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ROLE OF SMALL DIAMETER AFFERENTS IN REFLEX INHIBITION DURING HUMAN MUSCLE FATIGUE

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SUMMARY

1. Previous work has shown that the H reflex excitability of the human soleus motoneurones is reduced during fatigue and is accompanied by a corresponding decrease in electromyographic (EMG) activity during maximal voluntary contractions. These findings were consistent with the existence of a reflex whereby α-motoneurones are inhibited by sensory input from the fatigued muscle.

2. To elucidate the contribution of different-sized afferents in such reflex inhibition, compression of the sciatic nerve was used in an attempt to block large myelinated afferents prior to fatigue.

3. Fatigue of the soleus muscle was induced under ischaemic conditions by intermittent electrical stimulation at 15 Hz in ten healthy subjects. These subjects also participated in a control test in which the compression block was followed by ischaemia without fatigue.

4. Following nerve compression alone, both the mean maximal plantarflexion torque and the associated EMG for all ten subjects declined by $18{\cdot}8 \pm 16{\cdot}2\%$ (S.D.) and $13{\cdot}4 \pm 17{\cdot}2\%$, respectively.

5. Following fatigue, there were five subjects in whom the large afferents remained blocked and the experimental findings were consistent with the existence of reflex inhibition during fatigue. The mean maximal plantarflexion torque decreased further by $36{\cdot}2 \pm 7{\cdot}6\%$ from the value following the compression block compared to a decrease of $5{\cdot}0 \pm 9{\cdot}9\%$ in the ischaemia control. The mean EMG associated with these contractions also decreased from post-block values by $56{\cdot}8 \pm 19{\cdot}6\%$ following fatigue and by only $6{\cdot}4 \pm 8{\cdot}0\%$ following ischaemia alone.

6. The peripheral excitability of the neuromuscular junction and muscle fibre membrane was adequate following fatigue as evidenced by only modest changes in the M wave (muscle compound action potential). The descending motor drive was deemed sufficient because of the absence of any large interpolated twitches superimposed upon the maximal voluntary contraction in all but two subjects.

7. The declines in maximal plantarflexion torque and the associated EMG activity were very similar to those found in a previous study in which the sensory input was unaltered. The findings demonstrated that any reflex inhibition of the α-motoneurone

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pool during fatigue was probably not mediated by large diameter afferents. Rather, it is suggested that the reflex is mediated by smaller diameter afferents originating from the fatigued muscle.

INTRODUCTION

Recent work has shown that the H reflex excitability of the human soleus motoneurones is reduced fatigue and is accompanied by a corresponding decrease in electromyographic (EMG) activity during maximal voluntary contractions (Garland & McComas, 1990). The reduction in α-motoneurone excitability in that study could not be accounted for by a failure of central (descending) motor drive or by peripheral inexcitability. Nor could it be explained as an artifact of the stimulation regimen or ischaemia employed to produce the fatigue. Rather, the findings were consistent with the existence of reflex inhibition of the α-motoneurone pool brought on by sensory input from the fatigued muscle (Woods, Furbush & Bigland-Ritchie, 1987).

The purpose of the present study was to determine the type of afferent fibre mediating the putative reflex inhibition during fatigue. This information would help to elucidate the nature of the stimulus which may serve to match motoneurone output to the functional status of the muscle fibres during fatigue. The sensory discharge could arise from receptors sensitive either to mechanical changes in the contractile properties of the exercising muscle or to metabolic and ionic changes (Bigland-Ritchie, Dawson, Johansson & Lippold, 1986), or to both. Large myelinated afferents responding to mechanical events include Ia and II afferents supplying muscle spindles and Ib afferents supplying Golgi tendon organs. Smaller diameter afferents among group III (Mense, 1977) and group IV (Kniffki, Mense & Schmidt, 1978) fibre populations can be activated by chemical stimulation as well as by muscle contraction (Kniffki *et al.* 1978). Some of the group III and IV mechanoreceptors also exhibit a low sensitivity to muscle stretch (Houk & Rymer, 1981).

Smaller diameter fibres are likely candidates because, both in our previous study (Garland, Garner & McComas, 1988) and that of Bigland-Ritchie *et al.* (1986), EMG during fatigue remained depressed as long as the limb was rendered ischaemic. This suggested a chemical stimulus and it is known that only the small diameter fibres are chemosensitive (Hasan & Stuart, 1984).

In this study, a partial compression block of impulse conduction in the sciatic nerve was employed to elucidate the contribution of different-sized afferents to the reflex inhibition. Compression blocks are known to be more effective for afferent than efferent fibres (Magladery, McDougal & Stoll, 1950; Moddel, Best & Ashby, 1977) and the impulse conduction block progresses according to fibre size, with large myelinated afferents being affected first, followed by small myelinated afferents and lastly by unmyelinated afferents (Zotterman, 1933; Torebjork & Hallin, 1973; MacKenzie, Burke, Skuse & Lethlean, 1975). In the present study, if the EMG decreased during a maximal plantarflexion contraction of the fatigued soleus muscle with impulse blockade of the large afferent fibres, then the small diameter afferents would be more likely to be implicated in the reflex inhibition. A brief report of this work has appeared elsewhere (Garland & McComas, 1988).

