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Fatigue and functional performance of human biceps muscle following concentric or eccentric contractions

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Smith ICH, Newham DJ. Fatigue and functional performance of human biceps muscle following concentric or eccentric contractions. *J Appl Physiol* 102: 207–213, 2007. First published September 21, 2006; doi:10.1152/japplphysiol.00571.2006.—A long-lasting fatigue was measured in human biceps muscle, following 40 maximal isokinetic concentric or eccentric contractions of the forearm, as the response to single-shock stimuli every minute for 4 h. This protocol allowed new observations on the early time course of long-lasting fatigue. Concentric contractions induced a novel progressive decline to 30.2% (SE 7.8, $n = 7$) of control at 23 min with complete recovery by 120 min. Eccentric contractions lead initially to a smaller force reduction of similar time course followed by a slower decline to 40.0% (SE 5.1, $n = 7$) control at 120 min with recovery less than half complete at 4 h. A 50-Hz test stimuli overcame both fatigues, identifying low-frequency fatigue. EMG recordings from the biceps muscle showed moderate (<20%) changes during the fatigue. A visual-tracking task showed no decrement in performance at the time of maximal fatigue of the single-shock response. Because the eccentric contractions have a similar activation, a larger force, but much smaller metabolic usage than concentric contractions, it is concluded that the initial decline is related to the effects of metabolites, whereas the slower phase after eccentric contractions is associated with higher mechanical stress.

skeletal muscle; motor control; skill

PERIPHERAL MUSCLE FATIGUE can be both short term, with a simultaneous recovery of force and phosphocreatine largely complete within 1 min (36, 37), and long-lasting, remaining for at least 0.5 h after exercise (13). This later failure to develop tension is seen most clearly using low-frequency test stimuli, thus the nomenclature of low-frequency fatigue (19). It remains long after metabolic recovery and is associated with reduced calcium release per action potential (8, 9). In addition, it has long been recognized that high-intensity eccentric contractions give rise to further force reduction that lasts several days and is associated with muscle damage (30, 29, 35), although the mechanisms for the initial decline in force are still uncertain (2, 31). In this paper, which studies force reduction for up to 4 h after brief but intense fatiguing concentric or eccentric exercise, we refer to the force reduction by either protocol as fatigue. The time scale of the development of long-lasting fatigue remains unclear because it has been experimentally lost either by using a long period of fatiguing exercise or through infrequent test measurements of the degree of fatigue. Normally, the fatigue is shown as having developed by the first measurement point, leading to the assumption that it develops during the fatiguing exercise. However, it was recently found that, in response to short maximal isometric contractions, low-frequency fatigue developed between 3 and 9 min after the exercise (11). Thus, to achieve a faster time resolution, long-lasting fatigue is measured here using a protocol of *1*) a brief period of maximal exercise and *2*) frequent single-shock test stimuli, rather than the ratio of low- to high-frequency stimulation normally used to characterize low-frequency fatigue.

One of the hallmarks of long-lasting fatigue is, unlike metabolic and late (12+ h) eccentric fatigue, that it is not accompanied by pain. Indeed the term "insensible fatigue" would be a more characteristic name. In his review of long-lasting fatigue, Jones (19) noted that the severe decrement of mechanical response, at action potential frequencies of 10–20 Hz typical of natural activation, might be expected to give rise to substantive errors in motor performance after fatiguing exercise. Although errors in proprioception have been noted (4), motor errors have not been reported, and Jones questioned whether this was because there was an efficient neural correction for the decreased response or simply that an effective test of skill had not yet been utilized. Subsequently, a decrease was shown (17) in lower limb-tracking performance immediately after exercising to 50% exhaustion, i.e., short-term metabolic fatigue. However, this type of error can largely be compensated for visually (27, 43), and there is indeed a proportionate enhancement of central motor effort during short-term (18) and long-term (6) fatigue. In addition, there is a slower reaction time to auditory stimulus during postexercise balance control (42), suggesting an additional attentional demand during fatigue.

