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IMPAIRMENT OF NEUROMUSCULAR PROPAGATION DURING HUMAN FATIGUING CONTRACTIONS AT SUBMAXIMAL FORCES

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SUMMARY

1. The purpose of the study was to examine the dependence of neuromuscular propagation impairment on the level of isometric force sustained to the endurance limit. The task involved human volunteers sustaining a submaximal abduction force with the index finger by activating the first dorsal interosseous muscle as long as possible.

2. The submaximal force was sustained at one of three levels (20, 35 or 65% of maximum) by increasing motor unit activity, as indicated by the electromyogram (EMG), during the fatiguing contraction. Although the EMG increased during the fatiguing contraction, the EMG was significantly less than maximum at the endurance limit for all subjects (deficit of 19–55% of maximum). This deficit was inversely related to the level of the sustained submaximal force.

3. The maximum voluntary contraction and twitch forces were significantly reduced following the fatiguing contraction. As with the EMG, the degree of force reduction was greatest for the subjects who sustained the low target forces.

4. The fatiguing contraction caused a 12–23% decline in M wave amplitude, a 33–51% increase in M wave duration, and no change in M wave area. The decline in M wave amplitude, which is an index of neuromuscular propagation impairment, was greatest among the subjects who sustained the low target forces.

5. The mean power frequency of the EMG decreased by a similar amount (50–57%) during the fatiguing contraction for all three groups of subjects.

6. A model representing the interaction of processes that enhance and impair force was developed to explain the recovery of twitch force following the sustained contractions at different target forces.

7. We conclude that the fatigue experienced by a subject when force is sustained at a submaximal value does involve an impairment of neuromuscular propagation. This impairment is one factor that limits muscle excitation during a submaximal, fatiguing contraction and contributes to the diminished force capability by the end of the fatigue task.

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INTRODUCTION

Although the maximum voluntary force that a human subject can exert may decline during a fatiguing contraction, the reduction in force is not thought to be caused by a diminution of the descending drive provided by suprasegmental centres or by an impairment of neuromuscular propagation. This conclusion is based on evidence such as the ability of subjects to sustain the central drive (as assessed by the twitch superimposition technique), the absence of changes in the amplitude of the compound muscle action potential (M wave), an equivalence of voluntary and electrically elicited forces, and an increase in the EMG during submaximal contractions (Merton, 1954; Bigland-Ritchie, Furbush & Woods, 1986*c*; Kukulka, Russell & Moore, 1986; Thomas, Woods & Bigland-Ritchie, 1989). Because these studies have examined a variety of experimental conditions, including both maximal and submaximal contractions, sustained and intermittent tasks, and contractions of short and long duration, these investigators have concluded that the mechanisms underlying fatigue in voluntary contractions are dominated by the failure of processes within muscle fibres. In contrast, the inability of subjects to increase the EMG to maximal levels during submaximal fatiguing contractions (Lind & Petrofsky, 1979) and significant changes in the M wave with fatigue (Stephens & Taylor, 1972; Milner-Brown & Miller, 1986; Bellemare & Garzaniti, 1988) have led others to suggest that an inadequate excitation of muscle may contribute to the decline in force.

The purpose of the study was to examine the dependence of neuromuscular propagation impairment on the level of isometric force sustained to the endurance limit. We examined changes in the M wave and EMG of first dorsal interosseous that were associated with a sustained abduction force of the index finger at one of three submaximal levels. We observed significant changes in the M wave, which varied with the magnitude of the target force, that could not be explained by movement of the stimulating or recording electrodes. Although the voluntary EMG increased during the fatiguing contraction due to an increase in motor unit activity, the EMG amplitude at the endurance limit was less than the maximal level. This apparent inability to fully activate muscle also appeared to depend on the target force. These results suggest a force-level-dependent impairment of neuromuscular propagation that may be partially responsible for the limitation in neural excitation of muscle observed during sustained, submaximal contractions. Some of these data have been reported previously (Fuglevand, Huey, Zackowski & Enoka, 1991).

METHODS

The measurements were obtained from thirty-two healthy subjects (14 female, 18 male) between 20 and 40 years of age. The procedures were approved by the institutional Human Subjects Committee and all subjects gave their informed consent to participate in the study. The subjects were right-hand dominant and the experiments were performed on the first dorsal interosseous muscle of the left hand. First dorsal interosseous is a bipennate muscle with fibres that originate on the medial side of metacarpal I and the lateral side of metacarpal II and insert on the lateral side of the base of the proximal phalanx of the index finger. First dorsal interosseous is the primary muscle to abduct the index finger at the metacarpophalangeal joint and is one of several muscles to flex the index finger.

Mechanical recording

The study was conducted with the subjects seated facing an oscilloscope. The left arm was abducted to a horizontal plane passing through the shoulder with the hand and forearm pronated and resting on the manipulandum. The elbow joint was at about a right angle. The manipulandum allowed for the hand and forearm to be immobilized by several restraints: (1) two forearm straps, (2) a support for the thumb that held the angle between metacarpals I and II at approximately 1·0 rad, (3) a strap over fingers III–V, and (4) a brace that prevented flexion at the metacarpophalangeal joint of the index finger. In addition, the index finger was placed in an individualized mould (polyvinyl silicone) and strapped to an L-shaped aluminium splint that was positioned along the lateral and ventral surfaces of the finger and kept the interphalangeal joints extended. The hand was placed in the manipulandum so that the proximal interphalangeal joint was aligned with two force transducers (Sensotec model 13), one transducer sensing the abduction force and the other sensing the flexion force. The aluminium splint served as an interface between the finger and the transducers. The signals from both transducers were displayed on an oscilloscope and recorded on analog FM tape (bandwidth DC to 10 kHz).

Electrical recording

Electromyographic (EMG) signals were obtained from surface recordings with bipolar electrodes (silver–silver chloride) that were positioned over the first dorsal interosseous muscle, along the radial side of the metacarpal II, and over the abductor digiti minimi muscle, on the ulnar side of the hand between the metacarpophalangeal V joint and the pisiform bone. The EMG was measured with 4 mm diameter electrodes that were attached with an inter-electrode distance of about 10 mm. The abductor digiti minimi EMG was used to monitor the response to stimulation of the ulnar nerve (M wave) and allowed detection of changes that may have occurred in the position of the stimulating electrode. The reference electrode for each muscle was placed on the dorsal aspect of the hand. The EMG signals were differentially amplified, filtered (0·01–10 kHz), displayed on an oscilloscope, and stored on analog FM tape.

Electrical stimulation

The first dorsal interosseous and abductor digiti minimi muscles were activated by percutaneous electrical stimulation of the motor nerve with a Grass S88 stimulator. The ulnar nerve was stimulated by passing single current pulses (0·1 ms duration) through a saline-soaked felt pad (1·0 cm diameter) located on the ventromedial surface of the forearm just proximal to the wrist. A large plate anode (4 × 5 cm) was fixed on the central, ventromedial aspect of the forearm. Initially, the position of the cathode was adjusted to find the location that yielded the largest EMG response in first dorsal interosseous to submaximal stimulus pulses. Once the optimal position was determined, the cathode was firmly secured at that location with velcro straps. The stimulus intensity was then increased to a supramaximal level and was maintained at that level for the remainder of the experiment.

In order to estimate axonal conduction velocity, ulnar nerve stimulation was also elicited with an additional pair of electrodes located near the elbow. The cathode was located posterior to the medial epicondyle of the humerus and the anode was fixed on the distal medial surface of the upper arm. Procedures similar to that described for wrist stimulation were used to optimize cathode location for elbow stimulation. Generally, each time M waves were elicited, three stimuli were delivered at the wrist followed by two at the elbow with an interstimulus interval of 2 s. The M waves obtained with elbow stimulation were used only in the estimation of axonal conduction velocity.

Experimental procedures

Subjects were asked to participate in one training and four experimental sessions. The purpose of the training session was to familiarize the subjects with the timing of the isometric maximum voluntary contraction (MVC) and the general experimental protocol. The four experimental sessions were separated by 4–7 days between each session and involved the subjects performing the same protocol in each session.

Three procedures were carried out during each experiment: ulnar nerve stimulation, maximum voluntary contractions (MVCs), and a fatigue task. The experiment was initiated by applying five pulses of supramaximal stimulation to the ulnar nerve (three at the wrist, two at the elbow) and

recording the EMG (M wave) and abduction force (twitch) responses to the stimulation. Subjects then performed two to three MVCs, with rest periods provided between each trial. The timing of the MVC task was based on a verbal count during which the subject graded the abduction force from zero to maximum in 3 s and then maintained this force for 2–3 s. Subjects monitored the gradation of force on the oscilloscope.