METHODS

Subjects

Ten healthy volunteers of both sexes, aged 20–36 years (mean of 26 years), participated in the study; approval was obtained from the University Ethics Committee. None had any history of neuromuscular or vascular disease.

Evaluation and fatigue procedure

Subjects sat upright in a hard chair with the head and arms supported. Both legs rested in metal supporting frames and were clamped into position, so that the knees and ankles were held at 90 deg; the right foot was strapped onto an aluminium foot plate which housed strain gauges to measure torque (Marsh, Sale, McComas & Quinlan, 1981). A blood pressure cuff was wrapped around the middle portion of the right thigh and was inflated to at least 350 mmHg during the experiment. Inflation of the cuff served to augment and maintain the fatigue process in soleus muscle (an inherently fatigue-resistant muscle). A differential compression block of the sciatic nerve was introduced prior to fatigue and maintained throughout the experiment.

After preparing the skin with alcohol and conducting cream, stimulating electrodes, constructed of lead-plate, were positioned bilaterally for the H reflex and M wave testing. The H (Hoffmann) reflex was evoked by electrical stimulation of Ia afferent fibres in the posterior tibial nerve. The M wave (muscle compound action potential) was evoked by supramaximal stimulation of the motoneurones in the posterior tibial nerve. For each leg, the cathode ($4{\cdot}5 \times 2{\cdot}5$ cm) was placed in the popliteal fossa over the posterior tibial nerve and the anode (8×8 cm) was placed superior to the patella. For H reflex testing, single rectangular pulses of 0·5 ms duration were delivered every 5 s from a stimulator (Devices Ltd, model 3072), itself controlled by a digital timing unit (Digitimer, model 3290). The stimulus intensity was adjusted until a maximal H reflex was recorded. Maximal M waves were elicited with the same stimulating electrodes and stimulator (50 μs pulses of 160–360 V).

The recording electrodes for H reflexes, M waves and the EMG associated with maximal voluntary contractions were silver disc electrodes, 1 cm in diameter, placed on both legs approximately 6 cm above the superior aspect of the calcaneus. The ground electrodes were attached to the skin between the stimulating and recording electrodes while the reference electrodes were fastened over the dorsum of each foot; all four electrodes were silver strips, $5 \times 0{\cdot}7$ cm.

EMG activity associated with the maximal voluntary contractions was amplified (10 Hz to 1 kHz) and displayed on a variable-persistence storage oscilloscope (Hewlett–Packard model 141B). The EMG was subsequently full-wave rectified and integrated for the first second of contraction by a programmable desk-top calculator (Hewlett–Packard model 9810A). The amplitude and area of the M waves were calculated with a computer program. All recordings of torque and EMG were stored on FM tape for subsequent analysis.

The right soleus was fatigued with submaximal indirect electrical stimulation (140–160 V) at 15 Hz under ischaemic conditions. This frequency was chosen to minimize peripheral fatigue (Garland *et al.* 1988) and to be within the physiological firing range for soleus motoneurones (Bellemare, Woods, Johansson & Bigland-Ritchie, 1983). The stimuli were rectangular voltage pulses of 50 μs duration; the stimulator (Devices, model 3072) received triggering pulses from a digital timing device (Digitimer, model 3290) through a gated pulse generator (Devices, model 2521). The stimulating electrodes were two lead plates; the cathode ($7{\cdot}5 \times 5{\cdot}5$ cm) lay over the soleus muscle belly 3 cm above the stigmatic recording electrode while the anode (12×7 cm) was slightly more proximal and over the distal gastrocnemius muscle bellies. The trains of stimuli at 15 Hz were repeated every 10 s (7 s on, 3 s off) for 4–5 minutes until the tetanic torque had fallen, in most experiments, by more than 80 % of the control value. The onset of any efferent block of motor axons was monitored with contractions of the flexor hallucis longus muscle during the rest period between trains of stimuli. Since both soleus and flexor hallucis longus are innervated by the tibial nerve, any block of the efferent axons due to compression would be evident in weakened contractions of the non-fatigued flexors of the great toe.

Experimental protocol

The ten subjects were tested on two different occasions. The tests consisted of: test 1, differential compression block of the sciatic nerve followed by fatigue under ischaemic conditions; and test 2,

differential compression block of the sciatic nerve followed by ischaemia but without fatigue (Fig. 1).

Pre-test measures consisted of the average of seven maximum H reflexes and two maximal M waves in each of the two legs. On the right side, recordings were also made of maximal plantarflexion torque (with an interpolated stimulus; two pulses at 100 Hz), and the associated

