afferent with 43 m/s conduction velocity) is uninfluenced by the gentle manipulation. The small changes in discharge at the onset and offset of tendon stimulation document the finding that following blockade more vigorous stimulation failed to provoke emg inhibition, or to induce significant variation in secondary ending discharge

of the muscle nerve at the end of the experiments, was normal. A reduction in average motor unit discharge rate could explain the effect, since muscle force is greatly reduced when the muscle nerve is stimulated at low frequencies (Joyce et al., 1969; and our own experimental observations).

Motor Unit Properties

A sample of motor unit recordings in three spinalized animals confirmed the anticipated reduction in average discharge rate. The mean rates of 11 units, examined at low isometric force levels (less than 1 N) ranged from 3.5 to 5.4 impulses per second, rates substantially lower than those reported by Grillner and Udo (1971) in the soleus muscle of the normal decerebrate preparation. Records of muscle force also showed abnormal fluctuations (Figs. 2A, 6 right) which could be felt manually as a 'gritty' type of tremor. These force fluctuations could have arisen from the cited low rates of motor unit discharge, or from abnormal synchrony between the discharge of normally asynchronous motor units. In a recent study of motor units in spastic patients motor unit discharge rates were found to be abnormally low (Andreassen, 1977); thus, it would appear that this alteration may prove to be a general characteristic of the spastic state that is well mimicked by the hemisected decerebrate animal.

Inhibitory Effects of Stimulation of the Tendon and Aponeurosis

The final alteration which we found characteristic of the lesioned state is an elevated sensitivity of the tendinous parts of the muscle to contact and to distortion, both of which produced inhibition of motor output. This hypersensitivity was very striking, as shown by the lower trace on the left in Fig. 5.

Gentle forceps pressure applied to the distal portion of the tendon produced a marked inhibition of the emg for the duration of the stimulation. The application of dilute procaine (1% aqueous solution) to the stimulated area completely blocked the local inhibitory response within a few minutes (Fig. 5, right), although the clasp-knife reflex persisted. Areas of hypersensitivity were distributed all along the tendon and across the aponeurosis, and the efficacy of one site of stimulation was uninfluenced by procaine blockade of another site.

Inhibitory responses to tendon manipulation can sometimes be elicited in the usual decerebrate preparation, although much stronger stimuli are then required. Presumably the spinal lesion simply lowers the central threshold for evoking the inhibition, which is in accord with the generalized reduction of flexor reflex thresholds following hemisection. In any case, the demonstration of this hypersensitivity in the present experiments raises the interesting possibility that the stretch-induced inhibition described previously may be mediated by the same receptors that mediate tendon hypersensitivity (see below).

Part II: Correlation of Clasp-knife Reflex with Patterns of Receptor Discharge

We examined the discharge patterns of 74 receptor afferents in six preparations showing clasp-knife behavior.

Primary Endings

It has been suggested previously (Eldred et al., 1953) that the clasp-knife response results from a reduction in Ia afferent input, induced by fusimotor inhibition. Moreover, stretch-induced fusimotor inhibition has been reported in the decerebrate preparation (Fromm et al., 1974; Ellaway and Trott, 1978). We recorded the discharge of 33 primary endings in six preparations and were unable to validate the Eldred et al. (1953) hypothesis. Figure 6 illustrates that primary ending discharge, monitored during the clasp-knife response, is not grossly inhibited, although a consistent rate inflection (arrow), near clasp-knife threshold could represent fusimotor inhibition. In six other primary endings there was a modest, progressive, decline in rate towards the end of the ramp consistent with fusimotor inhibition, however the remaining (26) primary endings showed no evidence of fusimotor suppression.

For fusimotor inhibition to be manifested, some background level of fusimotor discharge must clearly be present. Based upon the dual criteria of spontaneous spindle receptor discharge at short muscle lengths (–12 to –15 mm), and variability of discharge in the absence of extrafusal activity, the majority of primary endings (24/33) appeared to receive spontaneous fusimotor input.

