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INHIBITION OF MONOSYNAPTIC REFLEXES IN THE HUMAN LOWER LIMB

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SUMMARY

1. Presynaptic inhibition of muscle spindle Ia afferents by afferents from the same and other muscles has been studied in the human lower limb. The experiments have utilized conditioning of test monosynaptic reflexes by vibration of both the test and other muscles.

2. The pattern of inhibition invariably includes autogenetic actions.

3. There are powerful effects from flexor to extensor Ia afferents. Actions from flexor to flexor, and from extensor to extensor, are weaker. Actions from extensors to flexors are very weak.

4. The strength of presynaptic inhibition from one muscle type to another weakens as the muscles considered become more anatomically distant.

5. The inhibition studied both by vibration and by electrical conditioning stimulation of nerves becomes weaker during voluntary isometric contraction of the test muscle. It is strongest at rest and during antagonist contraction.

6. Evidence is provided suggesting that descending control is the primary cause of this modulation of inhibition during contraction.

7. Stimulation of afferents in cutaneous nerves reduces group I presynaptic inhibition of Ia afferents.

INTRODUCTION

Electrical stimulation of afferent axons from muscle spindles in the human soleus induces a monosynaptic reflex discharge in some of the motoneurones, the H reflex. Mechanical vibration of soleus also excites muscle spindles. However, vibration, far from facilitating the H reflex, actually inhibits it. This inhibition has consequently been termed 'paradoxical' (Desmedt & Godaux, 1978).

The generally held explanation for this phenomenon is that muscle spindle primary afferents provide both monosynaptic excitation of motoneurones and presynaptic inhibition of themselves. This presynaptic inhibition of the monosynaptic pathway outweighs the excitatory action during vibration of the human soleus.

A number of objections to this interpretation have been raised (see Discussion). In the present work an attempt has been made to examine systematically the

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vibration-induced inhibition of reflex activity in a number of muscles of the human lower limb. Other forms of conditioning stimulation have been used for comparison. The strength of all these putative presynaptic inhibitory actions has been monitored during voluntary muscle contraction.

A brief report of some of this work has been published (Iles & Roberts, 1981).

METHODS

Experiments were performed on sixteen young adult (18–39 years) subjects of both sexes with their informed consent. None had any history of neurological disease. At least one of the authors was used in every type of experiment. Subjects are identified by initials in some Figures.

The basic procedure was to set up a test monosynaptic reflex in a given muscle (the 'test' muscle) when it was at rest or maintaining a constant isometric force and then to evaluate the conditioning effect of vibration of the same or other muscles. This use of the expressions 'test reflex' and 'conditioned reflex' conforms to that of Lloyd (1946).

The test monosynaptic reflex

Subjects were placed in a sitting position with knee and ankle joints close to 120 and 100 deg respectively (Hugon, 1973); except for a few experiments involving stimulation of the femoral nerve when the subject was placed supine to improve access. Reflexes were induced at a frequency close to 0·2 Hz in any of the following ways.

Electrical stimulation of the muscle nerve. Long-duration square-wave voltage pulses (0·5–1·5 ms) from isolated stimulators (Digitimer Mk IV, DS2 and 3072) were used to favour excitation of afferent fibres. The stimulus was usually adjusted to produce a very small direct muscle response as a monitor of the stability of the stimulation conditions. The tibial nerve (soleus reflex) was stimulated in the popliteal fossa with a Simon (1962) electrode; the anode was placed on the medial side of the knee. The common peroneal nerve (tibialis anterior reflex) was stimulated at the head of the fibula, the cathode position being adjusted to favour tibialis anterior contraction over that of the peronei; the anode was located just below the patella. The sciatic nerve was stimulated with a cathode just under the edge of gluteus maximus and an anode 4·5 cm more lateral; the same type of electrode was used on the femoral nerve (quadriceps reflex), where it passes under the inguinal ligament (Smorto & Basmajian, 1979), though in some cases a separate anode was placed near the head of the femur.

Monosynaptic reflexes induced electrically will be referred to as H reflexes.

Rotation at the ankle joint (reflexes in tibialis anterior and soleus). The foot was strapped to a platform which could rotate around an axis aligned with the ankle joint. The platform was coupled to the shaft of a $\frac{3}{4}$ horse power single-phase induction motor. The start winding of the motor was permanently energized (110 V, 8 A r.m.s.). To generate torque pulses and rotate the ankle joint a variable proportion of the supply voltage was switched to the main motor winding (currents up to 20 A r.m.s.). The briefest torque pulse had a 10–90 % rise time of 2 ms, duration at half amplitude of 8 ms, and amplitude up to 8 N m.

Movement of the hallux (reflex in flexor hallucis longus). A probe, 14 mm in diameter with its end fashioned to an oval section, was attached to the driving spindle of a vibrator by a sliding sleeve incorporating a compression spring. The ball of the large toe was placed on the probe and pushed down until the spring was just completely compressed (two springs requiring forces of 4 and 8 N respectively could be used). The foot and proximal phalanx were clamped between rubber-cushioned rods. The vibrator (Ling Dynamic Systems U.K., model 200) was driven from a 12 V direct current supply (automobile battery). Relays were used to simply short circuit the battery through the vibrator winding for 15 ms. The probe moved with a velocity of 2 ms^{-1} for 1 ms and then slowed. The total movement was 3·5 or 4·5 mm, with the weaker and stronger springs, respectively. This high velocity of stretch favoured the appearance of monosynaptic over longer latency responses.

Percussion of the patellar tendon (quadriceps reflex), and of the tendon of the short head of biceps femoris. The same vibrator and probe as described above were used.

Monosynaptic reflexes induced by mechanical stimulation will be referred to as M_1 reflexes.

Control of voluntary contraction

During the experiment the subject maintained a constant voluntary force in the test muscle or its antagonist. In experiments on soleus and tibialis anterior, tension springs attached to an arm on the motor shaft provided calibrated torques resisting either plantar or dorsiflexion. Ankle angle was monitored with a potentiometer on the motor shaft. Position was displayed to the subject who was required to keep ankle angle at 100 deg. The experiments were thus performed under effectively isometric conditions. The same arrangement was used whether reflexes were induced by mechanical or electrical stimulation. Plantar flexion torque is defined here as positive; dorsiflexion torque as negative.

In experiments with biceps and quadriceps, voluntary effort was assessed with a spring balance attached to the limb, or from a rectified integrated electromyogram whose value was displayed to the subject (cf. Stokes, Iles & Young, 1985).

In the case of flexor hallucis longus, effort was determined by the choice of compression spring (4 or 8 N) in the vibrator probe (see above).