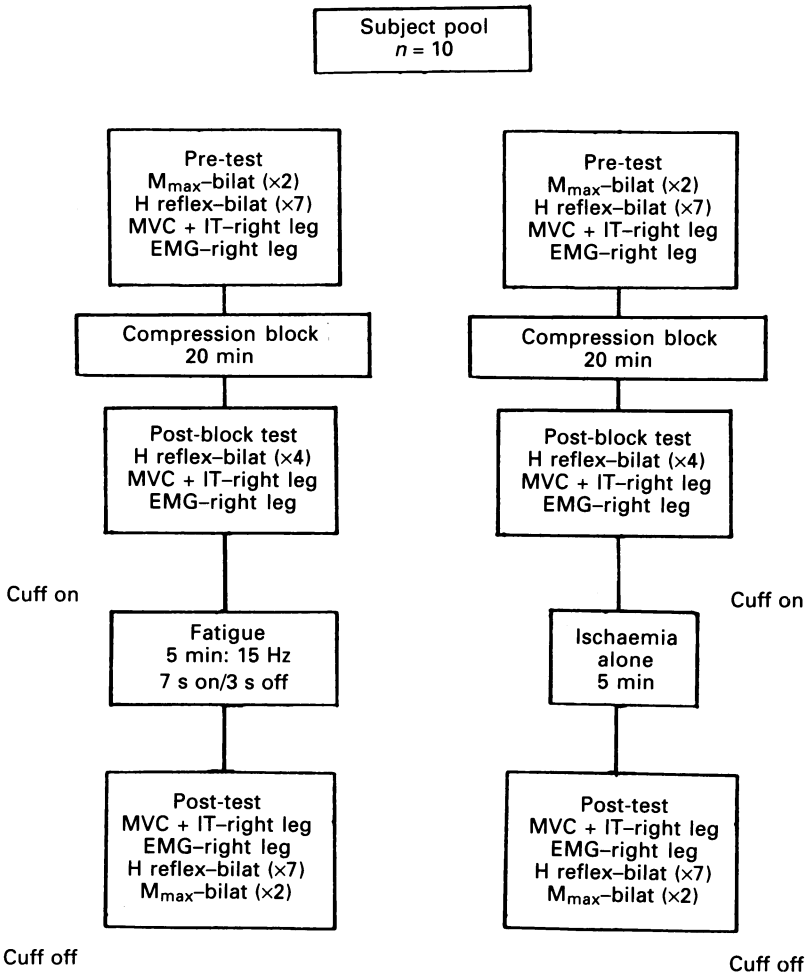

Fig. 1. Experimental protocol illustrating test 1 (fatigue) on the left and test 2 (ischaemia control) on the right. M_{max}, maximum M wave. MVC, maximal voluntary contraction. IT, interpolated twitch.

EMG activity from soleus muscle. The interpolated twitch technique served to assess the level of voluntary effort (cf. Belanger & McComas, 1981) and the presence of efferent conduction block (see below).

The differential compression block of the sciatic nerve was achieved by placing a wooden bar, 6 cm high and 2 cm wide, under the right thigh just distal to the ischial tuberosity. The subject sat with as much body weight as possible over the bar. The maximum right H reflex was monitored over the next 20 min until it was abolished. A very small H reflex (less than 0·2 mV) was permitted since the progressive effects of compression would ultimately block the H reflex completely. The stimulus intensity was adjusted, if necessary, throughout the experiment to ensure that the

maximal H reflex was being recorded. The left maximum H reflex served to demonstrate that the abolition of the right H reflex was a result of the block rather than any environmental factors. The maximal plantarflexion torque and the associated EMG were then retested (post-block test).

Following the compression block, subjects were aware of crude touch, yet there was noticeable hypaesthesia over the lower leg and foot. Subjects also reported a loss of position sense around the ankle joint and an inability to perceive the development of plantarflexion torque; they were therefore instructed to view the torque tracing on the oscilloscope while developing maximal voluntary contractions. During these maximal voluntary contractions, an interpolated stimulus was delivered to the muscle. If the interpolated twitch was small (less than 15% of the amplitude of the twitch in the rested muscle), then the experiment was continued. Such small interpolated twitches could have been the result of the loss of sensory feedback especially since Belanger & McComas (1981) found that approximately half of their subjects were unable to fully activate soleus muscle even under normal conditions (the mean interpolated twitch torque was 12% of the maximal twitch at rest). In four additional subjects who were excluded from this study, during an attempted maximal voluntary contraction the plantarflexion torque was markedly reduced and an interpolated twitch of equal size to the twitch evoked in a resting muscle was present. Thus the interpolated twitch technique could indicate the possibility of conduction block in the efferent fibres.

In test 1, fatigue was induced under ischaemic conditions by stimulating the muscle for 4–5 min while the compression block was maintained. In the control (test 2) experiment, the ischaemic cuff was inflated while the compression block was maintained, in the absence of electrical stimulation, for the same period of time as in the fatigue-inducing condition. Post-test measures, taken under ischaemic conditions, took another 2 min; these included maximal plantarflexion torque and the associated EMG followed by maximal H reflexes and M waves.

Statistical analysis

The statistical significance for the change in the maximal plantarflexion torque and the associated EMG was determined using repeated-measures analysis of variance (ANOVA), with subject and treatment (block, fatigue, ischaemia alone) as the factors, and Tukey's multiple comparisons. The effects of fatigue on the amplitude and area of the maximum M wave (pre-test − post-test) and the effect of the compression block on EMG and maximal plantarflexion torque (pre-test − post-block) were determined with Student's t tests. The α level of significance was set at $P = 0{\cdot}05$.

RESULTS

The data are organized to present the mean data for those subjects in whom the afferent input remained well blocked and there was no evidence of efferent block or decreased central drive during the testing. These data are followed by the results for all ten subjects.