In the performance of the fatigue task, the subjects observed a target force displayed on the oscilloscope and matched that force by isometric abduction of the index finger. Subjects were randomly assigned to one of three groups, which differed as to the magnitude of the target force (20, 35 or 65% MVC). The subjects were vigorously encouraged to sustain the target force for as long as possible. In addition, subjects were instructed to minimize the flexion force, which was also displayed on the oscilloscope. The fatigue task was terminated by one of the investigators when the force dropped below 90% of the target level for more than 2–3 s, the subject began to employ radial deviation of the wrist, or the subject began to extend the other fingers. The time at which the fatigue task was terminated was referred to as the endurance limit.

Immediately following the fatigue task, five M waves and twitches were elicited, and the subjects then performed two MVCs, with no rest period provided between trials. A 10 min recovery period ensued during which the subject relaxed the hand but did not alter its position. M waves and twitches were recorded every 10 s for the first minute of recovery, at 1 min intervals from 2 to 5 min, and then at 10 min of recovery. The subject then performed two to three MVCs and the experimental session was terminated.

Data analysis

Force and EMG data were digitally sampled (200 and 2000 samples/s, respectively, during the MVC and fatigue tasks and 1000 and 10000 samples/s, respectively, during ulnar nerve stimulation) and analysed off-line using the Spike 2 data analysis system (Cambridge Electronics Design, Ltd, Cambridge, UK) and custom-designed software. The M wave parameters measured were: peak-to-peak amplitude, peak-to-peak duration, total duration, area, and conduction time (latency from stimulus artifact to zero-crossing in the biphasic M wave). Axonal conduction velocity was estimated from the distance between the wrist and elbow stimulation cathodes divided by the difference in conduction times for the two stimulation sites. The measured abduction twitch force was due to the combined action of first dorsal interosseous and its antagonist, first palmar interosseous (also innervated by the ulnar nerve). Fatigue-induced changes in abduction twitch force, however, were attributed to alterations in the force exerted by first dorsal interosseous as it was assumed that the force of first palmar interosseous was relatively unaffected by the fatigue task.

Only the single MVC trial within each set of two to three trials that yielded the largest force was used in the analysis. The peak force was measured and the rectified average EMG was calculated for a 2·048 s epoch during the hold phase of the MVC. In addition, a fast Fourier transformation algorithm was implemented to calculate the power spectral density function of the unrectified EMG for the same 2·048 s epoch. The mean power frequency of the spectrum was calculated over the frequency range of 1–512 Hz and used as an index of the frequency content of the EMG signal. For the fatigue task, rectified average EMG, mean power frequency of the EMG, endurance time, and mean force were measured. Since endurance time differed among the subjects for the various target forces, time was normalized to the endurance limit. The rectified average EMG and mean power frequency were determined over a 2·048 s period in the middle of each 10% epoch of the fatigue task. Rectified average EMG data were normalized with respect to the EMG associated with the pre-fatigue MVC.

Data were analysed statistically by a factorial analysis of variance and comparison of means was performed with the Scheffe post-hoc test. Student's paired t tests were used to compare pre- and post-fatigue values for MVC and M wave parameters. Significance is reported at $P < 0{\cdot}05$. Reliability was determined from an intraclass correlation analysis using the SPSSX reliability program. The intraclass correlation coefficients are the ratios of the true variance to the observed variance. Accordingly, a correlation coefficient of 0·50 indicates that one-half of the observed variance was due to true variance (i.e. between subjects) while the remainder must be due to other factors, such as within-subject variance across sessions. Unless stated otherwise, the data are reported as means ± S.D.

RESULTS

The reliability of subject performance across the four experimental sessions was assessed for MVC force and endurance time. For MVC force, the group factor was collapsed and the data for all subjects were pooled by session. The intraclass correlation coefficients of MVC force across sessions were 0·97, 0·95 and 0·93 for before fatigue, immediately after fatigue, and following recovery, respectively. These coefficients indicate that most (93–97 %) of the variance in MVC force was due to differences between subjects and not due to within-subject variance across sessions.

The mean endurance time for the fatigue task declined with an increase in target force. Endurance times (mean ± S.D.) were significantly different among groups with mean values of 534 ± 195, 246 ± 110 and 66 ± 23 s, for the three target force groups (20, 35 and 65 % MVC), respectively. This trend was observed in all four experimental sessions as indicated by an analysis of variance that revealed no significant effect across the four sessions. For this reason, the data were collapsed across sessions and each subject contributed four values to the calculation of the mean. There were eleven subjects in each of the 20 and 35 % MVC groups and ten subjects in the 65 % MVC group. Calculations on the reliability of endurance time produced intraclass correlation coefficients of 0·69, 0·86 and 0·77 for the three groups (20, 35 and 65 % MVC), respectively. The endurance times showed a high reliability for the 35 % MVC group, and moderate reliability for the 20 and 65 % MVC groups; 69–86 % of the variance in endurance time was due to differences between subjects. In addition, the standard errors of measurement were 160, 72 and 17 s for the 20, 35 and 65 % groups, respectively.

Changes in EMG parameters during the fatigue task

Throughout the submaximal fatiguing contraction, the target force was maintained by an accompanying increase in EMG (Fig. 1). For the 20 and 35 % MVC target groups, EMG amplitude increased progressively over the fatigue task from 19·3 ± 4·8 to 45·2 ± 15·2 and from 31·5 ± 9·6 to 54·5 ± 17·6 % MVC-associated EMG, respectively (Fig. 2). These data represent 134 and 73 % increases in EMG amplitude for the 20 and 35 % MVC target groups, respectively. For the 65 % MVC target group, average EMG increased from 59·6 ± 13·9 to 81·4 ± 15·3 % MVC-associated EMG by the 60–70 % epoch of the fatigue task and then plateaued for the remainder of the task. This change represents a 37 % increase in EMG amplitude over the fatigue task. Despite the increase in EMG amplitude during the fatigue task and the cessation of the test at exhaustion, EMG amplitude failed to reach maximum levels at the endurance limit (Fig. 2).

There was a significant decline in mean power frequency for the three groups during the fatigue task (Fig. 3). Alteration in the frequency content of the EMG with fatigue is thought to reflect metabolite-induced changes in the propagation velocity of the muscle fibre action potentials (Lindström, Magnusson & Petersén, 1970; De Luca, 1984). The mean power frequency declined in parallel for all three groups and reached a similar value at the termination of the fatigue task. The mean power frequency changed from 128 ± 26 to 64 ± 20 Hz for the 20 % group, from 129 ± 34 to 55 ± 19 Hz for the 35 % group, and from 112 ± 17 to 51 ± 11 Hz for the 65 % group.

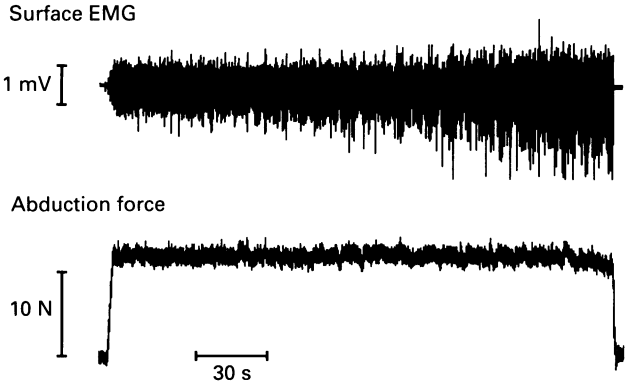

Fig. 1. Typical force and first dorsal interosseous EMG data from the fatigue test. The subject was able to sustain the target force (35% MVC) for 210 s with an increase in EMG.

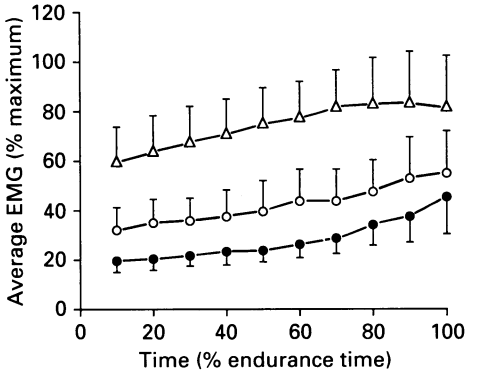

Fig. 2. Mean (±S.D.) changes in average EMG during the fatiguing contraction for the three groups of subjects (20, 35 and 65% MVC). The data were normalized relative to the average EMG associated with the pre-fatigue MVC and quantified at successive 10% epochs of the endurance time. ●, 20% group; ○, 35% group; △, 65% group. All subjects showed an increase in average EMG from the beginning to the end of the task.