Conditioning by vibratory stimulation

A physiotherapy vibrator (Pifco) operating at 100 Hz, peak to peak amplitude 0·5–1 mm under load, was applied to the muscle being used to produce the conditioning stimulus. Provided sufficient pressure was utilized there seemed to be no consistent difference between vibration of a muscle tendon or its belly. These parameters of vibration are known to provide effective presynaptic inhibition when used on soleus (Desmedt & Godaux, 1978). During control periods the vibrator was left active but lifted slightly away from the limb. For conditioning by quadriceps the vibrator was located over rectus femoris, though it must have activated receptors in most heads of the muscle.

In some experiments with soleus as test muscle pulsed vibration (2–3 cycles at 100 Hz) was applied to tibialis anterior as the conditioning stimulus. The vibration was timed to end 35–60 ms before each conditioned reflex.

Conditioning by electrical stimulation of muscle nerves

Electrical stimulation of nerves for conditioning was arranged using the same methods as described above for production of reflexes. An electromyograph was monitored in order that conditioning stimuli could be expressed in multiples of the strength just required to excite motor axons (alpha threshold: αT).

In some experiments the sural nerve was stimulated at the lateral malleolus at a strength 5 × perceptual threshold.

Recording monosynaptic reflexes

Electromyographic records were made with pairs of surface electrodes (electrocardiogram electrodes) attached over the chosen muscle. A single earth connexion was made close to these recording electrodes. In the case of flexor hallucis longus, the electrode positions were those used by Marsden, Merton & Morton (1976). Hamstring records were taken from the short head of biceps. Quadriceps records were taken with electrodes over the distal part of rectus femoris or vastus lateralis (Guiheneuc & Ginet, 1974).

The records were amplified, rectified and averaged as described in an earlier paper (Iles, 1977). Generally sixteen control and sixteen conditioned reflexes were averaged. Timing was controlled with a modified Digitimer D4030 Programmer and a BBC model B microcomputer. When muscle vibration was used as the conditioning stimulus control reflexes were recorded before the conditioned ones, and at least 3 s of vibration were applied before recording started. Reflexes were usually elicited throughout the experiment, whether being recorded or not, in order to avoid the period of depression of amplitude found at the beginning of a train of reflexes.

When electrical stimulation or pulsed vibration were used for conditioning, conditioned reflexes were interpolated between test reflexes, either randomly or alternately (no differences were noted between the two methods: cf. Fournier, Katz & Pierrot-Deseilligny, 1984).

The area above base line of the averaged reflexes was measured using an integration facility. The effect of conditioning stimulation was expressed by calculating the conditioned as a percentage of

the test reflex (C/T%; cf. Lloyd, 1946). In one subject in whom the reflex response from quadriceps appeared to have two components (Kudina, 1981) both were included in the integral.

In the experiment illustrated in Fig. 1*A* single rectified H reflexes were measured (base line to peak) using a Grafitek TSR3 recorder and BBC B computer.

Statistical methods

Up to ten paired averaging runs were performed under any set of conditions on one subject. To assess whether various muscles used for the conditioning vibration produce different strengths of action the Friedman 2-way analysis of variance by ranks was applied to the grand averages for all subjects; for comparison of actions from just two muscles the Wilcoxon matched pairs signed-ranks test was used (Siegel, 1956). In all cases the probabilities quoted refer to 2-tailed tests.

In order to test for a relation between strength of inhibition and voluntary torque the Spearmann rank correlation coefficient was calculated (cf. Iles, 1986).

Spread of vibratory conditioning stimulation

The data obtained in the present study showed that inhibition can be elicited in a test muscle by vibration of most other muscles of the lower limb. The possibility that this was simply due to spread of mechanical vibration was examined using the basic technique described by Dindar & Verrier (1975) which consists of examining the effect of blocking the common peroneal nerve on vibratory conditioning of a soleus test reflex.

Xylocaine (10 ml of 2% (w/v) solution with adrenaline 1:200000) was injected close to the common peroneal nerve behind the head of the fibula. This produced deep anaesthesia in the region of innervation and foot drop lasting 3–4 h.

Data from two blocking experiments on subject J.F.I. were combined. The inhibition produced by soleus vibration fell by about 8% (range 0–19) during the nerve block and the effect of semitendinosus vibration showed no clear change. The effectiveness of vibrating tibialis anterior fell by about 76% (range 72–79). The small remaining inhibition from pretibial vibration presumably results from vibration spread to triceps surae. This experiment indicates rather limited spread of the conditioning stimulus between pretibial and post-tibial compartments and across the knee joint.

Dindar & Verrier (1975) reported a reduction of inhibition from gastrocnemius–soleus vibration of 28%; this is significantly greater than the 8% we have found. The difference can probably be accounted for by the fact that our experiments were performed during soleus contraction (+5 N m): this may have made its muscle spindles more sensitive to vibration than those in the passive pretibial muscles.

The following abbreviations have been used on the Figures: b., biceps femoris; g.–s., gastrocnemius–soleus; q., quadriceps; s.t., semitendinosus; t.a., tibialis anterior; αT, alpha motoneurone axon threshold for electrical stimulation; C/T%, the action of a conditioning stimulus on a test reflex expressed in the form conditioned reflex as a percentage of the test reflex; D_1, long latency inhibition of a soleus monosynaptic reflex from the common peroneal nerve; H reflex, Hoffmann reflex: M_1 reflex, monosynaptic reflex induced by muscle stretch.

RESULTS

Variability in reflex amplitude and conditioning action

The reliability of the experimental method was investigated in experiments on subjects J.F.I. and J.V.P. using soleus test reflexes.

The amplitude of 256 successive H reflexes is illustrated in Fig. 1*A*. During the second and fourth quarters of the recording period ankle and knee flexor muscles were vibrated respectively. Both conditioning stimuli inhibited the reflexes, the ankle flexor vibration having most effect. The inhibition had a rapid onset and offset under these conditions of steady voluntary contraction (all reflexes were recorded; cf. Delwaide (1973) for autogenetic actions at rest).