Effects of compression block

Following sciatic nerve compression for approximately 20 min, the mean peak-to-peak amplitude of the H reflex was completely abolished during post-block testing in six subjects during the fatigue test (test 1) and in eight subjects during the ischaemia control test (test 2). No subject had an H-reflex amplitude greater than 0·2 mV. The mean of all ten subjects decreased by $97{\cdot}0 \pm 6{\cdot}1$ % in test 1 and decreased by $97{\cdot}0 \pm 5{\cdot}6$ % in test 2 for a pooled mean decrease of $97{\cdot}0 \pm 5{\cdot}7$ %.

There were seven subjects in whom interpolated twitch responses were absent during the maximal voluntary contraction. In these subjects, the mean plantarflexion torque fell $15{\cdot}7 \pm 12{\cdot}8$ % in test 1 and $9{\cdot}5 \pm 18{\cdot}7$ % in test 2 and the EMG activities decreased by $10{\cdot}4 \pm 18{\cdot}3$ % in test 1 and by $16{\cdot}0 \pm 25{\cdot}0$ % in test 2. Since the changes elicited by the compression block in test 1 and test 2 were not significantly

different, the data could be combined. The pooled means of 12·8 ± 15·4 and 13·2 ± 20·8 % for plantarflexion torque and EMG activity, respectively, were significantly lower than pre-test values.

In the other three subjects, interpolated twitch responses were detected during the maximal voluntary contraction in both test 1 and 2, and these were 10, 12, 13, 13,

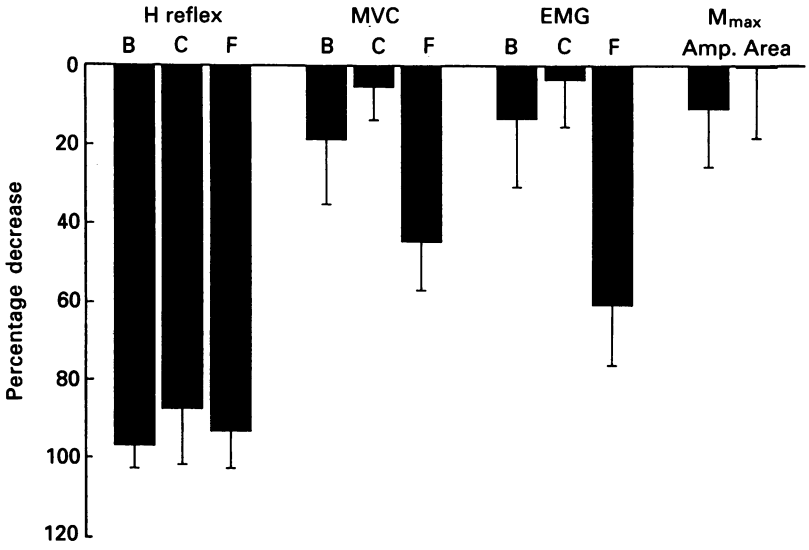

Fig. 2. Mean changes (±S.D.) for all ten subjects in maximum H reflex amplitude, maximal plantarflexion torque (MVC), EMG activity resulting from the compression block (B), ischaemia-only control (test 2, C) and fatigue (test 1, F); C and F represent further decreases from the post-block level. The maximum M wave (M_{max}) amplitude and area changes are following fatigue in test 1. The mean EMG declines following fatigue are marked compared to the modest mean decreases in the maximum M wave. This indicates that the decrease in EMG could not be explained by changes at the neuromuscular junction or muscle fibre membrane.

14 and 17 % of the maximal twitch torque in the post-compression period. When these subjects were included, the mean maximal plantarflexion torque for all ten subjects fell 21·7 ± 14·8 % in test 1 and 15·9 ± 17·9 % in test 2 after administration of the compression block. The EMG activity associated with the maximal voluntary contraction fell 11·1 ± 15·3 % in test 1 and 15·7 ± 19·4 % in test 2. The pooled mean decreases of maximal plantarflexion torque and EMG activity were 18·8 ± 16·2 and 13·4 ± 17·2 %, respectively. The pooled mean changes for all ten subjects following the compression block are depicted in Fig. 2.

Effects of ischaemia control

In test 2, after the period of ischaemia, the H reflex remained either completely blocked in four subjects or well blocked, i.e. less than 0·2 mV, in two additional subjects. In four subjects there was moderate return of the H reflexes during this ischaemia test (mean decline of 73·5 ± 12·1 %). This could be explained by the subjects inadvertently shifting their body weight off the wooden bar because of local

discomfort or excessive effort that resulted in hip movement during the maximal voluntary contraction trials. The mean decline of the H reflex in the ten subjects was 87·4 ± 14·4 %.

There were five subjects in whom the H reflex remained well blocked and interpolated twitch responses were not evident during maximal voluntary contraction. Data from these subjects indicate that the maximum plantarflexion torque decreased 5·0 ± 9·9 % and the associated EMG activity fell 6·4 ± 8·0 % from the post-block value.