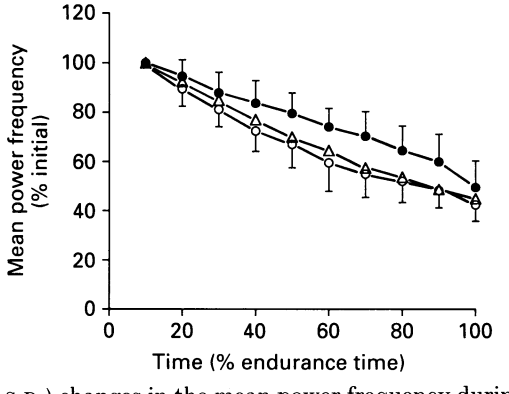

Fig. 3. Mean (±S.D.) changes in the mean power frequency during the fatigue test for the three groups of subjects (20, 35 and 65% MVC). The S.D.s were similar for all three groups and are shown for two of the groups. ●, 20% group; ○, 35% group; △, 65% group. On average, the mean power frequency for the three groups declined in parallel and reached a similar value at exhaustion.

By the final 10% epoch of the fatigue task, the average mean power frequency had decreased to 50, 43 and 45% of the initial value (10% epoch) for the three groups, respectively.

Changes in the MVC after the fatigue task

The pre-fatigue MVC forces for the 20, 35 and 65% MVC target force groups were 35·3 ± 9·7, 32·2 ± 6·5 and 33·6 ± 9·5 N, respectively. At the conclusion of the fatigue

TABLE 1. Percentage changes in maximum voluntary force and the associated average EMG and mean power frequency for the three MVC groups 15–20 s after the fatigue test and following 10 min recovery

	After		
	20%	35%	65%
Force	60·1 ± 10·3*†	70·1 ± 10·1*†	81·2 ± 9·6*
Average EMG	83·2 ± 20·1*†	97·9 ± 28·2‡	98·7 ± 24·9‡
Mean power frequency	67·9 ± 11·1*	56·8 ± 9·6*†‡	73·5 ± 11·6*
	Recovery		
	20%	35%	65%
Force	77·6 ± 11·1*†	79·3 ± 12·4*†	92·0 ± 8·9*
Average EMG	88·6 ± 21·6*	89·3 ± 19·4*	89·0 ± 14·0*
Mean power frequency	107·6 ± 23·3	109·5 ± 13·3	109·3 ± 10·0

Values expressed as a percentage of pre-fatigue and are means ± S.D.
* Significantly different from pre-fatigue ($P < 0·05$).
† Significantly different from the 65% MVC group ($P < 0·05$).
‡ Significantly different from the 20% MVC group ($P < 0·05$).

task, the subject relaxed for about 15–20 s while five M waves were elicited and then the subject performed two MVCs. The MVC force following the sustained, submaximal contractions declined significantly (Table 1) for all three groups (60·1, 70·1 and 81·2% of pre-fatigue for the 20, 35 and 65% MVC groups, respectively) and remained depressed following 10 min of recovery (77·6, 79·3 and 92·0% of pre-fatigue, respectively). The changes in MVC force were inversely related to the target force during the sustained contraction, with the subjects sustaining the lowest target force during the fatigue task yielding the greatest decline in MVC force and vice versa. This association was maintained following 10 min of recovery.

The average EMG values associated with the MVC (Table 1) at 15–20 s after the fatigue task were 83·2, 97·9 and 98·7% of pre-fatigue, respectively, for the 20, 35 and 65% MVC groups. The EMG was significantly depressed at this time only for the 20% MVC group. The EMG remained depressed for the 20% MVC group following 10 min of recovery (88·6%) and showed a significant decline below pre-fatigue values for the 35 and 65% MVC groups (89·3 and 89·0% respectively). In a similar way to the changes in MVC force seen after the fatigue task, the group that sustained the lowest target force also showed the greatest decline in EMG from pre-fatigue values.

The mean power frequency of the EMG associated with the MVC for all groups was

significantly lower after the fatigue task (67·9, 56·8 and 73·5% of pre-fatigue for the 20, 35 and 65% MVC groups, respectively). The subjects who performed the 35% MVC target force showed a significantly greater decline in mean power frequency than either the 20 or 65% MVC groups (Table 1). Unlike the force and EMG

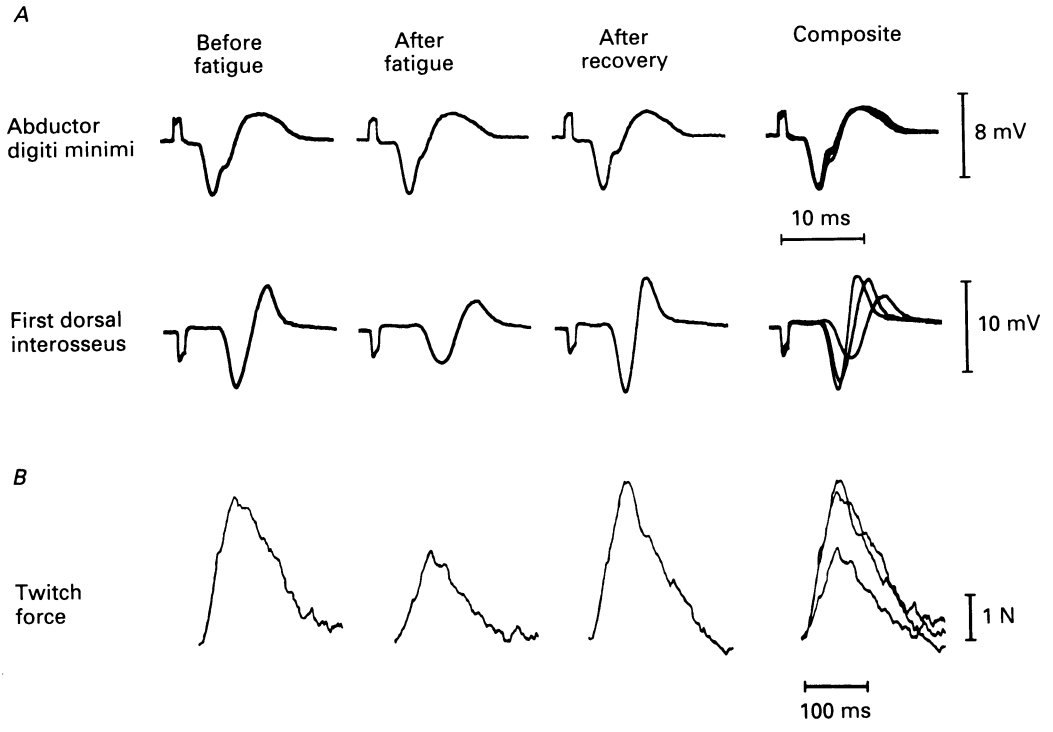

Fig. 4. Typical M waves (*A*) and twitch forces (*B*) elicited by stimulation of the ulnar nerve. The M waves were obtained concurrently in the first dorsal interosseous and abductor digiti minimi muscles before, immediately after the fatigue test, and following 10 min recovery. On average, the fatigue test produced a transient reduction in the amplitude of M waves elicited from the first dorsal interosseous with no corresponding change in the abductor digiti minimi M wave. Additionally, a significant increase in peak-to-peak duration occurred following the fatigue test. The absence of a change in the M waves for abductor digiti minimi suggests that the stimulus remained constant during the experiment. The changes in M wave amplitude for first dorsal interosseous were accompanied by similar changes in twitch amplitude.

amplitude for the MVC, mean power frequency recovered to greater than pre-fatigue values following the recovery period (107·6, 109·5 and 109·3%, respectively).

Fatigue-related changes in M waves

M waves were elicited in the first dorsal interosseous and abductor digiti minimi muscles by single maximal shocks of the ulnar nerve and were recorded before and immediately after the fatigue task, and following 10 min of recovery. Typical M waves are shown in Fig. 4*A*. The absence of a change in the abductor digiti minimi M wave during an experiment was taken as evidence that a constant stimulus was

applied to the ulnar nerve. Accordingly, changes in the first dorsal interosseous M wave were attributable to a factor other than variation in the effective stimulus intensity.