In Fig. 1*B* the experiment was repeated with the reflexes averaged in groups of

sixteen. The same relative effect of ankle and knee flexor vibration can be seen (the test reflex was somewhat smaller, and the level of inhibition slightly higher in this stage of the experiment: no adjustments were made to the test stimulus). More importantly, the standard error of the mean reflex amplitude was identical whether

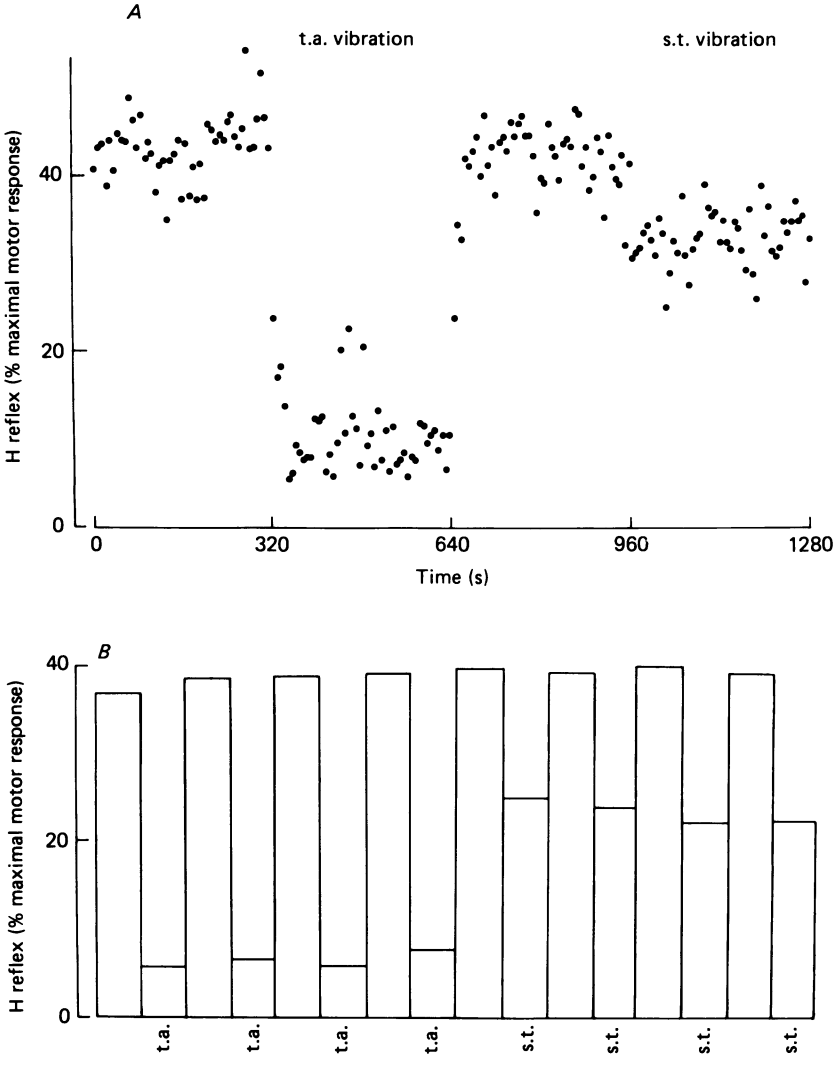

Fig. 1. The effect of muscle vibration on the soleus H reflex (subject J.F.I., torque +4 N m, plantar flexion). *A*, the peak amplitudes of 256 successive reflexes induced at 0·2 Hz are plotted as a percentage of the maximal motor response that could be recorded from the muscle. In the second quarter of the recording period vibration was applied to tibialis anterior; in the fourth quarter vibration was applied to semitendinosus. *B*, the same experiment was performed (shortly after *A*) but groups of sixteen reflexes were averaged to produce the histogram columns. Although the data are represented on the same time scale as *A* and involve the same total number of reflexes, a rest period of about 1 min was employed between each average and vibration was applied for about 6 s before averaging commenced.

calculated from measurement of forty-eight individual reflexes or from four averages each of sixteen reflexes.

The amplitude of the control reflex was $0{\cdot}431 \pm 0{\cdot}005$ and $0{\cdot}413 \pm 0{\cdot}007$ from the two periods with single reflexes; $0{\cdot}382 \pm 0{\cdot}005$ and $0{\cdot}393 \pm 0{\cdot}002$ from the two periods with grouped reflexes (mean $\pm$ S.E. of mean). This level of variability within an averaging run was typical of both subjects examined. The variability between averaging runs was typical of all subjects.

Since grouping the reflexes into a series of averages had no effect on estimates of the mean or of its standard error this experimentally convenient method of grouping data was used.

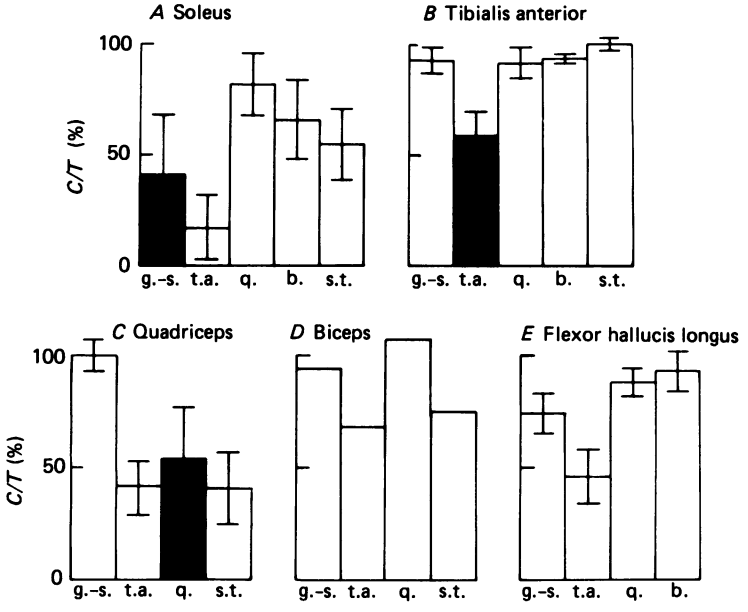

Fig. 2. Summary of the effects of muscle vibration on monosynaptic reflex amplitude for all subjects. The identity of the test muscle is given above each histogram. The conditioning effect is expressed in the form conditioned reflex as a percentage of test reflex amplitude (C/T%, ordinate, 100% is no effect). The muscles used for conditioning vibration are identified by abbreviations (see Methods) below the histogram columns. Filled columns refer to autogenetic actions. Each column represents the mean for all subjects with an estimate of the standard deviation.

The pattern of action from muscle vibration

Inhibition by muscle vibration of the reflexes in five different muscles is shown in Fig. 2 (*A–E*). The data for soleus are from eight different subjects studied during plantar flexion (Fig. 2*A*). Friedman's analysis of variance indicated highly significant differences in inhibition from the various conditioning muscles ($P < 0{\cdot}001$). In six of eight cases tibialis anterior produced most inhibition and quadriceps least. Inhibition from tibialis anterior was significantly greater than from gastrocnemius–soleus itself (Wilcoxon test: $P = 0{\cdot}05$). The same result was obtained in experiments in which the test reflex was induced mechanically by rotation of the ankle joint (M_1 reflex). Very weak inhibition was obtained from vibration of gluteus maximus in two subjects.