The sign of the Ia afferent synaptic connection was tested using tendon vibration, a specific stimulus to primary endings (Brown et al., 1968). Figure 6 (right) shows that longitudinal tendon vibration produces strong reflex excitation, evidenced by a marked emg elevation preceding muscle stretch – i.e.,

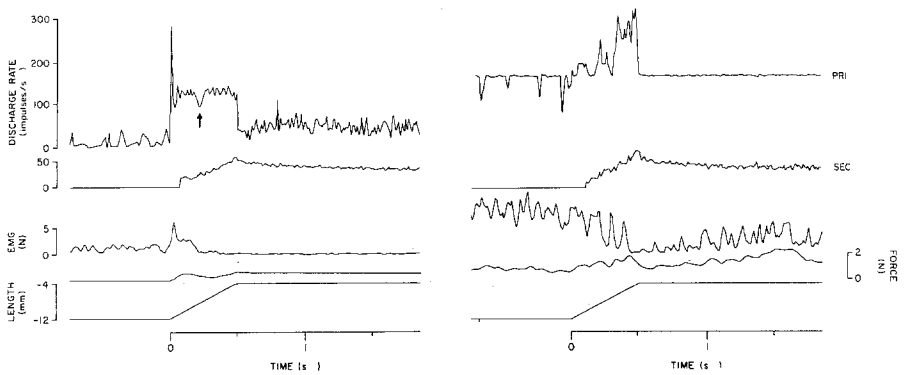

Fig. 6. Preservation of the clasp-knife response during tonic vibration. Left figure depicts ensemble averages (based on 4 trials using 12 ms sample intervals) in which an 8 mm stretch produces a marked decline in force and emg. Upper-most traces depict accompanying discharge of a primary ending (afferent conduction velocity 105 m/s) and a secondary ending (afferent conduction velocity 33 m/s) recorded simultaneously. The secondary ending has no pre-ramp discharge – – – threshold is reached only following 2 mm of stretch. The primary ending response shows a discrete, transient decline in rate about the mid-point (arrow) of the ramp following which the slope of the response is *slightly* reduced; both the transient dip and slope change could be caused by modest stretch induced inhibition of fusimotor neurons. The right figure, which shows ensemble averages based on 3 trials (same sample interval as left figure) represents the response to an identical stretch, applied during tendon vibration (100 μ peak to peak amplitude, 160 Hz). Vibration produced a tonic vibration reflex (increased initial force and emg) but did not affect the stretch induced inhibition. Secondary ending response was uninfluenced by the vibration, but the primary afferent discharge rate is clamped at the vibration frequency (with some dropping of spikes prior to the stretch, and extra spikes activated during the ramp)

Ia central connections maintain a net excitatory effect on soleus motoneurons in the clasp-knife preparation. However, stretch of the vibrated muscle still provokes a steep decline in emg (Fig. 6 right), in spite of added primary ending discharge. Similar observations were made in two other preparations. In sum, our observations do not support either fusimotor inhibition or changing central Ia synaptic action as the source of clasp-knife behavior in this preparation.

Golgi Tendon Organs

As might be expected, tendon organ discharge proved to be most clearly related to net muscle force. In two preparations in which muscle force output was limited, the discharge rate of four receptors was low, and discharge was dominated by passive forces. Specifically, tendon organ discharge continued for several seconds during the plateau phase of stretch even when no emg was evident, and the force was therefore of passive origin. However, in three other preparations, active muscle forces were much higher, and tendon organ discharge rates followed force output quite closely. Figure 7A illustrates the averaged response from one such afferent. The receptor discharges during the