There were three subjects that demonstrated interpolated twitch responses during maximal voluntary contraction; two of these subjects were the same subjects that demonstrated interpolated twitch responses following compression block. These superimposed twitch responses were 17, 20 and 25 % of the resting twitch torque in the post-ischaemic period.

The mean maximal plantarflexion torque for all ten subjects only decreased 4·3 ± 9·3 % from the post-block value. Similarly, the EMG for all ten subjects only decreased 3·5 ± 11·8 % from the post-block value. These mean changes for all ten subjects in the ischaemia control experiment are presented in Fig. 2. The data from one subject are illustrated in Fig. 3; there is little change in the maximal plantarflexion torque or the associated EMG activity despite the total block of the H reflex and 5 min of ischaemia.

Effects of fatigue

By the end of 5 min of fatiguing stimulation, the block had been in place for 25–30 min. The H reflexes remained completely blocked in six subjects or well blocked, less than 0·2 mV, in one additional subject. The other three subjects had moderate recovery of the H reflex such that the mean decline in these three subjects was 80·7 ± 5·1 %. However, the mean decline of the H reflex in all subjects was 93·2 ± 9·5 % and this suggested that most of the large myelinated afferents supplying soleus remained blocked.

There were five subjects in whom the H reflex remained completely blocked and interpolated twitch responses were not evident during maximal voluntary contraction. Data from these subjects indicated that the maximum plantarflexion torque decreased 36·2 ± 7·6 % and the associated EMG activity fell 56·8 ± 19·6 % following fatigue (test 1) compared to MVC declines of 5·0 ± 9·9 % and EMG declines of 6·4 ± 8·0 % following ischaemia alone (test 2). These declines in MVC plantarflexion torque and the associated EMG activity were markedly greater following fatigue than that following the control (ischaemia only) test 2. Furthermore, the decline in mean maximal plantarflexion torque was similar to the value of 38·5 ± 8·6 % found in a previous study (Garland & McComas, 1990) in which the fatigue was induced without the compression block. The reduction in mean EMG activity may be compared with the value of 51·9 ± 17·9 % found in the previous study without the block (Garland & McComas, 1990). Hence, fatigue produced very similar changes in maximal plantarflexion torque and EMG activity both with and without the majority of sensory input from large diameter afferents.

As in test 2 (see above), the same three subjects showed evidence of small interpolated twitches during the maximal voluntary plantarflexion contraction.