Data from all subjects has been averaged to produce Fig. 2. The absolute amount of inhibition varied between subjects. This variation was greater than that expected from repeated measurement on one individual (cf. Fig. 1*B*).

These early experiments were performed at a variety of torque levels (1·5–14 N m) but correction to a single torque level (using a relation derived from Figs. 3 and 4) did not reduce the variance to any extent.

This suggests that there are genuine differences in the strength of inhibition evoked by muscle vibration in different subjects (see also Fig. 1 in Iles & Roberts, 1986). For this reason the mean and an estimate of the standard deviation of the mean have been plotted in Fig. 2. This problem of individual differences in over-all level of inhibition was avoided in our statistical analysis by using the analysis of variance by ranks.

It was not always possible to elicit reflexes from tibialis anterior. Data from five subjects in whom a reflex was present during active dorsiflexion are presented in Fig. 2*B*. In all cases vibration of tibialis anterior itself produced inhibition, whereas vibration of other muscles had little effect (Friedman's analysis of variance: $P = 0{\cdot}03$).

Data from quadriceps in four subjects is illustrated in Fig. 2*C*. Vibration of quadriceps itself, the knee flexor semitendinosus and the ankle flexor tibialis anterior all produced inhibition. The ankle extensors were without effect (Friedman's analysis of variance: $P = 0{\cdot}03$). The same pattern of effects was found whether the reflex was induced by electrical or mechanical stimuli.

Reflexes from biceps femoris were induced by mechanical stimulation of the tendon of the short head and recorded from over the belly of the muscle. Vibration of semitendinosus and tibialis anterior both produced some inhibition in the one subject in whom a test reflex was easily evoked (Fig. 2*D*).

Reflexes in flexor hallucis longus were elicited by mechanical stimulation only. In the two subjects studied, vibration of tibialis anterior produced strong inhibition, and vibration of gastrocnemius–soleus had a smaller effect (Fig. 2*E*). Vibration of muscles acting about the knee joint was almost without action (Friedman's analysis of variance: $P = 0{\cdot}04$).

Muscle vibration failed to induce a tonic vibration reflex in most subjects under these conditions (steady voluntary isometric contraction). However, in some cases vibration of the test muscle did induce a reflex firing of its motoneurones. In these subjects autogenetic actions could not be studied. Clonus was not induced (though it did appear in spastic subjects: Iles & Roberts, 1986).

The data described above suggested a ranking of the strength of inhibitory action from different muscles in the following order (strongest first): (i) from the anatomically closest flexors (including autogenetic actions if the test muscle is a flexor), (ii) autogenetic actions if the test muscle is an extensor, (iii) flexor muscles operating at neighbouring joints, (iv) the nearest extensor muscle, (v) distant extensor muscles. This was confirmed by calculation of a Spearman rank correlation coefficient between conditioning muscle ranked in the above way and conditioning action from the data in Fig. 2. The correlation coefficient ($r_s = 0{\cdot}99$) is highly significant ($P < 0{\cdot}0005$).

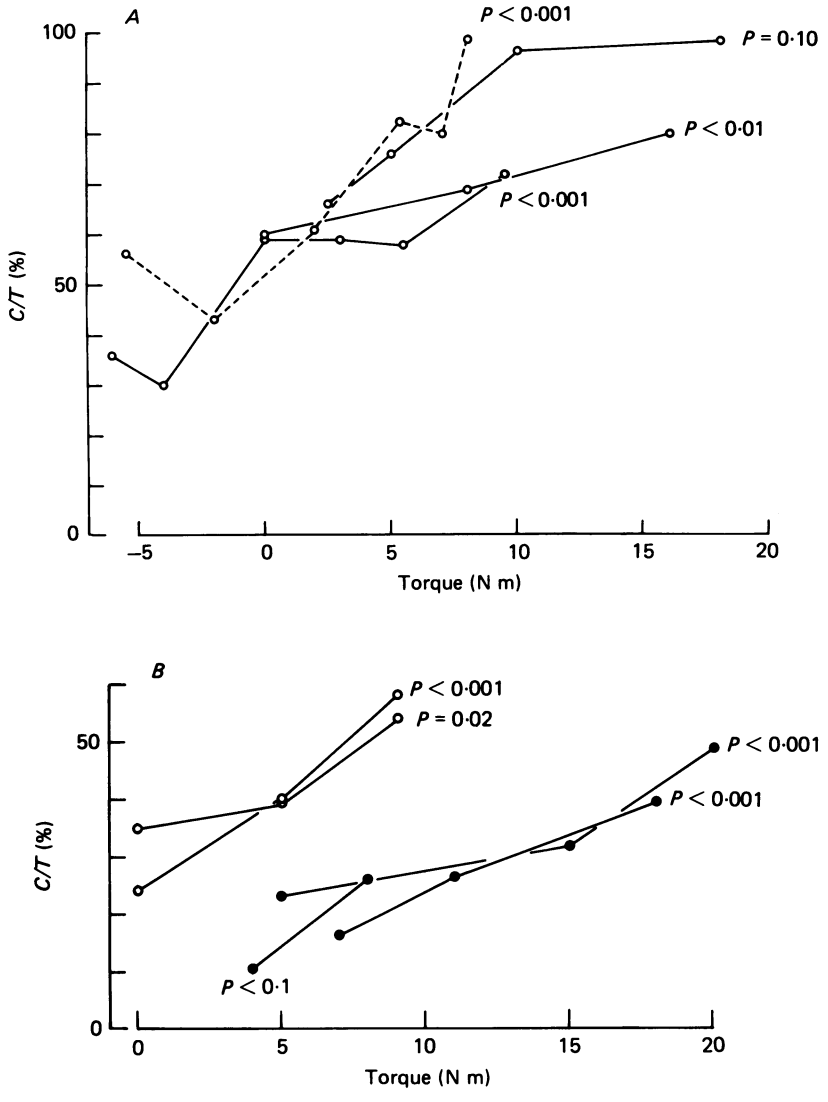

Fig. 3. *A*, soleus monosynaptic reflexes conditioned by vibration of knee flexor muscles (semitendinosus in two subjects, semitendinosus and biceps femoris in a third) at different levels of voluntary torque. Ordinate: inhibition expressed as the ratio of conditioned to test reflex amplitude (C/T%). Abscissa: torque (− torques refer to dorsiflexion and + torques to plantar flexion at the ankle). Spearmann rank correlation coefficients between C/T and torque were in all cases significantly different to zero (the 2-tailed probabilities are indicated). Each point in this and subsequent Figures represents the mean of the C/T values obtained from at least two pairs of averages (i.e. at least sixty-four reflexes). *B*, soleus H reflexes conditioned by pulsed vibration (open circles) and continuous vibration (closed circles) of tibialis anterior in three subjects at different torques. In these experiments the amplitude of the test reflex was maintained constant at different torques by adjustment of the test stimulus.