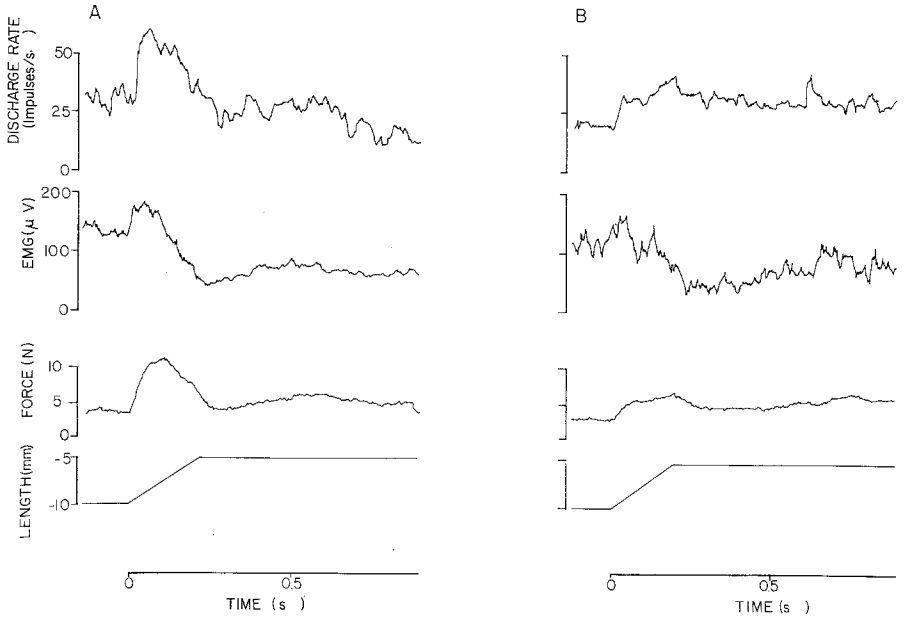

Fig. 7. A The relation between tendon organ discharge and the clasp-knife reflex. Initial discharge rate is relatively high, in response to increased isometric force, and rate then follows muscle force change during stretch. Since the afferent discharge falls with declining force, it is unlikely to be responsible for the prolonged inhibition. Afferent fiber conduction velocity was 86 m/s. **B** The response of a secondary spindle afferent, recorded during the clasp-knife reflex. The presence of static fusimotor bias is supported by the occurrence of spontaneous afferent discharge at –10 mm, the initial length. Since the unit is discharging before stretch onset, its threshold is quite different from that of the clasp-knife response. Afferent conduction velocity, 48 m/s. Each trace is an ensemble average of 8 trials, matched for initial isometric force. Sampling interval is 8 ms. Emg is low-pass filtered with 25 ms, time constant

isometric initial phase, and then follows net muscle force during the subsequent stretch sequence.

It would be difficult to attribute the onset of inhibition to the discharge of receptors such as that illustrated in Fig. 7A, and in fact 12/17 tendon organs in our sample were active during the initial isometric and early stretch phase. The threshold of the clasp-knife is therefore unlikely to correspond with that of tendon organ activation; some additional central threshold mechanism or an alternative receptor source has to be invoked.

We were also unable to produce sustained inhibition of force and emg following electrically induced muscle twitch (the standard procedure used to characterize prospective tendon organ afferents). Isometric twitches induced the anticipated burst of discharge in tendon organ afferents; however, when these twitches were superimposed upon a substantial background level of force and emg, there followed only a transient reduction in emg, (i.e., a silent period), far briefer than that observed during the clasp-knife response. This observation suggests that the Ib afferent pathway is unable to induce prolonged inhibition, at least under the circumstances of our experiment. Moreover, tendon organ

discharge in our sample was not significantly influenced by gentle manipulation of the surface aponeurosis, even though this procedure consistently induced profound inhibition.

At very low force levels, tendon organ discharge displayed a characteristic, irregular bursting behavior, showing bursts every 200 to 250 ms. The bursts were almost certainly induced by the discharge of a single motor unit (because of the stable periodicity, and because of correlated emg potentials in some instances), and their low rate thus provides further evidence in support of the proposed low motor unit discharge rate in the clasp-knife preparation.