Fatiguing submaximal contractions at all three target forces significantly decreased M wave amplitude from pre-fatigue values (Table 2). Furthermore, the

TABLE 2. Fatigue-induced changes in M wave parameters for the three target forces immediately after the fatigue test and following 10 min recovery

	After		
	20%	35%	65%
Amplitude	76·2±14·3*†	73·6±18·9*†	88·3±16·0*
Duration	139·8±23·7*	150·9±28·4*†	132·9±18·8*
Area	101·9±19·9	102·0±30·6	106·8±22·2
	Recovery		
	20%	35%	65%
Amplitude	102·9±11·3	103·4±19·9	106·0±17·8*
Duration	84·9±8·9*	87·4±14·4*	91·2±8·7*
Area	96·0±10·7	95·0±20·9	97·5±17·0

Values expressed as a percentage of pre-fatigue and are means±S.D.
* Significantly different from pre-fatigue ($P < 0·05$).
‡ Significantly different from the 65% MVC group ($P < 0·05$).

subjects who were assigned the 20 and 35% MVC target forces performed the task longer and showed a significantly greater decline in M wave amplitude than the 65% MVC group (76·2, 73·6 and 88·3% of pre-fatigue values for the 20, 35 and 65% groups, respectively). This decline in M wave amplitude, however, was transient and following 10 min of recovery the amplitude had returned to levels slightly greater than pre-fatigue values (101·9, 103·4 and 106·0% respectively).

In addition to the decline in M wave amplitude, the fatigue task also resulted in significant increases in M wave peak-to-peak duration for the three target force groups. While the increases in M wave duration were similar for the 20 and 65% MVC groups, the 35% MVC group exhibited a significantly greater increase in duration as compared to the 65% MVC group (139·8, 150·9 and 132·9% of pre-fatigue for the 20, 35 and 65% MVC groups, respectively). Following 10 min of recovery, the M wave duration had returned to levels less than pre-fatigue values (84·9, 87·4 and 91·2%, respectively). The changes in M wave duration (Table 2) were inversely related to changes in mean power frequency (Table 1) for the three groups. The 35% MVC group showed the greatest increase in M wave duration and the greatest decrease in mean power frequency immediately after the fatigue task.

In contrast to the significant changes in M wave amplitude and duration, the fatiguing contraction resulted in no significant changes in M wave area compared to pre-fatigue values (101·9, 102·0 and 106·8% of pre-fatigue for the 20, 35 and 65% MVC groups, respectively). The stability in the M wave area reflects the significant

changes in both M wave amplitude and duration (Table 2). The opposing decrease and increase in M wave amplitude and duration, respectively, resulted in non-significant changes in M wave area. For this reason, the measure of M wave area provides a limited assessment of the changes in neuromuscular propagation following a sustained submaximal contraction.

Influence of sustained contraction on axonal conduction velocity

The mean conduction time (latency from stimulus application to zero-crossing in biphasic M wave) obtained before the fatigue task was $12{\cdot}8 \pm 1{\cdot}4$ and $9{\cdot}6 \pm 1{\cdot}1$ ms for elbow and wrist stimulation, respectively. Generally, conduction time increased 1–3 ms immediately following the fatigue task for both elbow and wrist stimulation sites; the mean increases in conduction time with elbow stimulation were $1{\cdot}46 \pm 0{\cdot}86$, $2{\cdot}05 \pm 0{\cdot}76$ and $1{\cdot}54 \pm 0{\cdot}71$ ms and with wrist stimulation the increases were $1{\cdot}57 \pm 0{\cdot}81$, $2{\cdot}14 \pm 0{\cdot}75$ and $1{\cdot}47 \pm 0{\cdot}64$ ms for the 20, 35 and 65% MVC groups, respectively. Conduction time includes delays for action potential propagation along the axons, neuromuscular transmission, and propagation of action potentials along the muscle fibres and past the EMG recording electrodes. The difference in the conduction times for elbow and wrist stimulation was used to estimate axonal propagation time between the two stimulation sites. The distance between the two stimulation sites (typically 22–26 cm) was divided by the conduction time difference to estimate axonal conduction velocity. The mean values for axonal conduction velocity before the fatigue test were $76{\cdot}4 \pm 15{\cdot}2$, $81{\cdot}1 \pm 20{\cdot}0$ and $80{\cdot}1 \pm 16{\cdot}1$ m/s for the 20, 35 and 65% MVC groups, respectively. Axonal conduction velocity was minimally affected by the fatigue test with values of $105{\cdot}5 \pm 17{\cdot}7$, $105{\cdot}1 \pm 18{\cdot}1$ and $99{\cdot}7 \pm 14{\cdot}9$% of the pre-fatigue value for the 20, 35 and 65% MVC groups, respectively; the increase in axonal conduction velocity exhibited by the 20% MVC group was significant. Following 10 min of recovery, the axonal conduction velocity for all three groups was not different to pre-fatigue values ($103{\cdot}9 \pm 13{\cdot}2$, $99{\cdot}6 \pm 13{\cdot}3$, $100{\cdot}8 \pm 10{\cdot}8$% pre-fatigue, respectively). Increased conduction time (1–3 ms) with fatigue, therefore, must have been due entirely to slowing of muscle fibre action potentials and possibly to an increase in neuromuscular transmission delay.

Our estimates of axonal conduction velocity were substantially higher than those reported for the ulnar nerve in clinical studies (e.g. 58·7–66·5 m/s; Kimura, 1984). Three factors may have led to this difference. First, we chose to measure M wave latencies as the time to the zero-crossing in the biphasic waveform, rather than the time to M wave onset (the conventional method), because the zero-crossing is a distinct and easily identified feature of M waves. The specific time of M wave onset, however, is often not easily discerned. We re-analysed a set of sixty M waves using the conventional method and found the variability in estimated conduction velocity to increase compared to the zero-crossing method. Interestingly, the mean conduction velocity estimated using M wave onset latencies was significantly lower (by 4·4 m/s) than that determined using the zero-crossing method. Secondly, axonal conduction velocity increases with activity level (Sammeck, 1975) and decreases with age (Kanda & Hashizume, 1989). Our subjects were primarily university students studying exercise science and were young ($27{\cdot}3 \pm 5{\cdot}1$ years), healthy and physically active. Thirdly, monopolar nerve recordings yield axon conduction velocities that are 5 m/s lower than those obtained with a bipolar electrode configuration (Gordon, Hamm, Enoka, Reinking, Windhorst & Stuart, 1987). The majority of clinical studies have recorded M waves using a monopolar electrode configuration whereas we used a bipolar configuration. These three factors (method of latency measurement, subject differences, and electrode configuration) probably

contributed to our higher estimates of conduction velocity compared to those generally reported in the clinical literature.

Fatigue-related changes in twitch force

Abduction twitch force was significantly depressed for all three target force groups immediately following the fatigue task (45·4 ± 21·3, 46·0 ± 23·4, 90·0 ± 39·9 % of pre-fatigue values for the 20, 35 and 65 % MVC target groups, respectively). Furthermore, the degree of twitch reduction for the 20 and 35 % MVC groups was significantly greater than that of the 65 % MVC group. This pattern of reduction in twitch force paralleled the depression in M wave amplitude (Table 2) seen immediately following the fatigue test (Fig. 4*B*).

After 10 min of recovery, the twitch force for both the 20 and 35 % MVC target groups remained depressed (79·3 ± 19·2 and 84·5 ± 27·2 % of pre-fatigue values, respectively). These values were significantly different from pre-fatigue levels and from the twitch force of the 65 % groups, which had recovered completely by 10 min (103·4 ± 18·5 % of pre-fatigue value). The prolonged depression of twitch force in the two groups that sustained low-level force contractions (20 and 35 % MVC) must be influenced by factors other than those related to the M wave because the M wave was fully recovered by 10 min for all three groups (Table 2). The depressed MVC force at 10 min of recovery (Table 1) paralleled the reduction in twitch force for all three groups.

Time course of M wave and twitch recovery following the fatigue task

The time course of recovery in M wave amplitude over the 10 min period following the fatigue test is shown for all three target force groups in Fig. 5*A*. The recovery curves for the three groups were similar; M wave amplitude recovered in an approximately exponential fashion with a time constant of about 100 s. Recovery was nearly complete by 200–240 s and then stabilized for the remainder of the recovery period.