Eccentric, compared with concentric, contractions are characterized by the development of high forces but a considerable lower metabolic turnover (1). Differences in subsequent fatigue development should thus highlight either metabolic causes following concentric contractions or the effect of high cross-bridge forces following eccentric contractions, such as damage by overstretch of unstable sarcomeres (39, 26). Although the long-term recovery over several days from eccentric fatigue has been described (e.g., Refs. 20, 34), the immediate differences in type and time course of fatigue are not clear. The intentions in this paper are thus *1*) to compare the size and time course of long-lasting fatigue for equal concentric and eccentric contractions in human muscle at high temporal resolution and *2*) to determine what affect the fatigue has on task-dependent performance.

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METHODS

Fatiguing exercise. Maximal voluntary isokinetic contractions and extensions of the elbow flexors were made against a motor-controlled dynamometer (Kin-Com 500H, Chattecx, Chattanooga, TN). The subjects were strapped at the waist and shoulders to the dynamometer chair so that the contractile force was largely developed by forearm flexors. The moving arm of the dynamometer was strapped to the subject's wrist with the pivot in line with the elbow joint and at an initial included joint angle of 100° for concentric, or the complementary 45° for eccentric, work of the biceps. The exercise was 4 sets of 10 contractions through 55° at a speed of 100°/s. This speed was chosen to obtain an approximately maximal power output. There was a 4-s rest period between sets, giving an exercise period of ~2 min. In a third series of experiments with the same protocols, either two sets (20 contractions) or eight sets (80 contractions) were required. Test responses were started ~2 min afterward, the time required to unstrap the Kin-Com wrist cuff and set the response recording system. Each subject undertook concentric contractions on the first experimental day and eccentric contractions on the second experimental day, 2 -7 days later, using the nondominant arm.

Electrical stimulation and recording of response. Single electrical shocks were applied at the top third of the biceps via two 5 × 5-cm conductive rubber electrodes using constant-current 0.1-ms stimuli (model DS7, Digitimer, Welwyn Garden City, Hertfordshire, UK). EMG signals were recorded from the belly of biceps with a MA-110 active electrode probe (Motion Lab Systems, Baton Rouge, LA) in all experiments except the skill series. Subjects were seated with the elbow joint at 90°, and the auxotonic twitch response was recorded as the inertial flexion of the forearm using a potentiometer connected via a lightly loaded (compliance ~10°/N) wrist strap. Maximal twitch responses were ensured by recording stimulus-response curves for each subject before and at hourly intervals during the experiment. Responses were recorded every minute for 15 min before and 240 min after the fatiguing exercise. To compare these twitch measurements with conventional low-frequency fatigue, tetanic stimuli with 5 shocks at 1 Hz and 10 Hz and then 10 shocks at 50 Hz were given in a second series of experiments each minute for 15 min before and 20 min after the exercise. Results for these are given as the average of 10 tests during *minutes 6-15* of the control period and for *minutes 11–20* after exercise. All mechanical records were measured at the peak response. In all cases, the timing of the stimuli and of the skill test was computer controlled throughout the recording period.

Skill test. In the series of experiments using tetanic stimuli, a 10-s tracking test was also performed every minute during the 15-min preexercise period and the 20-min recovery period. The subjects were asked to point at a moving target on a computer screen using a laser pointer that was strapped to the lower arm, the position of which was measured by the same potentiometer system as for recording the twitch response. The vertically moving target was synthesized for each test from 10 harmonic sine waves with random amplitude and base frequency of 1 wave each 10 s. The movement range, referred to the elbow joint, was 10°. Tracking performance was quantified in several ways. First, the lag between the target and response trace was calculated by finding the time difference for maximum coherence between the two signals. In all subsequent analyses, the target signal was shifted forwarded by this lag so that, for an ideal tracking performance, the signals would exactly superimpose. The movement error was calculated as the standard deviation of the difference between the new traces. The movement error was further analyzed to test the hypothesis that errors should be larger during activation of the fatigued biceps muscle than during activation of the unfatigued triceps muscle or while allowing the action of gravity. Because it is muscle force that accelerates the arm, the tracking signal was double differentiated and used to separated the tracking errors into those occurring during positive acceleration (biceps activation) and negative acceleration (triceps activation or gravity). The ratio of the standard deviation of each of these error types was used to estimate the symmetry of error between biceps and triceps. Results given are for the average of 10 tests during *minutes 6–15* of the control period and for *minutes 11–20* after exercise.