The effect of level of voluntary contraction on inhibition

This was examined in experiments using soleus as the test muscle.

Conditioning with muscle vibration. Inhibition was strong at rest and during ankle dorsiflexion but decreased with contraction of soleus itself. The statistical significance of the changes was tested by calculating the Spearman rank correlation coefficient between C/T and torque. The coefficients were always positive and the 2-tailed probability of a coefficient actually being zero was in all cases small (see legend to Fig. 3*A*).

In these experiments no attempt was made to keep the amplitude of the test reflex constant during changes in voluntary torque. When experiments were repeated with constant amplitude test reflexes (obtained by adjustment of the stimulus to the tibial nerve), identical results were obtained. This is illustrated for conditioning with continuous vibration of tibialis anterior in Fig. 3*B* (filled circles; compare with data in Iles & Roberts, 1986, Fig. 1).

Data obtained using a short burst of vibration to tibialis anterior as the conditioning stimulus is also illustrated in Fig. 3*B* (open circles). The inhibition produced by pulsed vibration was strong at rest and declined as voluntary contraction of soleus increased in strength.

Conditioning with electrical stimulation. Stimulation of the common peroneal nerve with a single shock, or two at 330 Hz produced inhibition of the soleus H reflex. Two phases of inhibition could be distinguished: one maximal at an interval of around 2 ms, the other extending from 10 to at least 100 ms. Both phases were recruited with conditioning stimuli at $0{\cdot}65 \times \alpha T$ (multiples of motor threshold). For subsequent experiments the conditioning stimulus was set just at motor threshold and a very small direct motor response was recorded from tibialis anterior as a monitor of constancy of the conditioning stimulus. With three or four conditioning stimuli the first phase of inhibition was somewhat obscured but the later phase was stronger and showed a clear peak about 25 ms after the last conditioning stimulus (Fig. 4*A*). This late phase of inhibition will be referred to as D_1 inhibition (Mizuno, Tanaka & Yanagisawa, 1971; Tanaka, 1974).

During contraction of soleus, both the early and late phases of inhibition from the common peroneal nerve were reduced. The behaviour of the late, D_1 inhibition is shown in detail in Fig. 4*B*. In all four subjects examined, inhibition declined with plantar flexion (the absolute levels of inhibition differed between subjects: this could reflect differences in the response of the conditioning nerve to stimulation or in central transmission; cf. results with vibratory conditioning). The inhibition did not seem to increase further during strong dorsiflexion.

The quadriceps H reflex was inhibited by electrical stimulation of the sciatic nerve at a strength close to motor threshold for biceps femoris. Just as with soleus, early and late phases of inhibition could be distinguished and the late phase of inhibition declined during stronger quadriceps contraction. Very little long-latency inhibition was apparent when tibialis anterior reflexes were conditioned by electrical stimulation of the tibial nerve. This is consistent with the conclusion drawn from experiments with vibratory conditioning that there is little presynaptic inhibition directed from ankle extensors to the flexor monosynaptic pathway.

The soleus H reflex was inhibited at long latency by electrical stimulation of the femoral nerve with shocks below threshold for direct or reflex activation of quadriceps motoneurones, thus

supporting the conclusion from experiments using vibration that there is weak inhibition directed from quadriceps to soleus. The reverse pathway could not be established unequivocally with electrical stimulation.

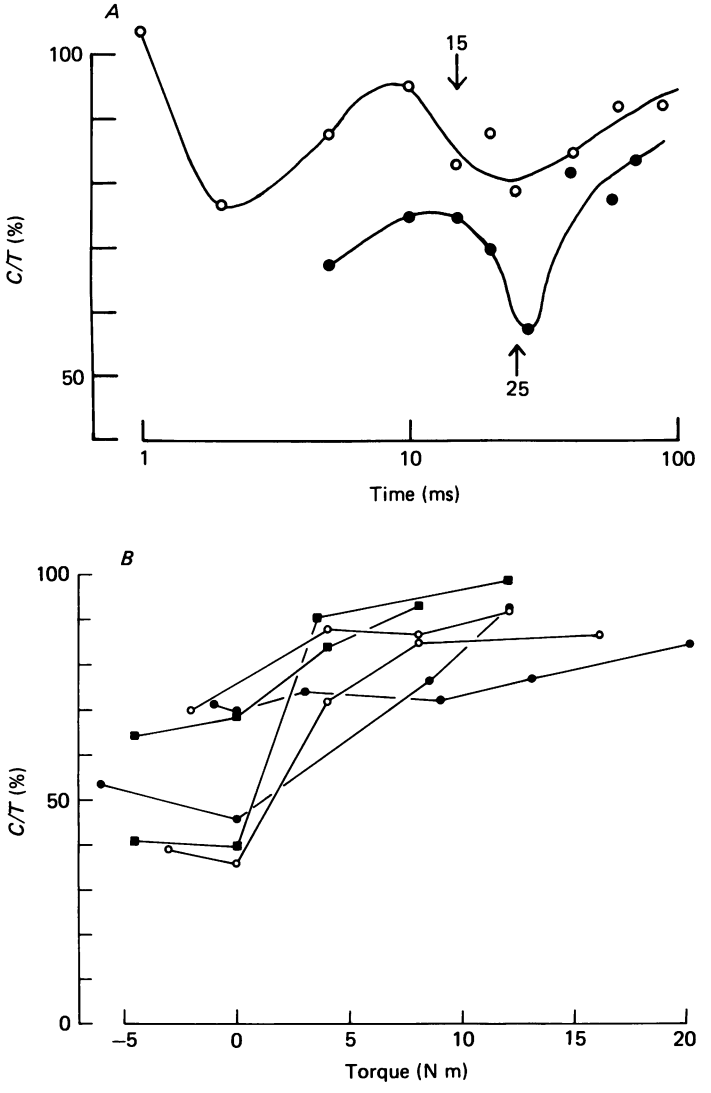

Fig. 4. *A*, time course of inhibition of the soleus H reflex produced by electrical stimulation of the common peroneal nerve (strength $1 \times \alpha T$) at rest. Inhibition was induced by either one (open circles) or three conditioning shocks (closed circles). All data points were obtained from one experimental session, though results from other experiments on the same subject (J.F.I.) were used as a guide when drawing the curves through the points. Note the logarithmic time scale. Vertical arrows at 15 and 25 ms indicate the conditioning intervals used in subsequent experiments. *B*, D_1 inhibition of soleus H reflexes at different levels of voluntary torque. Experiments with one to two conditioning shocks and three to four conditioning shocks are distinguished by circular and square symbols respectively. Open symbols refer to experiments without control of test reflex amplitude, closed symbols with constant test reflexes. Data from four subjects. There was a significant rank correlation between C/T and torque in all experiments ($P < 0{\cdot}05$, 2-tailed).