In contrast, twitch recovery was more complex and the pattern varied across the three target force groups (Fig. 5*B*). Over the initial 20–30 s, the 20 and 35 % MVC groups (● and ○, respectively) showed an almost identical rapid increase in twitch amplitude. This early recovery restored twitch amplitude for these two groups from about 45 to 70 % of the pre-fatigue level. The twitch force for the 65 % MVC group (△) potentiated during this early phase, rising from 90 to about 110 % of the pre-fatigue level. A transition to an increased rate of twitch recovery was evident at about 60 s for the 35 and 65 % target groups. This secondary phase was not seen in the 20 % MVC group, which maintained a slow rate of recovery throughout the remainder of the 10 min period. Twitch recovery peaked (127·1 ± 40·1 % of pre-fatigue) at 180 s for the 65 % group and slightly later (240 s) for the 35 % MVC group (94·7 ± 30·1 % of pre-fatigue). For both of these groups, twitch amplitude then slowly decayed from the peak value and at 10 min was 103·4 ± 18·5 and 84·5 ± 27·2 % of pre-fatigue levels for the 65 and 35 % MVC groups, respectively.

Twitch recovery in first dorsal interosseous following a sustained 65 % MVC seen in this study was nearly identical in amplitude and time course to that observed by others in tibialis anterior (Vandervoort, Quinlan & McComas, 1983) and quadriceps

femoris (Grange & Houston, 1991) following sustained, 60 s MVCs. We believe that these twitch recovery curves can be explained by the co-existence of fatigue-related and potentiating processes.

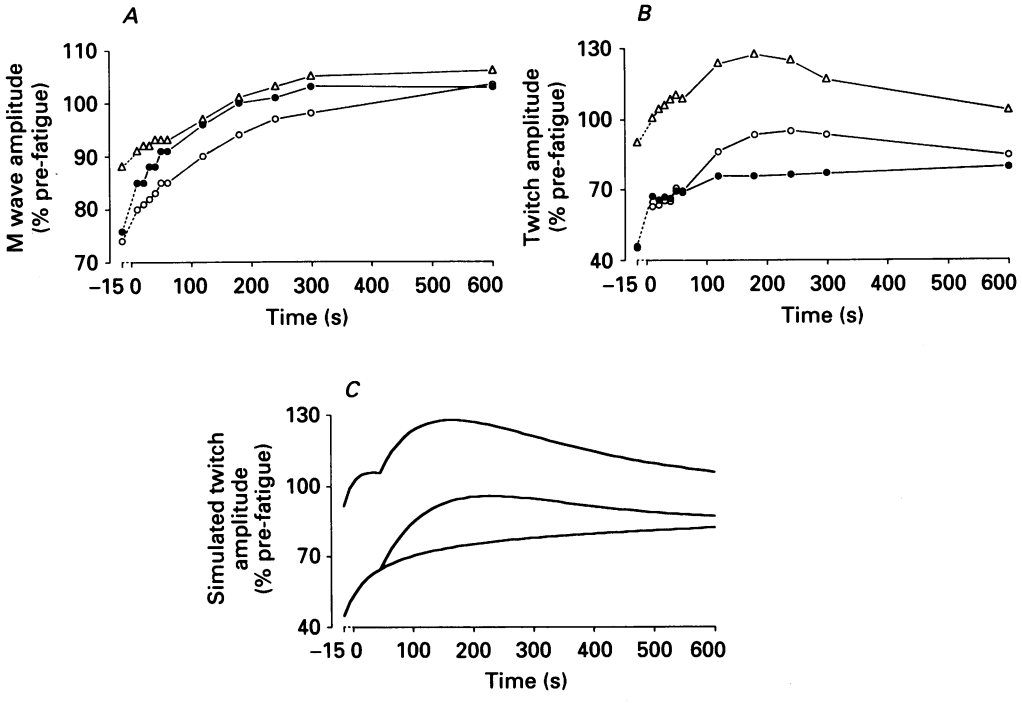

Fig. 5. Mean changes in M wave amplitude (*A*), experimentally measured twitch amplitude (*B*), and simulated twitch amplitude (*C*) from the end of the fatigue test through the 10 min recovery. ●, 20% MVC group; ○, 35% MVC group; △, 65% MVC group. The first measures of twitch amplitude (indicated at −15 s on the graph) were obtained immediately after the fatigue task, whereas the 10 min recovery period did not begin (time 0 s) until after the final set of MVCs. M wave amplitude recovered to equal (20 and 35% groups) or slightly greater (65% group) than pre-fatigue values within 10 min. The time course of recovery in twitch amplitude, however, was different for the three groups. The simulated twitch–recovery curves (*C*) were based on a model of processes that can concurrently potentiate and diminish force. The initial simulated values were obtained at time zero (eqns (1)–(3)) but the curves were moved graphically to the left in order to coincide with the experimental measurements. The time courses for the experimentally measured and simulated values for twitch amplitude were similar for all three groups of subjects.

DISCUSSION

The major findings of this study were a failure of voluntary EMG to attain maximal levels during a sustained, submaximal contraction, a fatigue-related decline in M wave amplitude, and a time course of twitch recovery that suggested the impairment of several processes during the fatiguing contraction. These results suggest that neuromuscular propagation was impaired by this task, which probably contributed to the inability of subjects to fully activate muscle during a sustained,

submaximal contraction and contributed to the diminution of force by the end of the fatigue task. These effects, however, varied with the target force and the duration of the contraction, and underscore the task-dependent nature of fatigue (Enoka & Stuart, 1992).

Impairment of neuromuscular propagation

The conclusion that neuromuscular propagation is impaired during a sustained, submaximal contraction is based on the observation of significant declines in M wave amplitude. This reduction was greater for the subjects who sustained the low target forces and performed the task longer (23·8 and 26·4 % decreases for the 20 and 35 % MVC groups, respectively) compared to those who held the 65 % MVC force (11·7 % decrease). In contrast, it has generally been found that M wave amplitude is maintained during short-duration (60 s), sustained maximum voluntary contractions (Bigland-Ritchie, Kukulka, Lippold & Woods, 1982; Bigland-Ritchie *et al.* 1986*c*; Kukulka *et al.* 1986; Thomas *et al.* 1989). However, when the maximum voluntary contraction was sustained for longer durations (up to 5 min), comparable reductions in M wave amplitude to that seen in the present study have been reported in adductor pollicis (Bellemare & Garzaniti, 1988), first dorsal interosseous (Stephens & Taylor, 1972; Milner-Brown & Miller, 1986; Thomas *et al.* 1989), and tibialis anterior (Milner-Brown & Miller, 1986). Thus contraction duration appears to be one task parameter that may influence the degree of neuromuscular propagation impairment.

It has been suggested that the decrease in M wave amplitude can be caused by a failure of neuromuscular transmission (on all-or-none event that will not affect M wave duration), a reduction in the amplitude of the muscle fibre action potentials, or an increase in the dispersion time over which the muscle fibre action potentials are detected by the electrode. For three reasons, however, the effect of the latter factor on M wave amplitude is minimal. Firstly, simulations have shown that increased temporal dispersion has a negligible effect on the amplitude of motor unit action potentials when detected with surface electrodes (Boyd, Lawrence & Bratty, 1978; Gootzen, Stegeman & Van Oosterom, 1991). Secondly, because fatigue has little effect on axonal conduction velocity, an increased dispersion in the arrival times of the axonal action potentials at the endplates seems unlikely. Thirdly, fatigue probably causes a compression in the range of muscle fibre conduction velocities. Motor units with low recruitment thresholds have lower muscle fibre conduction velocities than do high threshold units (Andreassen & Arendt-Nielsen, 1987). Only fatiguable units exhibit a marked increase in action potential duration with fatigue (Enoka, Trayanova, Laouris, Bevan, Reinking & Stuart, 1992), which indicates a reduced conduction velocity in these units (Lindström *et al.* 1970). Because these units have the highest conduction velocities initially, fatigue may tend to compress, rather than enhance the differences in conduction velocity across the population of motor units. This effect would tend to decrease temporal dispersion of the motor unit action potentials elicited during an M wave.