Subjects. Subjects were healthy untrained men and women with a median age of 22 yr (range 20–53 yr). Experiments were conducted in three series with different, but overlapping, subject groups. The first series of experiments, using 40 eccentric or concentric contractions followed for 4 h of test twitch stimulation, had 7 subjects. The second series with six subjects involved the skill test and tetanic stimulation, although one subject chose not to complete the tetanic stimulation. A third series with 5 subjects compared 20 or 80 contractions. The experimental protocols were approved by the College Research Ethics Committee, and all subjects provided written informed consent. Data are given as means ± SE where n refers to the number of subjects. Significance was set at $P < 0.05$ using paired or unpaired t-tests.

RESULTS

Forty maximal concentric isokinetic contractions resulted in a progressive decline in the response to single electrical stimuli with a minimum response 23 min after the end of exercise of 30.2 ± 7.8% (means ± SE, $n = 7$) of the preexercise control (Fig. 1*A*). This was followed by a steady recovery with half recovery at 55 min and full recovery after ~2 h. The response at the first measurement, ~2 min after the end of the exercise, was depressed to only 78% control with a half-maximal decline in 6–7 min. Subjects, when asked about this delayed decline, reported no sense of fatigue; indeed, some were incredulous of the observed decline in their response.

The temporal pattern of fatigue following 40 maximal eccentric contractions was markedly different. The decline was much slower with a minimum response taking ~2 h. By the end of the experiment at 4 h, recovery was still just less than half complete. Half-maximal decline occurred in 12 min, but there was an early rapid decline, similar in time scale to that for concentric contractions, followed by a much slower decline. The maximal decline was smaller following eccentric contractions (40.0 ± 5.1% of control at 120 min). The force exerted during the isokinetic concentric contractions, as might be expected from the Hill relationship, was about half the force produced during eccentric contractions (Fig. 1*B*) (58% for the first contractions falling to 40% for the final contractions). Thus, despite having developed a lower force, concentric contractions produced a greater long-lasting fatigue.

To test whether the long-lasting nature of the fatigue observed is due to low-frequency fatigue (13), the second series of experiments were performed where the fatigue was measured with stimuli at 1, 10, and 50 Hz. Figure 2 shows that the initial fatigue (11–20 min) was relieved at 50 Hz for both concentric and eccentric fatiguing routines, thus defining the observed fatigue as low frequency. The 10-Hz-to-50-Hz ratio showed significant declines to 0.56 ± 0.09 of its initial value for concentric and 0.80 ± 0.09 for eccentric contractions, values in similar proportion to the twitch decline (Fig. 1) but of smaller amplitude. To investigate the relationship between exercise intensity and fatigue, a third series of experiments were conducted using either 20 or 80 maximal concentric contractions in the fatiguing period (i.e., 2 or 8 sets instead of 4). The twitch response at 20 min after 20 contractions was 72 ± 2.2%, and after 80 contractions it was 50 ± 6.0% control ($n = 5$). There was no significant difference between 40 and 80