Changes in test reflex size

During changes in voluntary contraction test and conditioned reflex amplitudes *both* varied. As a strong plantar flexion was reduced the soleus test reflex fell in size, slowly at first but rapidly near zero torque. With dorsiflexion the reflex eventually vanished. However, in most of our subjects the strength of inhibition was unaffected by changes in test reflex amplitude *per se*, and a change in inhibition with changed torque was still observed if the test reflex was maintained at the same amplitude by adjustments to the test stimulus. A similarly small change in the strength of

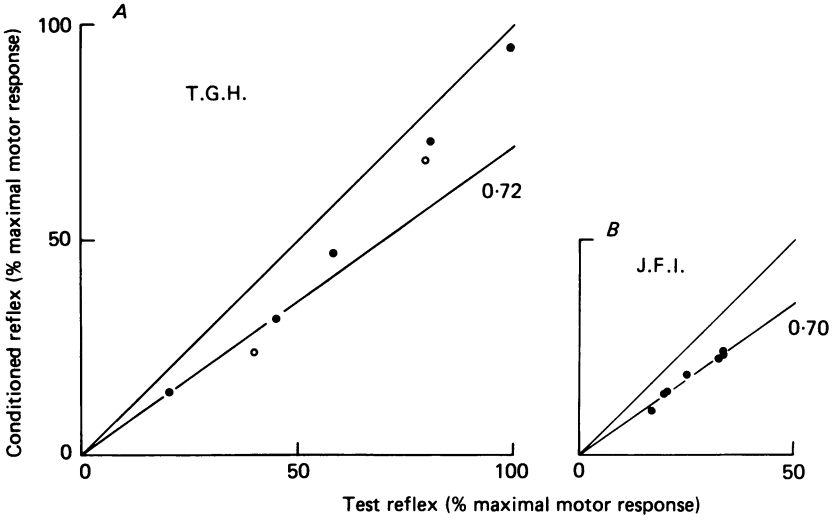

Fig. 5. Estimates of D_1 inhibition with different sized test reflexes. *A*, subject T.G.H. at rest (closed circles), conditioning stimulus 1·1 × αT, 15 ms before test. Note that for test reflexes < 50 % maximal motor discharge C/T is 0·72, for larger reflexes it is closer to 1. All the data points are from a single experimental session. Other experiments confirmed that the level of inhibition assessed with small reflexes corresponded to a C/T of around 0·7. Data obtained during dorsiflexion of −10 N m is indicated by open circles. *B*, subject J.F.I. at rest, all other parameters as for T.G.H. All reflexes are < 35 % maximal motor discharge and C/T is constant at 0·7. Randomized conditioning stimulation.

presynaptic inhibition over this range of reflex amplitudes can be seen in the H reflex recruitment curves presented by Delwaide (1971; our experiments were performed on the ascending limb of the recruitment curve). Desmedt & Godaux (1980) have also concluded, from a study of motor unit recruitment, that presynaptic inhibition is fairly uniformly spread over the population of monosynaptic afferents and motoneurones.

However, H reflexes in most of our subjects were small, not exceeding about 40 % of the maximal motor response. A different result was obtained in a subject (T.G.H.) in whom a maximal H reflex could be elicited in soleus without any direct muscle response, even during voluntary ankle dorsiflexion. The relation between estimate of D_1 inhibition and reflex size in this subject (and J.F.I. for comparison) is illustrated in Fig. 5. Conditioned reflex amplitude is plotted against test reflex amplitude, both

expressed as a percentage of the maximal direct muscle response (cf. Mazieres, 1983). For subject J.F.I., where the test reflex is always small, the data points fall on a regression line demonstrating a constant ratio, $C/T = 0{\cdot}7$. For subject T.G.H., data points for test reflexes less than 50 % of maximal motor response show about the same inhibition. However, estimates of inhibition made with larger test reflexes are smaller (the points fall closer to the line of unit slope). The same deviation was found in experiments performed during voluntary dorsiflexion and plantar flexion (cf. Iles & Roberts, 1986, Fig. 4).

The above result suggests that test reflex amplitude should be maintained constant by adjustment of the test stimulus in experiments of the present kind. However, this manoeuvre is not likely to produce exactly equivalent test reflexes (in terms of the population of motoneurones discharged) at different torques. Furthermore, it has the disadvantage of changing the size of the monosynaptic input volley which is being inhibited.

In order to demonstrate presynaptic inhibition of a constant afferent volley with constant amplitude of test reflex, an experiment analogous to that described by Morin, Pierrot-Deseilligny & Hultborn (1984) was performed. A small soleus H reflex was conditioned by a single mechanical stimulus to the Achilles tendon. This stimulus was kept sufficiently small so as not to itself induce a reflex discharge at zero torque. When the conditioning and test volleys were arranged to be coincident the reflex was facilitated. This facilitation can be attributed to Ia afferent action elicited by the mechanical stimulus. When the test reflex was preceded by a stimulus to the common peroneal nerve the facilitation from mechanical stimulation was reduced (from $C/T = 1{\cdot}93$ to $1{\cdot}32$, average of ten experimental runs on J.F.I.; the difference is statistically significant: Mann–Whitney U test, $P < 0{\cdot}002$, 2-tailed). The reduction in Ia action occurred even though the amplitude of the test reflex was kept constant by adjustment of the electrical stimulus to the tibial nerve. Thus a stimulus to the common peroneal nerve produces inhibition of a constant Ia input with a constant amplitude test reflex. Unfortunately, it is not prove feasible to use this experimental approach to study presynaptic inhibition during soleus contraction. This was because during soleus contraction conditioning facilitation always itself modulated discharge of soleus motoneurones. It was not possible to produce a subthreshold conditioning effect.

Effects on inhibition of stimulation of a cutaneous nerve

The effect of sural nerve stimulation was tested on D_1 inhibition of soleus in two subjects. The sural stimulus was applied before both test and conditioned reflexes (intervals between 21 and 37 ms; torque was changed between dorsiflexion and strong plantar flexion). The sural stimulus itself had very little effect on the soleus reflex at these intervals (cf. Delwaide, Crenna & Fleron, 1981).