Because of the unlikely effect of dispersion time on M wave amplitude, changes in M wave amplitude are largely determined by alterations in neuromuscular junction transmission and variation in the amplitude of muscle fibre action potentials, both of which appear to change with sustained activity (Sandercock, Faulkner, Albers &

Abbrecht, 1985; Eerbeek & Kernell, 1991). There is some evidence, however, which suggests that a decline in action potential amplitude may not necessarily lead to a change in force. Action potentials have been shown to decline in frog muscle fibres in response to direct stimulation at high frequencies ($\geqslant 50$ Hz) without a concomitant decrease in isometric force (Lüttgau, 1965). Such observations suggest that there may be a safety margin within which sarcolemmal action potentials can vary without affecting the force exerted by the contractile machinery. In contrast, most evidence obtained in mammalian muscle (including human) has shown that diminished action potential amplitude during repetitive stimulation is associated with reduced force in single fibres (Metzger & Fitts, 1986), single motor units (Reinking, Stephens & Stuart, 1975; Kugelberg & Lindegren, 1979; Sandercock *et al.* 1985; Gardiner & Olha, 1987), and in whole muscle (Milner-Brown & Miller, 1986; Kernell, Donselaar & Eerbeek, 1987; Enoka, Rankin, Stuart & Volz, 1989). Indeed, it is difficult to find any demonstration in mammalian muscle of a safety margin for activation, namely, a reduction in action potential amplitude without a change in muscle force. Without such evidence, the observed decline in M wave amplitude following a sustained, submaximal contraction must be interpreted as a decrement in muscle activation.

If there was a complete loss of force prior to a change in action potential amplitude, then it would be difficult to argue that impaired neuromuscular propagation contributed to the decline in force. Indeed, it is possible to design a fatigue protocol that will elicit a decline in force prior to a reduction in action potential amplitude (Burke, Levine, Tsairis & Zajac, 1973). However, such protocols tend to evoke parallel declines in action potential amplitude and force when applied over a longer duration (Reinking *et al.* 1975; Gardiner & Olha, 1987). Similarly, M wave amplitude is relatively stable during sustained maximum voluntary contractions of short duration (Merton, 1954; Bigland-Ritchie *et al.* 1982). The results of the present study, however, show that M wave amplitude is reduced during submaximal contractions and that the effect is greater when the target force is low (20 and 35% MVC) and the task is performed for a long duration compared to a moderate force (65% MVC) that is sustained for a shorter duration. The mechanisms responsible for the decline in force, therefore, appear to depend on the details of the fatiguing protocol (Enoka & Stuart, 1992).

Limited increase in voluntary EMG

When human subjects perform maximal voluntary contractions there are parallel declines in force, EMG and M waves that have been interpreted to indicate a significant role in fatigue for impairment of neuromuscular propagation (Stephens & Taylor, 1972; Milner-Brown & Miller, 1986; Bellemare & Garzaniti, 1988). However, it has been suggested that when a human subject sustains a submaximal, isometric force to the endurance limit and the EMG of the involved muscle increases (Lippold, Redfearn & Vuco, 1960), that the central nervous system, in well-motivated subjects, remains capable of fully activating muscle and that the reduction in force can result only from failure of the muscle contractile apparatus (Bigland-Ritchie *et al.* 1986*c*). The increase in EMG is generally thought to reflect a neural-based compensation for contractile failure whereby there is an increase in motor unit activity, both in recruitment and discharge rate, due to an enhancement of the descending drive

provided by suprasegmental centres (Lippold *et al.* 1960; Bigland-Ritchie, Cafarelli & Vøllestad, 1986*a*). When the M wave area immediately after the fatiguing contraction is not different to pre-fatigue values (Table 2), the increase in EMG amplitude must have been minimally affected by peripheral factors (Fuglevand, Winter, Patla & Stashuk, 1989) and largely determined by an increase in motor unit activity.

Despite the observed increase in EMG amplitude during the submaximal contraction by all three groups of subjects in this study, a significant feature of the data was the failure of the EMG to reach the maximal values that were obtained during an MVC. The observation that subjects reached their endurance limit despite a submaximal EMG has been reported previously for handgrip contractions (Lind & Petrofsky, 1979) and biceps brachii (Petrofsky, Glaser, Phillips, Lind & Williams, 1982), and for soleus but not quadriceps femoris (Bigland-Ritchie *et al.* 1986*c*). As with our data, Lind & Petrofsky (1979) and Petrofsky *et al.*(1982) also found that a subject was more likely to attain a maximal EMG, or close to it, when the target force was high rather than low. For example, in Fig. 2 the 20% MVC group reached a final EMG value that corresponded to 45% MVC while the EMG for the 65% MVC group was comparable to 81% MVC at the endurance limit.

The ability of subjects to maintain a sufficient level of neural excitation to muscle despite a declining force capacity of active motor units during sustained contractions probably depends on the interaction of several competing processes: increased excitation of the motoneuron pool by descending drive; intrinsic adaptation in motoneuron excitability (Kernell & Monster, 1982); peripheral inhibitory feedback from metabolite-sensitive muscle receptors (Bigland-Ritchie, Dawson, Johansson & Lippold, 1986*b*); a reduction in muscle spindle (Macefield, Hagbarth, Gorman, Gandevia & Burke, 1991) and Golgi tendon organ (Zytnicki, LaFleur, Horcholle-Bossavit, Lamy & Jami, 1990) afferent inputs; an increase in recurrent inhibition (Kukulka, Moore & Russell, 1986; McNabb, Frank & Green, 1988), and impairment of neuromuscular propagation. The time course of the voluntary EMG during the fatiguing contraction indicates the net effect of these processes (Fig. 2). The EMG data for the 65% MVC groups, for example, indicated that neural excitation increased over the first 70% of the contraction and then remained constant (△ in Fig. 2). At the endurance limit, the EMG amplitude was 19% less than maximum. This failure to attain maximum excitation may be due, in part, to an impairment of neuromuscular propagation, as reflected in a 12% decrease in M wave amplitude. Greater deficits in voluntary EMG and M wave amplitude were observed for the two groups that sustained lower target forces. We suggest, therefore, that the limitation in neural excitation of muscle during fatiguing contractions may be partially due to impaired neuromuscular propagation in addition to factors that reduce the net output of the motoneuron pool.

Time course of twitch recovery

It has been proposed that the complex pattern of force restoration following a sustained contraction is attributable to the co-existence of processes that both diminish and enhance force (Jami, Murthy, Petit & Zytnicki, 1983; Rankin, Enoka, Volz & Stuart, 1988; Grange & Houston, 1991). We concur with this view and have attempted, through an analytical examination of twitch force recovery, to

understand the potential interaction among these processes. A possible system of processes that may affect force output following a sustained contraction in response to motor nerve stimulation is shown in Fig. 6. In this scheme, the processes are arbitrarily arranged to proceed from the most proximal site of an event

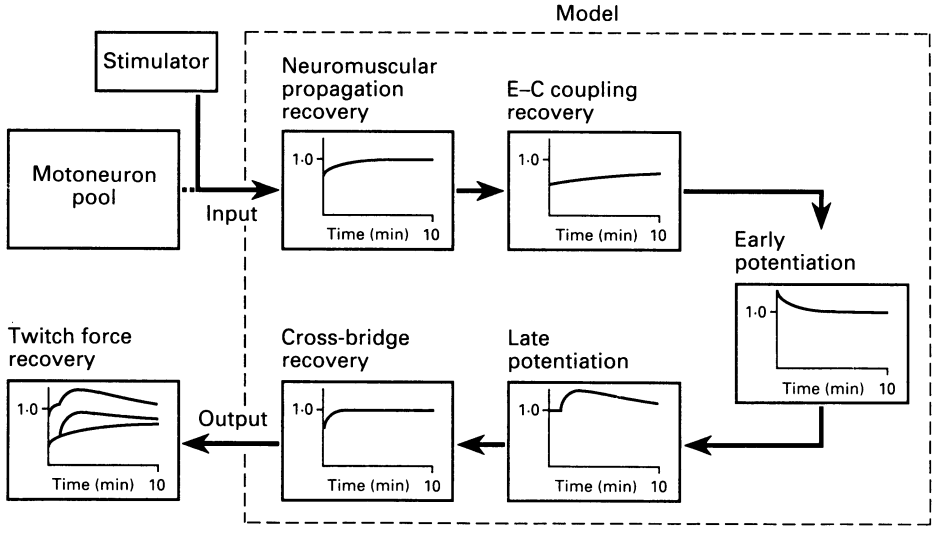

Fig. 6. Model used to simulate the recovery of twitch force after the fatigue task. The model consists of five processes that can influence the recovery of twitch force; three of these processes diminish force (impairment of neuromuscular propagation, excitation–contraction coupling, and cross-bridge function) while two processes can enhance it (early and late potentiation). A schematic time course of each process is indicated in the insets; an ordinate value of 1·0 indicates recovery to pre-fatigue values. In the model, the processes are arranged anatomically proceeding from the most proximal site (neuromuscular junction) to the most distal (cross-bridge). The input to the model is electrical stimulation of the muscle nerve (stimulator), as used to elicit twitches. The output of the model is twitch force. The time course of twitch force recovery is determined by the task-dependent interaction among the five processes.