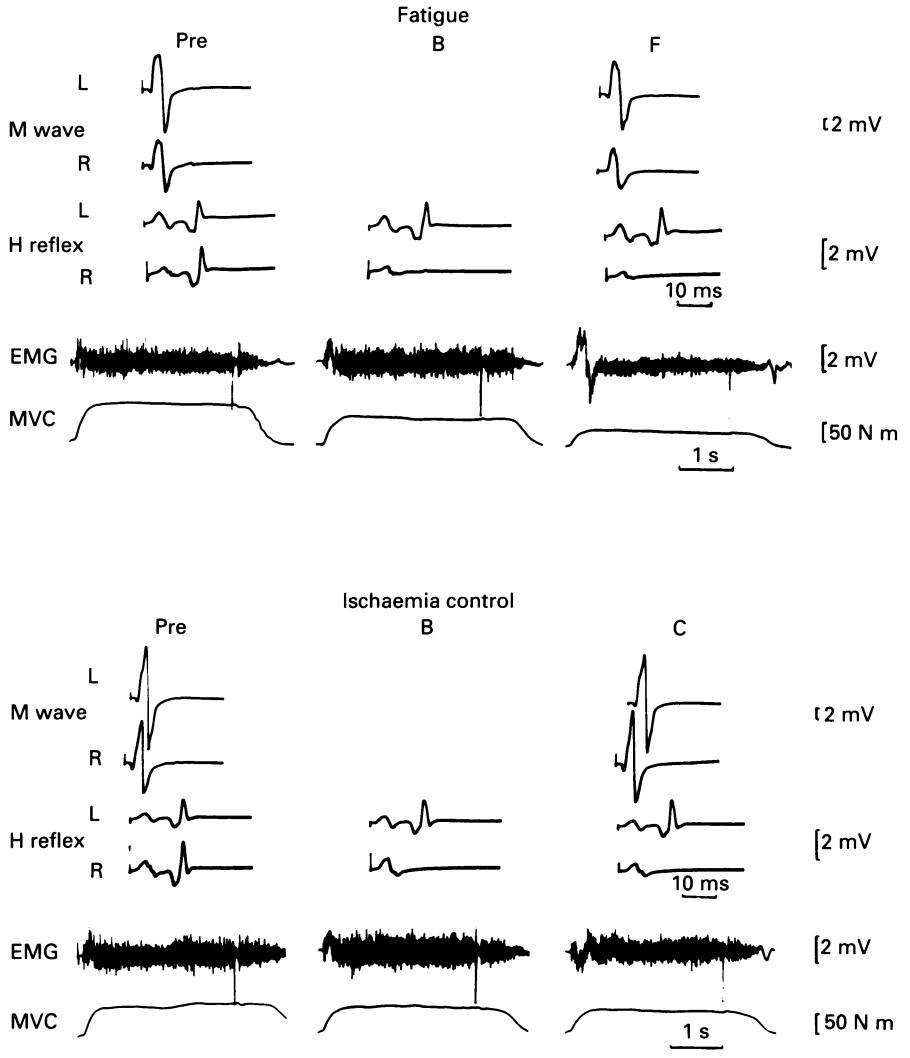

Fig. 3. Top, data from one subject illustrating the effectiveness of the compression block and the substantial decline in the maximal plantarflexion torque and the associated EMG following fatigue. Top two rows, maximum M waves from control (left) leg above and right (experimental) leg below. Middle two rows, maximum H reflexes from left leg above and right leg below. Bottom two rows, EMG above and maximal plantarflexion torque recordings below for the right leg. Left column are pre-test values, middle column are post-block values and right column are post-fatigue values. Note the abolition of the right H reflex post-block which was maintained post-fatigue. Bottom, same subject's data in the ischaemia control test. These data illustrate little change in the maximal plantarflexion torque and the associated EMG despite total block of the H reflex and 5 min of ischaemia.

Despite the tester's encouragement, and obvious effort on the part of the subject, this could not be overcome. Due to the presence of fatigue, these small interpolated twitches represented 17, 50 and 57% of the maximal twitch torque in the post-

fatigue period. Hence, two of the subjects probably had some degree of failure of central drive during fatigue.

The mean maximal plantarflexion torque for all ten subjects showed a statistically significant decrease of another 44·6 ± 12·4 % from the post-block value. The mean maximum twitch torque, evoked by supramaximal stimulation of the tibial nerve with two pulses at 100 Hz, declined by 30–40 %. The plantarflexion torque evoked by the submaximal fatiguing stimulation of the soleus muscle declined by more than 80 % by the end of stimulation. The difference between the large decline in plantarflexion torque during fatiguing stimulation and the smaller declines during the MVC and the maximum twitch probably reflected the submaximal fatiguing stimulation intensities and illustrated the contribution that the non-fatigued gastrocnemius muscle was able to make to the MVC and maximal twitch torque.

The mean EMG associated with the maximal voluntary plantarflexion torque for all ten subjects also showed a statistically significant decrease of another 60·4 ± 15·6 % from post-block levels. The declines in EMG and MVC were significantly different from the control values (test 2, ischaemia only).

If the declines in plantarflexion torque and EMG activity following ischaemia were subtracted from those data following fatigue for each subject, then the mean decrease in plantarflexion torque and EMG 'attributable' to fatigue was 43·3 ± 21·6 and 56·9 ± 22·8 %, respectively. Thus it makes little difference how the data were manipulated in that the effect of fatigue on the maximal plantarflexion torque and the associated EMG remained substantial despite the blockade of the majority of large diameter afferents.

The changes in the M wave were not statistically significant. The mean amplitude of the maximum M wave fell 10·8 ± 14·7 % from the pre-test value and the corresponding area of the M wave fell by 0·2 ± 18·0 %. Hence the changes in maximal M wave were modest in comparison to the decreases in EMG activity.

The mean changes for all ten subjects following fatigue are illustrated in Fig. 2. In Fig. 3, the data from one subject shows the effectiveness of the block and the substantial decline in maximal plantarflexion torque and the associated EMG activity during fatigue. In this subject the M wave also showed a larger than average decline.

DISCUSSION

The main impetus for this research was to attempt to clarify the role of large and small diameter afferents in the reflex inhibition of motoneurones observed during fatigue. The study was designed to implicate reflex inhibition of motoneurones in the mechanism for the declining EMG activity during fatigue. This was accomplished by minimizing the contribution of peripheral inexcitability of the neuromuscular junction and muscle fibre membrane (as evidenced by only modest changes in the M wave) and maintaining sufficient motor drive to the muscle (as evidenced by the absence of any large interpolated twitches superimposed on the maximal voluntary contraction in the majority of subjects).

There were two subjects, however, in whom some of the fatigue could be attributable to failure of motor drive on the basis of rather large interpolated twitch

responses. This was not surprising considering the complexity of and discomfort associated with the experimental protocol.

Many subjects also had difficulty achieving maximal plantarflexion torques following compression block. While three subjects demonstrated small interpolated twitch responses, others did not. Small declines in maximal plantarflexion torque may go undetected by the interpolated twitch technique since the sensitivity of the technique has been shown to decrease at plantarflexion torque levels above 85–90% of maximum (Belanger & McComas, 1981). Declines larger than 15% in maximal plantarflexion torque were evident in the absence of any interpolated twitch or decreased EMG activity. The explanation for these declines in MVC plantarflexion torques following compression block is probably that the introduction of the wooden bar (which was not present during the pre-test) made it difficult to exert the same force upon the foot plate despite the subject's maximal effort.

Nevertheless, the present findings demonstrated that following fatiguing stimulation, the maximal plantarflexion torque and the associated EMG declined despite blockade of the majority of large myelinated afferents; this suggested that input from these afferents was unlikely to mediate the presumed reflex inhibition.