No effect of sural stimulation could be found, although in the same experiments there was some increase of the shorter latency reciprocal inhibition. In the spinal cat, stimulation of flexor reflex afferents in the sural nerve inhibits Ia to Ia presynaptic inhibition (Lund, Lundberg & Vyklicky, 1965; Rudomin & Dutton, 1969). However, Rudomin, Jiminez, Solodkin & Duenas (1983) have shown that *strong* stimuli have to be applied to large cutaneous nerves to produce substantial effects in the cat.

In three subjects the experiment was repeated using a train of six shocks to the sural nerve at 300 Hz (19–39 ms before test). In these cases, sural stimulation consistently reduced D_1 inhibition (C/T changed from 0·69 to 0·77 in T.G.H., from 0·77 to 0·87 in J.F.I., from 0·72 to 0·77 in J.V.P., all subjects studied at rest). These reductions were significant when analysed by the Mann–Whitney U test ($P = 0{\cdot}036$, $P = 0{\cdot}025$, $P = 0{\cdot}075$ respectively, 1-tailed tests). The effect was confirmed using

pulsed vibration of tibialis anterior as conditioning stimulus to elicit presynaptic inhibition (C/T changed from 0·47 to 0·62 in J.F.I.; $P = 0·015$, 1-tailed). Thus the phenomenon described in the cat can be observed in man when using sufficient temporal summation of the sural action.

DISCUSSION

The nature of vibratory inhibition

In this paper one experimental approach has been to condition monosynaptic reflexes by muscle vibration. Many possible explanations could be put forward for the inhibition produced including specific presynaptic inhibitory mechanisms. The reasons for believing that the predominant action is presynaptic inhibition of Ia afferents have been discussed in detail (Ashby, Verrier & Carleton, 1980; Ashby, Verrier, Carleton & Somerville, 1980). Their reviews deal particularly with the action of vibration of the test muscle, and the arguments will not be repeated here. However, it can be noted that the choice of several *different* muscles for the conditioning stimulus in the present experiments also argues against some alternative explanations for the phenomenon. For example, inhibition produced by vibration of a distant muscle can hardly be attributed to occlusion of the test afferent volley or transmitter depletion in the monosynaptic pathway.

The pattern of inhibition was the same when either M_1 or H test reflexes were used in those muscles where the comparison was possible. Thus although M_1 and even H reflexes might include multisynaptic actions (Burke, Gandevia & McKeon, 1983), they nevertheless behaved identically. In the following discussion it will be assumed that the test reflexes are predominantly monosynaptic.

Greater difficulties accompany any attempt to distinguish quantitatively between presynaptic and post-synaptic components of the inhibition. In the cat, Cook & Cangiano (1972) showed that muscle vibration can reduce monosynaptic reflexes with no change in membrane potential or steady firing rate of a single motoneurone (though in some cases there were also post-synaptic changes). The analogous experiment has been performed in man by Ashby & Verrier (1980) who showed that vibration reduces the response of a single firing motoneurone to a Ia volley, even when mean firing rate was kept constant. This strongly suggests a presynaptic mechanism. To the extent that maintenance of constant torque in the present experiments reflects constant motoneurone firing, the inhibition of reflexes produced by muscle vibration will be predominantly presynaptic (see Iles & Roberts, 1986).

The pattern of presynaptic inhibitory action

The results described here suggest that Ia afferents from all muscles receive homonymous and/or heteronymous group I presynaptic inhibition (our experiments with vibration cannot distinguish homonymous and heteronymous actions). We will refer to these actions as autogenetic. In addition, there are powerful actions *from* flexor *to* extensor Ia afferents, weakening as the muscles examined become more anatomically distant. The converse action from extensors to flexors is very weak. Actions from flexors to flexors and from extensors to extensors acting about other joints are weak. This pattern is summarized in Fig. 6.

The pattern of local sign accommodates other observations reported on man. Many authors have noted autogenetic actions from soleus vibration. Autogenetic inhibition in another extensor, quadriceps, is mentioned by DeGail, Lance & Neilson (1966). Amongst flexors, Ashby & Verrier (1980) describe autogenetic actions in tibialis anterior and Delwaide (1971) reports a weak autogenetic action in biceps femoris. Strong actions directed from flexors to extensors are noted by Ashby, Verrier & Carleton (1980) and Delwaide (1971).

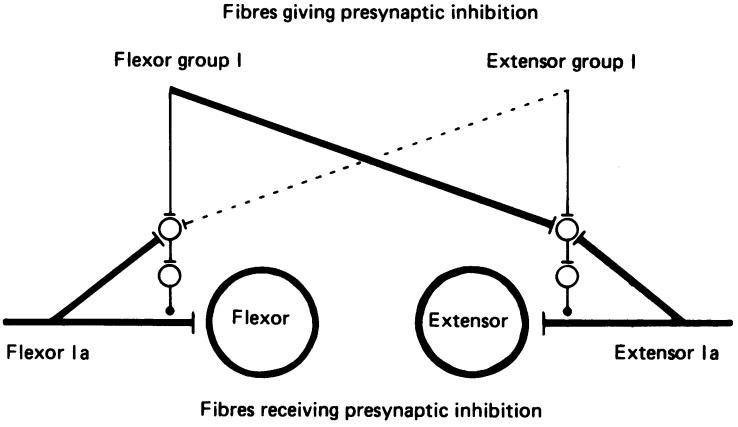

Fig. 6. Diagrammatic representation of the local sign of muscle group I to Ia presynaptic inhibition for the human lumbar cord. The thickness of the lines indicates the strength of the actions.

Older work on the cat demonstrated powerful effects directed from flexors to extensors, but only very circumscribed extensor actions (autogenetic actions in quadriceps: Eccles, 1964; Schmidt, 1971; but see Decandia, Provini & Taborikova, 1967, for triceps surae). More recently, other weak extensor effects have been described (Fu, Hultborn, Larsson & Lundberg, 1978; Brink, Jankowska & Skoog, 1984). With the rather incomplete data available for the cat, obtained from a variety of preparations, it is difficult to make a detailed comparison with man.

Changes in inhibition during voluntary contractions

In addition to continuous muscle vibration three other forms of conditioning action on the soleus monosynaptic reflex have been used: pulsed vibration of the antagonist, electrical stimulation of the antagonist nerve with one to two shocks and a 15 ms conditioning interval, electrical stimulation with three to four shocks and 25 ms interval. These have permitted investigation over a greater range of voluntary contraction.