(neuromuscular junction) to the most distal (cross-bridge). These processes are shown to interact in a serial manner and to have a multiplicative effect on one another such that they function as a cascade of mechanisms.

We assumed that at least three peripheral processes may be impaired during sustained contractions which can lead to a reduction in twitch force: neuromuscular propagation, excitation–contraction coupling and cross-bridge function. Each process was assumed to follow a different time course of recovery from fatigue (see Appendix for computational details). Firstly, impairment of neuromuscular propagation was assumed to follow an intermediate time course, similar to that observed for M wave amplitude in this study. Secondly, force loss due to impaired excitation–contraction coupling appears to recover slowly (30–60 min; Edwards, Hill, Jones & Merton, 1977; Metzger & Fitts, 1987); therefore, excitation–contraction coupling recovery was assigned a long time constant. Thirdly, recovery of force loss due to metabolite-induced impairment of cross-bridge function seems to occur

rapidly (Miller, Giannini, Milner-Brown, Layzer, Koretsky, Hooper & Weiner, 1987; Sahlin & Ren, 1989), which suggested a brief time constant for recovery of cross-bridge function.

In contrast to these impairment effects, there is evidence in the literature for at least two processes that enhance twitch force following sustained contractions. An early potentiation occurs after brief contractions that exceed 50% MVC force (Vandervoort, Quinlan & McComas, 1983), which decays relatively quickly. After a delay of about 60 s a late potentiating process becomes evident (Vandervoort *et al.* 1983; Grange & Houston, 1991; see also Fig. 5*B*) that reaches a peak at about 200 s, and then decays to control levels by 8–12 min of recovery. These two processes (early and late potentiation) were included in the model with the observed time constants. The mechanisms underlying these potentiation processes are not completely understood but appear associated with alterations in calcium kinetics (Duchateau & Hainaut, 1986) and the phosphorylation of myosin P light chains (Houston, Green & Stull, 1985).

To simulate the recovery of twitch force, the expression of these five processes was assumed to vary among the three target force groups. The assumptions included: (1) impaired neuromuscular propagation was present in all three groups, in direct proportion to the degree of M wave depression seen for each group at the end of the fatigue task; (2) impairment of excitation–contraction coupling is limited to contractions of long duration (Lännergren & Westerblad, 1991), which excluded an effect for the 65% MVC group but meant that the recovery of twitch force was influenced by impairment of excitation–contraction coupling for the 20 and 35% MVC groups; (3) a similar degree of metabolite-associated impairment of cross-bridge function was assumed for all three groups, because mean power frequency, an indirect index of alteration in the metabolic environment of muscle with fatigue (Lindström *et al.* 1970; De Luca, 1984), declined by the same amount for all three groups (Fig. 3); and (4) early potentiation affected only the 65% MVC group (Vandervoort *et al.* 1983) whereas late potentiation affected twitch force recovery of both the 35 and 65% MVC groups.

Based on these assumptions, the time course of twitch force restoration following a sustained 20% MVC, $F_{20}(t)$, was estimated from the serial cascade of force recovery associated with the impairment of neuromuscular propagation (F_{NP}), excitation–contraction coupling (F_{EC}), and cross-bridge function (F_{CB}) as:

$$F_{20}(t) = F_{NP}(t) \times F_{EC}(t) \times F_{CB}(t). \quad (1)$$

Under this scheme, the initial restoration of force following a 20% MVC (Fig. 7*A*) occurred quickly because of the combined rapid recoveries in neuromuscular propagation and cross-bridge function. The twitch remained depressed, however, after both of these processes (F_{CB} and F_{NB}) had recovered fully because of the slow recovery of excitation–contraction coupling (F_{EC}).

Recovery of twitch force following a sustained 35% MVC (F_{35}) was similar to that following a 20% MVC but with the additional effect of late potentiation (F_{LP}):

$$F_{35}(t) = F_{NP}(t) \times F_{EC}(t) \times F_{CB}(t) \times F_{LP}(t). \quad (2)$$

Late potentiation was superimposed on the long-lasting impairment of force due to

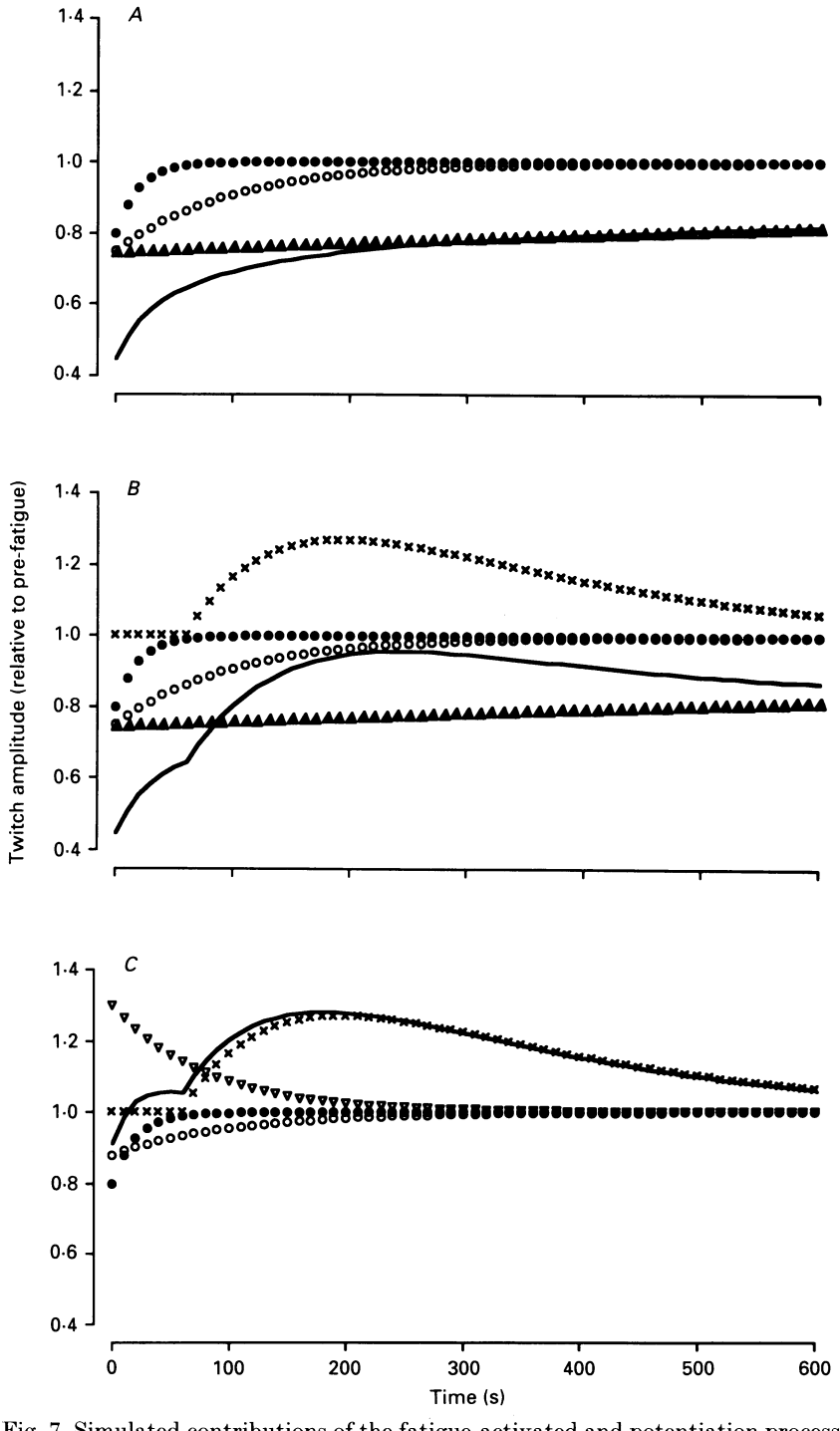

Fig. 7. Simulated contributions of the fatigue-activated and potentiation processes to the recovery of twitch force. In each panel, the simulated values for twitch force are indicated by the continuous line, while the contribution of each process is shown by the following symbols: ○, impairment of neuromuscular propagation; ▲, impairment of excitation–contraction coupling; ▽, early potentiation, ×, late potentiation; and ●,

incomplete restoration of normal excitation–contraction coupling (Fig. 7*B*). The apparent secondary depression of twitch force seen for this condition (Fig. 5*B*) after about 240 s of recovery can be explained by the decay in late potentiation.