The smaller diameter afferents are thinly myelinated fibres (Aδ or group III) and unmyelinated fibres (C or group IV); in the present study, these afferents were probably left unaffected by the compression block and were therefore the prime candidates for putative coupling of motoneurone output to the functional status of the muscle fibres. Approximately half of the small diameter afferents have been shown to respond to noxious chemical, mechanical and thermal stimuli, (Kniffki, Mense & Schmidt, 1981). Other small afferents are activated by moderately innocuous stimuli such as stretch, contractions and touch (Kniffki *et al.* 1981, Kaufman, Waldrop, Rybicki, Ordway & Mitchell, 1984). Group III and IV afferents can be activated by chemical agents associated with muscle pain, i.e. bradykinin and potassium (Mense, 1977; Hnik, Vyskocil, Ujec, Vejsada & Rehfeldt, 1986), lactate and phosphate (Kniffki *et al.* 1978), most of which are known to increase during fatigue (Fitts & Holloszy, 1976; Dawson, Gadian & Wilkie, 1980; Sjogaard, Adams & Saltin, 1985).

The central actions of noxious stimuli could induce inhibition at the spinal and/or supraspinal level. Nociceptive group III and IV afferents are known to synapse in the dorsal horn of the spinal cord, the pathway to the somatosensory cortex and the frontal brain continuing via the brain stem reticular formation and thalamus (Mense, 1983). It is possible that these terminations could influence α-motoneurone excitability via reticulospinal tracts or via frontal and premotor areas feeding the motor cortex (Schell & Strick, 1984). Hence, it is possible that stimulation of nociceptive afferents during fatigue produces inhibition of motoneurones via spinal or long-loop reflexes. If there is long-loop reflex inhibition, the descending motor drive to the motoneurones during maximal voluntary contractions is still able to fully utilize the available force-generating capacity of the muscle (as evidenced by the absence of interpolated twitches in seven subjects).

To date, no studies on fatigue-induced reflex inhibition have demonstrated whether the nature of the sensory input is mechanical or chemical. In the present experimental protocol, chemical changes during fatigue were more likely than

mechanical changes to have mediated reflex inhibition for several reasons. First, both in this study and that of Bigland-Ritchie *et al.* 1986, the EMG associated with maximal voluntary contractions following fatigue remained depressed for 2 or 3 min while the limb was rendered ischaemic. In Bigland-Ritchie *et al.* 1986, the EMG demonstrated near-full recovery in 3 min if the blood supply was intact; this suggested a chemical stimulus. Second, it was shown in a previous study that release of the ischaemic cuff was associated with a reduction in muscle pain (Garland *et al.* 1988; presumably due to wash-out of metabolites), and many of the chemosensitive afferents are known to be nociceptive (Mense, 1983). Third, Marsden, Meadows & Merton, (1983) were unable to demonstrate any change in motor unit firing rates by slowing muscle contraction through cooling rather than fatigue; hence in the absence of chemical changes associated with fatigue, the EMG activity (motor unit discharge rate) was unaffected. Lastly, the magnitude of chemical changes observed in fatigue, e.g. extracellular K^+ concentrations rising as high as 15 mM (Hnik *et al.* 1986), and the strong correlation between the decline in force and the concentration of diprotonated inorganic phosphate (Nosek, Fender & Godt, 1987; Miller, Boska, Moussavi, Carson & Weiner, 1988) have lent support to the contention that the decline in EMG activity which occurs in fatigue could also be mediated by such chemical changes.

To conclude, there appears to be a reflex inhibitory system active during fatigue; it serves to decrease motoneurone activity in conjunction with the reduction in force. This reflex is probably not mediated by large diameter afferents; rather it seems more likely that the reflex is mediated by small diameter afferents from within the fatigued muscle. Whether this reflex is chemical in nature (consequent to metabolite accumulation or deprivation of energy substrate) or mechanical (consequent to altered sensitivity to stretch, contraction or pressure) requires further investigation.

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REFERENCES

BELANGER, A. Y. & MCCOMAS, A. J. (1981). Extent of motor unit activation during effort. *Journal of Applied Physiology* **51**, 1131–1135.

BELLEMARE, F., WOODS, J., JOHANSSON, R. S. & BIGLAND-RITCHIE, B. R. (1983). Motor unit discharge rates in maximal voluntary contractions of three human muscles. *Journal of Neurophysiology* **50**, 1380–1392.

BIGLAND-RITCHIE, B. R., DAWSON, N. J., JOHANSSON, R. S. & LIPPOLD, O. C. J. (1986). Reflex origin for the slowing of motoneurone firing rates in fatigue of human voluntary contractions. *Journal of Physiology* **379**, 451–459.

DAWSON, M. J., GADIAN, D. G. & WILKIE, D. R. (1980). Mechanical relaxation rate and metabolism studied in fatigued muscle by phosphorus nuclear magnetic resonance. *Journal of Physiology* **299**, 465–484.

FITTS, R. H. & HOLLOSZY, J. O. (1976). Lactate and contractile force in frog muscle during development of fatigue and recovery. *American Journal of Physiology* **231**, 430–433.

GARLAND, S. J., GARNER, S. H. & MCCOMAS, A. J. (1988). Reduced voluntary electromyographic activity after fatiguing stimulation of human muscle. *Journal of Physiology* **401**, 547–556.