Group II Afferent Discharge

There appeared to be three major types of response pattern evident in our population of 24 group II afferents.

One group of eight afferents, derived from three preparations, (conduction velocities 45–61 m/s) behaved like classical secondary endings, with modest, but definite gamma bias. For example the discharge was activated by stretch and suppressed during muscle twitch. Moreover, there was typically spontaneous discharge present at –10 to –15 mm, detectable acceleration of discharge with crossed extensor or cutaneous stimulation and a small dynamic response during ramp stretch. The threshold for activation of these afferents bore no relation to the clasp-knife threshold, and they were insensitive to surface stimulation. The averaged response of one such receptor is illustrated in Fig. 7B.

A second group of 12 afferents (27–67 m/s conduction velocity) was again activated by stretch and silenced by muscle twitch, but the afferents did not discharge spontaneously at –10 mm. Their responses were like those of deefferented secondaries, in that they did not show maintained discharge until they were stretched to near maximum length, they had little response to stretch, and they were also silenced readily by increasing isometric force (induced by crossed extensor reflex activation). A typical example is shown in Fig. 6 (left). The threshold for activation of these units often lay close to that of the clasp-knife (as in Fig. 6), but there was no systematic correlation. Furthermore, increases in the initial isometric force level often induced a more obvious clasp-knife effect (as described previously), yet the discharge of these endings was often markedly reduced by this force increase, even during stretch. Finally, the receptors were insensitive to localized surface stimulation.

The third type of response manifested by 4 afferents, (conduction velocities of 26, 27, 32, and 58 m/s) was quite uncharacteristic of secondary spindle receptor afferents, in that the discharge was usually activated at the peak of the muscle twitch, at which point the receptors discharged only a few impulses. The receptors were also rather insensitive to muscle stretch, discharging sometimes only towards the end of the ramp. A typical example is illustrated in Fig. 8; there is a modest rate increase during the ramp and also some sporadic low-frequency discharge continuing during the maintained phase of the stretch.

These afferents were also activated by direct local mechanical stimulation of the muscle or tendon, (although only one ending was sensitive to very light

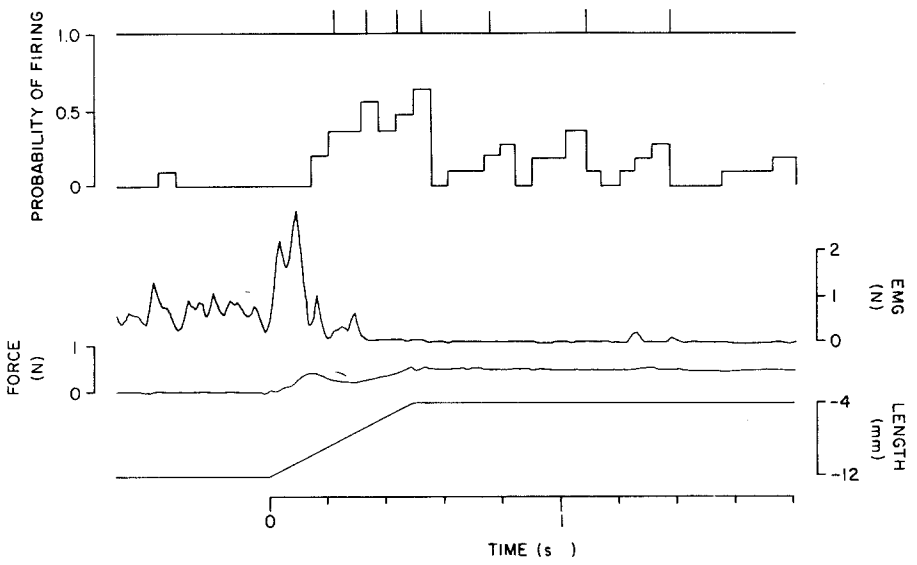

Fig. 8. Relation between the discharge of a low-sensitivity stretch receptor and clasp-knife inhibition. The receptor discharge commences at a point corresponding, approximately, with the onset of emg inhibition. Both the single trial (upper trace) and the post-stimulus histogram (second trace) document the prominent dynamic response but also verify the maintained discharge at constant length. The latter discharge could cause some persistent inhibition during ramp plateau. Analog samples were collected at 6 ms intervals, and the post-stimulus histogram was calculated over 11 trials as the firing probability in successive 60 ms time bins