Recovery of twitch force following a 65% MVC (Fig. 7*C*) was assumed not to involve impairment of excitation–contraction coupling because of the relatively short duration of the contraction. The efficacies of neuromuscular propagation and cross-bridge function were assumed to be diminished by this target force and would, by themselves, lead to a reduction in twitch force. Competing with these fatigue processes, however, were two forms of potentiation, early (F_{EP}) and late (F_{LP}) potentiation. Thus, force recovery following a sustained 65% MVC (Fig. 7*C*) was estimated as:

$$F_{65}(t) = F_{NP}(t) \times F_{CB}(t) \times F_{EP}(t) \times F_{LP}(t). \quad (3)$$

As with the 20 and 35% MVC conditions, both neuromuscular propagation and contractile function recovered quickly following a sustained 65% MVC. Because the reduction in force due to these processes was accompanied by an early potentiation which decayed with time, the rate of twitch recovery plateaued briefly and declined slightly. Late potentiation dominated the remainder of the recovery period because excitation–contraction coupling was assumed not to be impaired in this condition.

The pattern of force recovery derived from these assumptions captured most of the features of twitch force restoration seen experimentally (compare time courses in Fig. 5*B* and *C*). While experimental verification of the assigned parameter quantities is required to validate the model, the analytical description illustrates the following points: (1) the eventual inability of human subjects to sustain force at a particular target level is impaired at several sites in the sequence of processes involved in force production; (2) the degree to which each process is altered depends on the characteristics of the task (e.g. duration, intensity); (3) after a sustained contraction, processes that enhance force may co-exist with those that impair force; (4) the interaction of these processes, each with a different time course, shape the history of force restoration in the recovery period; and (5) the impairment of neuromuscular propagation probably contributes to the diminution of force following the sustained, submaximal contractions used in this study.

The effect of the level of sustained force on the processes involved in fatigue and recovery probably reflects, to some extent, differences in the time course of activation of the motor units utilized in the different tasks. For example, the high force contraction would have been accomplished, from the outset, by the activation of a greater proportion of high-threshold motor units compared to the low force contraction. Fast-twitch, fatigable motor units, which presumably have high recruitment thresholds, exhibit marked force potentiation whereas low-threshold units show little potentiation (Jami *et al.* 1983; Gordon, Enoka & Stuart, 1990). In the present study, potentiation was apparent following the two highest force contractions but was absent following the lowest force contraction. Furthermore, potentiation of fast-twitch, fatigable units, which have the highest recruitment

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impairment of cross-bridge function. The contributions of the five processes to twitch force recovery differed among the 20% (*A*), 35% (*B*), and 65% (*C*) MVC groups. The simulated values for the recovery of twitch force should be compared to those measured experimentally (Fig. 5*B*).

thresholds, has a relatively brief duration (Gordon *et al.* 1990). The only condition that appeared to display an early, fast-decaying potentiation (which we termed early potentiation) was the brief, high force task (65% of MVC). The early potentiation was not evident in the longer duration contractions (20 and 35% MVC), presumably because either fast-twitch, fatigable units were not activated during these tasks or because the mechanisms underlying this type of potentiation had subsided prior to cessation of these long duration contractions.

In conclusion, we have reported a decrease in the amplitude of the M wave in first dorsal interosseous after a submaximal, isometric contraction was sustained to the endurance limit. The magnitude of the decline in M wave amplitude, which we interpret as evidence of neuromuscular propagation failure, was greater for low target forces. We suggest that the impairment of neuromuscular propagation contributed to the observed limitation in muscle excitation during the fatiguing contraction and hence the force that could be exerted. A model of twitch force recovery underscored the task-dependent interaction of processes than can impair and enhance force.

APPENDIX

Restoration of twitch force during the 10 min of recovery was simulated based on the observation that the diminution and potentiation of force can operate concurrently following sustained contractions. Furthermore, the degree to which these effects are exhibited depends on the force level sustained during fatiguing contractions. The recovery of twitch force was modelled by accounting for five processes that can influence twitch force; a block diagram of the model is shown in Fig. 6. This cascade of mechanisms operates on the input (motor nerve activation) and affects the twitch force output in a multiplicative fashion.

The model consists of five processes, three that reduce force and two that enhance it (Fig. 6). The processes that are impaired and reduce force include neuromuscular propagation (NP), excitation–contraction coupling (EC), and cross-bridge (CB) function. It was assumed that these processes recovered exponentially but with different time constants. In Fig. 6, an ordinate value of 1·0 indicates the recovery to pre-fatigue values. The recovery in twitch force associated with restoration of neuromuscular propagation, $F_{NP}(t)$, was modelled as (see Fig. 7, ○):

$$F_{NP}(t) = 1 - \delta_{NP} e^{-(t/\tau_{NP})}, \tag{A 1}$$

where τ_{NP} is the time constant for neuromuscular propagation recovery and δ_{NP} represents the decrease in twitch force, relative to pre-fatigue values, caused by impairment of neuromuscular propagation immediately after the fatiguing contraction. Similarly, twitch force recovery associated with excitation–contraction coupling $F_{EC}(t)$ and cross-bridge function $F_{CB}(t)$ were modelled as (see Fig. 7, ▲ and ●, respectively):

$$F_{EC}(t) = 1 - \delta_{EC} e^{-(t/\tau_{EC})} \tag{A 2}$$

and

$$F_{CB}(t) = 1 - \delta_{CB} e^{-(t/\tau_{CB})}, \tag{A 3}$$

respectively. The parameters δ_{EC} and δ_{CB} represent the decreases in twitch force caused by impaired excitation–contraction coupling and cross-bridge function, respectively, immediately following the fatigue task.

Parameter estimates for these force reduction equations were: (1) M wave amplitude was assumed to reflect the effectiveness of neuromuscular propagation and hence values for eqn (A 1) were based on experimental observations of M wave recovery (Fig. 5*A*). The time constant, τ_{NP}, was assigned a value of 100 s, and δ_{NP} was set at 0·25 for the 20 and 35 % MVC groups, and at 0·12 for the 65 % MVC group; (2) a long time constant was used to simulate excitation–contraction coupling recovery ($\tau_{EC} = 1800$ s, eqn (A 2)). Force decrement related to excitation–contraction coupling impairment was assumed to be the same for the 20 and 35 % MVC groups ($\delta_{EC} = 0{\cdot}25$) and was set to zero for the 65 % MVC group; and (3) the degree of metabolite-induced impairment of cross-bridge function (eqn (A 3)) was assumed to be equivalent for all three target force conditions ($\delta_{CB} = 0{\cdot}20$) and to recover quickly following the contraction ($\tau_{CB} = 20$ s).

The two force enhancement processes included in the model were early and late potentiation. However, early potentiation was assumed to be expressed only with the 65 % MVC target force whereas late potentiation was assigned to both the 35 and 65 % MVC groups. In the absence of force reducing processes, early potentiation (EP) would induce a 30 % increase in twitch force immediately following the contraction ($\delta_{EP} = 0{\cdot}30$). This type of potentiation was assumed to decay at a moderate rate ($\tau_{EP} = 80$ s). Increased twitch force due to early potentiation was modelled as (see Fig. 7, △):

$$F_{EP}(t) = 1 + \delta_{EP} e^{-(t/\tau_{EP})}. \quad \text{(A 4)}$$

In contrast, late potentiation (LP) was assumed to be initiated after a time delay (t_d) of 60 s. This potentiation was characterized by two time constants (one related to its rate of rise, τ_{LPr}, and the other to its decay, τ_{LPd}). The values of these time constants were selected ($\tau_{LPr} = 180$ s, $T_{LPd} = 200$ s) so that late potentiation peaked at a recovery time of around 200 s and decayed to control levels by 600 s. The equation used to model twitch force enhancement due to late potentiation was (see Fig. 7, ×):

$$F_{LP}(t) = 1 + (1 - e^{-(t-td)/\tau_{LPr}})\, e^{-(t-td)/\tau_{LPd}}), \quad t \geqslant 60 \text{ s}. \quad \text{(A 5)}$$

In Fig. 7*A–C*, these modelled processes are shown for the 20, 35 and 65 % MVC target force conditions, respectively. Twitch force recovery (Fig. 7, continuous lines; Fig. 5*C*) was simulated for each group as the product of these processes.

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