GARLAND, S. J. & MCCOMAS, A. J. (1988). Role of the small diameter afferents in reflex inhibition during fatigue of human soleus muscle. *Society for Neuroscience Abstracts* **14**, 62.

GARLAND, S. J. & MCCOMAS, A. J. (1990). Reflex inhibition of human soleus muscle during fatigue. *Journal of Physiology* **429**, 17–27.

HASAN, Z. & STUART, D. G. (1984). Mammalian muscle receptors. In *Handbook of the Spinal Cord*, vols 2 and 3: *Anatomy and Physiology*, ed. DAVIDOFF, R. A., pp. 550–607. Marcel Dekker Inc., New York.

HNIK, P., VYSKOCIL, F., UJEC, E., VEJSADA, R. & REHFELDT, H. (1986). Work-induced potassium loss from skeletal muscles and its physiological implications. In *Biochemistry of Exercise VI*, ed. SALTIN, B., pp. 345–364. Human Kinetics Publishers, Champaign, IL, USA.

HOUK, J. C. & RYMER, W. Z. (1981). Neural control of muscle length and tension. In *Handbook of Physiology*, section 1, vol. 2, *The Nervous System*: *Motor Control*, ed. BROOKS, V. B., pp. 276–280. Williams & Wilkins, Baltimore, MD, USA.

KAUFMAN, M. P., WALDROP, T. G., RYBICKI, K. J., ORDWAY, G. A. & MITCHELL, J. H. (1984). Effects of static and rhythmic twitch contractions on the discharge of group III and IV muscle afferents. *Cardiovascular Research* **18**, 663–668.

KNIFFKI, K.-D., MENSE, S. & SCHMIDT, R. F. (1978). Responses of group IV afferent units from skeletal muscle to stretch, contraction, and chemical stimulation. *Experimental Brain Research* **31**, 511–522.

KNIFFKI, K.-D., MENSE, S. & SCHMIDT, R. F. (1981). Muscle receptors with fine afferent fibers which may evoke circulatory reflexes. *Circulation Research* **48**, suppl. 1, I25–31.

MACKENZIE, R. A., BURKE, D., SKUSE, N. F. & LETHLEAN, K. (1975). Fibre function and perception during cutaneous nerve block. *Journal of Neurology, Neurosurgery and Psychiatry* **38**, 865–873.

MAGLADERY, J. W., MCDOUGAL, D. B. & STOLL, J. (1950). Electrophysiological studies of nerve and reflex activity in normal man. II. The effects of peripheral ischemia. *Bulletin of Johns Hopkins Hospital* **86**, 291–312.

MARSDEN, C. D., MEADOWS, J. C. & MERTON, P. A. (1983). "Muscular wisdom" that minimizes fatigue during prolonged effort in man: Peak rates of motoneuron discharge and slowing of discharge during fatigue. In *Motor Control Mechanisms in Health and Disease*, ed. DESMEDT, J. E., pp. 169–211. Raven Press, New York.

MARSH, E., SALE, D., MCCOMAS, A. J., & QUINLAN, J. (1981). Influence of joint position on ankle dorsiflexion in humans. *Journal of Applied Physiology* **51**, 160–167.

MENSE, S. (1977). Nervous outflow from skeletal muscle following chemical noxious stimulation. *Journal of Physiology* **267**, 75–88.

MENSE, S. (1983). Basic neurobiologic mechanisms of pain and analgesia. *American Journal of Medicine* **75** (5A), 4–14.

MILLER, R. G., BOSKA, D., MOUSSAVI, R. S., CARSON, P. J. & WEINER, M. W. (1988). ^{31}P Nuclear magnetic resonance studies of high energy phosphates and pH in human muscle fatigue. Comparison of aerobic and anaerobic exercise. *Journal of Clinical Investigations* **81**, 1190–1196.

MODDEL, G., BEST, B. & ASHBY, P. (1977). Effect of differential nerve block on inhibition of the monosynaptic reflex by vibration in man. *Journal of Neurology, Neurosurgery and Psychiatry* **40**, 1066–1071.

NOSEK, T. M., FENDER, K. Y. & GODT, R. E. (1987). Is it diprotonated inorganic phosphate that depresses force in skinned skeletal muscle fibres? *Science* **236**, 191–193.

SCHELL, G. R. & STRICK, P. L. (1984). The origin of thalamic inputs to the arcuate premotor and supplementary motor areas. *Journal of Neuroscience* **4**, 539–560.

SJOGAARD, G., ADAMS, R. P. & SALTIN, B. (1985). Water and ion shifts in skeletal muscle of humans with intense dynamic knee extension. *American Journal of Physiology* **248**, R190–196.

TOREBJORK, H. E. & HALLIN, R. G. (1973). Perceptual changes accompanying controlled preferential blocking of A and C fibre responses in intact human skin nerves. *Experimental Brain Research* **16**, 321–332.

WOODS, J., FURBUSH, F. & BIGLAND-RITCHIE, B. (1987). Evidence for a fatigue-induced reflex inhibition of motoneuron firing rates. *Journal of Neurophysiology* **58**, 125–137.

ZOTTERMAN, Y. (1983). Studies in the peripheral nervous mechanisms of pain. *Acta Medica Scandinavica* **130**, 185–233.