superficial stimulation). The threshold for unit activation was usually close to that of the clasp-knife reflex (as illustrated in Fig. 8), however, we made no systematic recordings of unit responses over a range of forces, so no detailed correlations could be established.

We are confident that the first group of afferents originated in secondary endings, and that the latter group of afferents was not derived from spindle receptors, however the situation with regard to the second group of afferents is less clear-cut – it remains possible that some proportion of these afferents did not originate on muscle spindles. To be more specific, the classical criteria of stretch activation and twitch unloading could apply to any receptor which lies in parallel with extrafusal muscle: receptor nerve endings within the inter-fiber connective tissue could also conform with such a response pattern, since they might also be activated by stretch, and undergo strain reduction during muscle twitch.

There is now available histological evidence (Barker et al., 1962; Stacey, 1969) that an appreciable fraction of group II afferents arises from non-spindle sources, i.e., responses such as those of our third type of group II afferents are not entirely unexpected. Furthermore, it also now apparent that many group III and some group IV afferents are activated by muscle stretch, contraction und surface mechanical stimulation (Paintal, 1960, 1962; Bessou and Laporte,

1961; Franz and Mense, 1975; Kniffki et al., 1976; Mense, pers. commun.). Moreover, the spinal actions of these group III and IV afferents are certainly inhibitory to extensor motoneurons and it seems possible that group II non-spindle afferents may have similar synaptic effects. In sum, these slowly conducting stretch and contraction sensitive endings may be the source of the clasp-knife response.

Discussion

The stretch-induced inhibition that follows dorsal hemisection of the spinal cord in decerebrate cats shows most of the characteristic features of the clasp-knife reflex seen in human pathology, and we agree with Burke et al. (1972) that it is probably a good experimental model of this clinical sign. However, one difference is that in six (of ten) animals the initial resistance to muscle stretch appeared to be less pronounced than that offered by a spastic limb. Presumably this is due to a more complete disruption of tonic descending activity in the dorsal reticulospinal system of these animals than results from most pathological lesions in man, although the extensive limb denervation in the cat model may also have contributed. Loss of reticulospinal inhibition may also explain the extreme hypersensitivity of the tendinous tissues of the cat soleus muscle to contact and manipulation, and an attempt to determine whether this is also a feature of the human spastic state should be made in the future. A further difference between the animal model and human spasticity is the apparent deficit in static fusimotor bias in many of our spindle receptors (since it is claimed that fusimotor bias is normal or even increased in the spastic state). If the animal model is relevant, one would conclude that fusimotor inhibition is not an obligatory component of the clasp-knife response. Another feature of the animal model brought out by the present experiments is the atypically low discharge rates of motor units, inferred from the deficit in force production, and supported by a sample of motor unit recordings. As noted earlier, this rate reduction corresponds with a similar alteration recently described in spastic patients (Andreassen, 1977).

The results reported here provide unequivocal evidence that clasp-knife inhibition in the animal model is autogenetically based, although it is clear that in the intact limb, non-autogenous receptors could also contribute. We also demonstrate that the threshold is much lower than in the decerebrate, and the extent of inhibition is increased by increases in either muscle length or the initial level of motor output (presumably indicating a dependence on muscle force). This dual dependence on length and force together with the tendon hypersensitivity released by the same lesions provide the main criteria used in our attempt to determine which muscle receptors are responsible for the autogenetic inhibitory actions.