With pulsed vibration of tibialis anterior a long conditioning interval was left between the end of vibration and the test reflex. This should allow time for any post-synaptic inhibition to decline, leaving longer latency presynaptic actions. The experiments are thus suitable for study at rest as well as during soleus contraction. However, they cannot be extended to active dorsiflexion because the muscle spindles of tibialis anterior may then become more sensitive to vibration (cf. Burke, Hagbarth, Lofsted & Wallin, 1976).

When using vibration of knee flexor muscles to provide the conditioning stimulus, the inhibitory actions could be predominantly presynaptic because post-synaptic actions are rarer between distant muscle groups (cf. Hongo, Lundberg, Phillips & Thompson, 1984, for the baboon and Pierrot-Deseilligny, Morin, Bergego & Tankov, 1981; Mao, Ashby, Wang & McCrea, 1984, for man). These experiments were therefore used over the full range of test and antagonist muscle contraction.

Electrical stimulation of the antagonist nerve provides a verifiably constant stimulus and also permits separation of post-synaptic and presynaptic components of inhibition on the basis of latency. The D_1 inhibition produced by three to four conditioning shocks has a time course very similar to the flexor group I presynaptic inhibition of extensor monosynaptic reflexes studied with the same parameters in the cat (Eccles, Schmidt & Willis, 1962). However, whereas experiments using mechanical conditioning stimulation can be expected to favour activation of muscle spindle Ia afferents, electrical stimulation will excite both components of the muscle group I and also some low threshold cutaneous afferents. In the cat cutaneous afferents make no contribution to presynaptic inhibition of Ia afferents (Eccles, Magni & Willis, 1962) except after L-DOPA (L-β-3,4-dihydroxyphenylalanine) treatment (see Lundberg, 1982). Nevertheless, with these provisos, electrical conditioning stimulation is suitable for the full range of test and antagonist muscle contraction.

Although each experimental protocol has its own limitations, it is likely that a component of group I presynaptic inhibition of Ia afferents is common to all of them. In all cases the strength of inhibition was maximal at rest and during antagonist contraction; it declined with contraction of the test muscle.

Descending and peripheral control of presynaptic inhibition

Although it might be assumed that the changes in strength of presynaptic inhibition observed during contraction result from descending control, this need not be the case. Muscle contractions excite flexor reflex afferents (Lundberg, 1979) which are known to reduce presynaptic inhibition of Ia afferents in the cat (Lund *et al.* 1965). Other peripheral receptors could also be involved. Peripheral and descending controls could converge at an interneuronal level.

In the experiments described here we were able to produce some reduction of presynaptic inhibition with peripheral (cutaneous nerve) stimulation. However, because there are differences in the strength of presynaptic inhibition and its voluntary control in subjects with upper motoneurone disease (Iles & Roberts, 1986), and changes have been reported during sleep (Shimoji, Ito & Channa, 1975), we are inclined to ascribe the modulation during contraction to some form of descending control. This interpretation is supported by the work of others (see below) which suggests that presynaptic inhibition is reduced before a voluntary contraction, and thus before any change in peripheral input.

Some reduction during contraction of the inhibition of soleus reflexes produced by vibration can be seen in Delwaide's work (1971, his Fig. 23), and Delwaide & Hugon (1969) reported that contraction abolished depression of the soleus reflex produced by sinusoidal ankle movement. A reduction of D_1 inhibition during soleus contraction is present in the data of El-Tohamy & Sedgwick (1983; the C/T ratio was 0·26 during dorsiflexion and 0·38 during plantar flexion).

An apparent reduction in presynaptic inhibition during soleus contraction could be produced by occlusion if increased soleus Ia afferent activity in an isometric contraction produces homonymous presynaptic inhibition. This explanation does not seem very likely because the presumably much greater Ia firing produced by soleus vibration did not occlude D_1 inhibition.

Two further difficulties attend experiments with contraction. First, contraction may, by movement, alter the conditioning stimulus. With electrical conditioning we checked thresholds and with vibration included distant muscles where movement should be slight. It would be surprising if undetected alterations in the different conditioning stimuli always led to the same changes in presynaptic inhibition with contraction. It is worth noting with respect to this problem that several authors have concluded that there is an increase in soleus presynaptic inhibition *before* a voluntary contraction of tibialis anterior and a decrease *before* contraction of soleus itself (see Discussion in Schieppati, Nardone & Musazzi, 1986). Since these changes precede the movement there can be no movement artifact.

The second difficulty is that reflex amplitude changes during contraction. This could by itself lead to changes in the estimates of inhibition (Mazieres, 1983). This problem and experiments designed to maintain constant-amplitude test reflexes are described in the Results. However, even with maintenance of a constant-amplitude reflex there is no certainty that precisely the same population of Ia afferent-motoneurone synapses is being studied at different levels of contraction. The possibility remains, therefore, that some of the changes in presynaptic inhibition with contraction reflect changes in the motoneurone pool (cf. Zengel, Reid, Sypert & Munson, 1983). This would not, however, diminish their functional significance.

Nevertheless, it seems likely that presynaptic inhibition is under descending control during voluntary movement and that peripheral control, or changes linked to the recruitment of motor units play a minor part. Pathways of descending control have been described in the cat (see Lundberg, 1982).

Functional implications

An autogenetic pathway of group I presynaptic inhibition has been detected in all the muscles examined. Such action will reduce the efficacy of feed-back from Ia afferents to motoneurones. Presynaptic inhibition from other muscle groups will contribute further to this. The descending inhibition of these pathways provides a mechanism for *selective* increase in the gain of servo-assistance during voluntary muscle contraction (cf. discussion of peripheral control in Mendell, 1972). The possibility remains open that in other motor tasks the gain of this pathway could be controlled more independently of the strength of muscle activation (e.g. different levels of presynaptic inhibition during walking and voluntary soleus activation have been inferred by Morin, Katz, Mazieres & Pierrot-Deseilligny, 1982). A clear analogy exists with the function proposed for descending control of recurrent inhibition by Hultborn, Lindstrom & Wigstrom (1979), except that in the latter case the changes in gain during voluntary contraction would apply *unselectively* to all the excitatory inputs of a pool of motoneurones, and extend also to γ-motoneurones and reciprocal inhibition.

The strongest component of presynaptic inhibition is directed from flexors to extensor Ia afferents. This pathway will contribute to reciprocal innervation (even

though the reverse action is weak; such a bias in inhibition from flexors to extensors has long been known to exist in the cat: Sherrington, 1906). Voluntary flexor muscle contraction with servo-assistance would automatically reduce the gain of the antagonist stretch reflex. During extensor muscle contraction, reduction in presynaptic inhibition would increase gain. This view is supported by data from subjects with upper motoneurone disease (Iles & Roberts, 1986).

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