Our observations of receptor response properties in lesioned animals suggest that none of the major muscle proprioceptors (spindles and tendon organs) have all of the response properties required to account for the characteristic features of the inhibitory reflexes. Most particularly, few spindle or tendon organ

afferents were responsive to tendon manipulation or had stretch activation thresholds close to that of the clasp-knife reflex, so that some *additional* central mechanism would have to be invoked. Although our observations do not exclude the possibility that different categories of receptor converge upon a common inhibitory pathway, and thus give rise to dependence on muscle length, force and localized pressure, the simpler hypothesis, that a single receptor type is responsible for all of the features, is proposed as a realistic alternative.

Previous studies of group III and IV muscle afferents together with our own observations on 4 group II afferents suggest that some of the receptors innervated by these fibers are responsive to stretch, contraction and pressure, and are therefore capable of explaining all of the features of the inhibitory responses. Furthermore, the reflex connections of these muscle afferents have been clearly established as inhibitory to extensor motoneurons (the flexor reflex pattern studie by Lloyd, 1943; Brock et al., 1951; Eccles and Lundberg, 1959; Kuno and Perl, 1960). The often observed after-discharge of flexor reflexes is consistent with the prolonged inhibition characteristic of the clasp-knife reaction and this prolonged after-discharge is not evident in the Ib pathway.

We believe that these correlations taken together provide strong support for the hypothesis advanced here, that the clasp-knife reaction is mediated by low-sensitivity stretch receptors innervated by afferents conducting in the group II, III and IV ranges. These low-sensitivity stretch receptors presumably belong to the mixed group that has been referred to as 'flexor reflex afferents' (Holmqvist and Lundberg, 1961). The enhanced transmission from flexor reflex afferents released by interruption of the dorsal reticulospinal descending system (Engberg et al., 1968) apparently has the effect of lowering the central threshold for transmission from these afferents which then provokes the clasp-knife reflex.

Tendon Organ Contributions

A reevaluation of the evidence upon which the proposed Ib contribution to the clasp-knife reflex was based is of considerable interest. These receptor afferents were considered responsible for clasp-knife inhibition by Ballif et al. (1925) and Fulton and Pi-Suner (1928) because mechanical pressure on the tendons produced a decline in muscle force, although it is now clear that such mechanical stimulation could also have activated the low sensitivity receptors discussed earlier. Later McCouch et al. (1950) showed that electrical stimulation of the musculotendinous portion of the crureus muscle in the decerebrate cat produced prolonged inhibition of the excitatory response to tendon tap, while infiltration of the area with local anaesthetic sharply reduced the inhibitory effect. Clearly, the electrical stimulation technique could also have served to activate the low-sensitivity stretch receptor afferents, particularly those of larger diameter. Overall, the original evidence supporting a tendon organ contribution to the clasp-knife reflex seems equally compatible with a mechanism based on the actions of non-spindle group II or III nerve afferents. However, a Ib related contribution to the clasp-knife phenomenon is difficult to discount completely, since these receptors are also activated by muscle stretch, and their central

inhibitory action would probably be enhanced in the spinal-lesioned animal (Engberg et al., 1968).

Evaluation of Group II Contributions

The classical views of muscle afferent action assigned secondary spindle receptor fibers to the general class of flexor reflex afferents (FRA), providing inhibition of extensors and excitation of limb flexors (Eccles and Lundberg, 1959; Holmqvist and Lundberg, 1961). Matthews (1969, 1972) has pointed out many of the uncertainties attending the interpretation of the reflex response to electrical stimulation of group II muscle afferents, citing evidence that a significant proportion of these fibers do not originate from spindle receptors (Barker et al., 1962), evidence which we support with present results. This suggestion is at variance with the results of Hunt (1954); however, the contradiction could be resolved if the selection criteria used (i. e., stretch sensitivity and twitch unloading) were also satisfied by some non-spindle afferents.

Other studies have relied upon muscle stretch to activate secondary spindle afferents. For example, Laporte and Bessou (1959), and more recently Cangiano and Lutzemberger (1972) observed inhibition of extensor motoneurons when muscle was stretched in the presence of group I electrical nerve blockade. This inhibition was attributed to secondary spindle receptor activation. However, it is quite possible that low-sensitivity stretch receptors were also activated by their stimulus.

In recent years a substantial body of indirect evidence has accumulated supporting an excitatory action of secondary spindle receptor afferents on extensor motoneurons (Matthews, 1969; Westbury, 1972; McGrath and Matthews, 1973; Kanda and Rymer, 1977). More recently, Kirkwood and Sears (1974), and Stauffer et al. (1976) have demonstrated the existence of an excitatory monosynaptic secondary afferent projection to extensor motoneurons.

While the existence of an excitatory secondary projection appears likely, the mechanism of the electrically induced inhibition remains to be explained. One current hypothesis requires that secondary spindle afferents also project to inhibitory interneurons, whose central action could be facilitated by supraspinal pathways, allowing "switching" between net synaptic excitation and inhibition (Lundberg et al., 1977). A simpler hypothesis (which we favour) suggests that secondary afferent projections to extensor motoneurons are exclusively excitatory in nature, whereas those of low-sensitivity stretch receptors are probably entirely inhibitory. Following partial spinal section, the inhibitory suppression which characterizes the decerebrate state is eliminated, and flexor reflexes arising from many afferents (including those from groups III, IV and non-spindle group II nerve endings) become manifest. Finally, electrical stimulation induces net inhibition because the low-sensitivity stretch receptor afferents are disproportionately potent (a proposition strongly supported by the dramatic effect of very localized stimulation of the muscle surface).

Evaluation of Human Studies

The interpretations advanced here are broadly consistent with published reports of clasp-knife behavior in quadriceps muscle of spastic man (Burke et al., 1970), in that the effect is manifested at the extremes of muscle stretch, and seems best developed when some level of force co-exists (Patton, 1965).

A more precise evaluation of the "low-sensitivity" stretch receptor hypothesis in man is presently limited by a lack of specific data; however, there are some observations which differ from our animal data. For example, Mark et al. (1968) and Burke et al. (1971) observed that slow extension of the triceps muscle in man, or maintained dorsiflexion of the ankle each produced clear-cut inhibition of the triceps H reflex. In both reports the effects were reproduced by tendon manipulation sufficient to alter muscle length, but inhibition was not reproduced by simple pressure on tendinous structures, i. e., muscle stretch receptors appeared to be necessary. This observation seems at variance with the marked tendon hypersensitivity observed in our animal preparations, however the differences may very well be produced by differences in central threshold in the spinalized vs. the intact state. Furthermore, it is not evident whether the reduction of the H reflex is directly related to the clasp-knife response or whether it is produced by some unrelated mechanism (such as occlusion or pre-synaptic inhibition). The clasp-knife reflex has also been reported to subside following muscle infiltration with dilute local anesthetic (Burke et al., 1970), suggesting that small diameter nerve filaments are involved. In addition, the reflex is preserved when large diameter afferent conduction is eliminated by ischemic limb blockade, further supporting a small fiber contribution. However, the latter procedures are relevant simply to fiber size and not to receptor origin; they do not distinguish between different types of groups II and III fibers.

Functional Role of the Clasp-knife Reflex

Groups III and IV muscle afferents respond to a variety of stimuli-thermal, chemical, noxious, and mechanical. Within the context of our experiments, the properties of the low-sensitivity stretch receptors would support some sort of protective role much like that originally proposed for tendon organs (Fulton and Pi-Suner, 1928). The central effects of these afferents could conceivably be manifested only following release of flexor afferent action, as in the spinalized state. Alternately, they could serve as a source of inhibition causing limb collapse when various muscles or tendons are subjected to major unexpected strain in normal subjects.

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