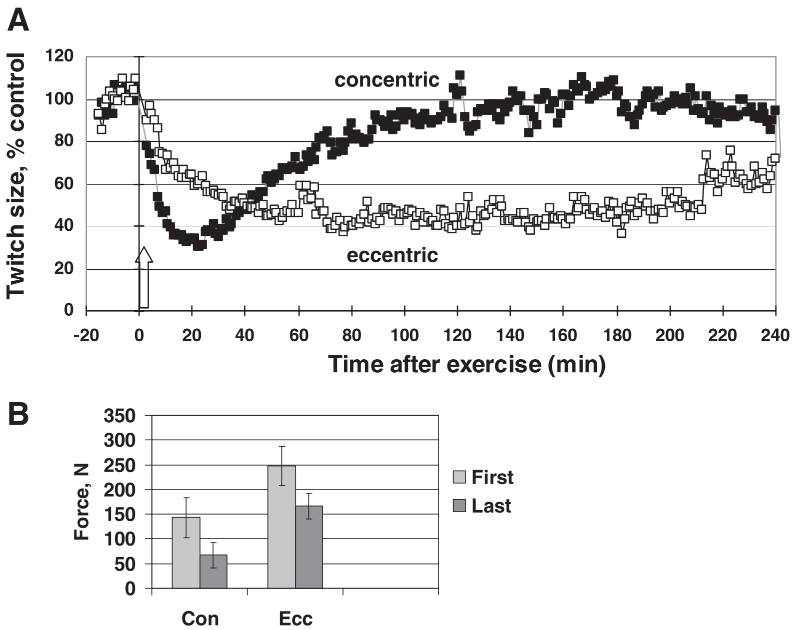

Fig. 1. Fatiguing responses to concentric (Con) and eccentric (Ecc) exercise. *A*: contractile responses to single-shock electrical stimulation of the biceps. Voluntary maximal isokinetic contractions (4 sets of 10 contractions) were performed at *time 0* (arrow) with either concentric (first experimental day) or eccentric (second day) contractions of the upper arm. Values were calculated as a percentage of the 15-min preceding control period for each subject and are shown as the average of the average for 7 subjects (after 210 min $n = 5$); modal mean ± SE of all points is 8%. *B*: peak force developed during the fatiguing contractions averaged for the first and last sets of 10 contractions (mean ± SE, $n = 4$).

contractions, but the fatigue was about halved for 20 contractions.

A reduction in electrically induced EMG (M wave) following fatiguing electrical stimulation has been reported in both rats (23) and humans (25) with a maximum depression of ~50% after 60 min. Figure 3*A* shows that in the present experiments, there was also a decline in the M wave but that this was <20% for both concentric and eccentric contractions (Fig. 3*C*). The time scale of decline and recovery of the M wave was similar to the decline of the mechanical response, although there was evidence of an initial potentiation of the M wave during the first few minutes after the fatiguing exercise.

To test whether the observed fatigue had an effect of skilled motor performance a tracking task was presented to subjects in the second series of experiments (Fig. 4*A*). The task was undertaken every minute during both the preexercise control period and during recovery. The results shown are for the average of 10 tests before and during *minutes 11–20* after exercise. The lag between the target trace and the tracking trace was ~200 ms (Fig. 4*B*) and showed no significant change after exercise or between exercise types. Paired differences before and after exercise were −11 ± 15 ms for concentric exercise and −6 ± 6 ms for eccentric exercise ($n = 6$ subjects). The corrected error of movement, measured as the standard deviation of the difference between the target trace and the lag-shifted tracking trace, also showed no significant change after exercise (106.2 ± 4.6% of the control period error for concentric exercise and 94.6 ± 2.5% for eccentric exercise). Finally, these corrected errors were separated, point by point, according to the direction of acceleration of the tracking movement. The ratio of these errors (Fig. 4*C*), which are assumed to reflect activity of biceps (positive acceleration) and triceps or gravity (negative acceleration) muscle, again showed no significant difference either before or after either exercise type.

DISCUSSION

These experiments show for the first time the slow development, as well as slow recovery, of long-lasting fatigue from both concentric and eccentric contractions. The study was designed to optimize the measurement of long-lasting fatigue, first by using high-power isokinetic contractions and second by testing the fatigue with single-shock stimulation with auxotonic recording. The protocol largely avoided the observation of early (metabolic) fatigue because the first test stimulus was given ~2 min after the end of exercise, by which time there is an almost complete recovery of creatine phosphate levels (38), although an early fatigue was seen during the exercise period (Fig. 1*B*). Other metabolite changes, such as lactate and pH, can be expected to be more moderate following our brief

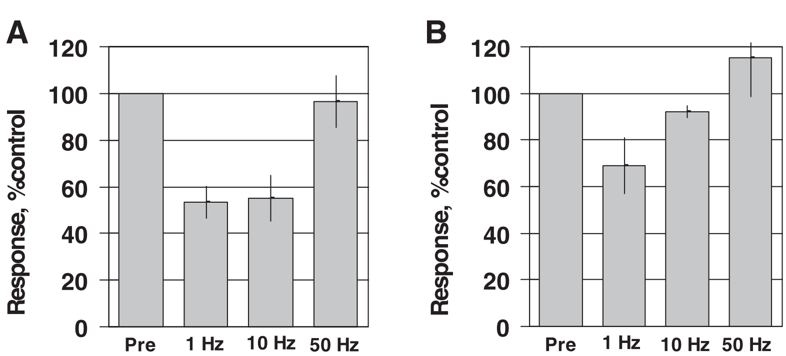

Fig. 2. Frequency dependence of the fatigued response. In a second series of experiments, tetanic responses were measured using stimuli delivered at 1 Hz, then 10 Hz, and finally 50 Hz every minute after 40 maximal concentric (*A*) or eccentric (*B*) contractions. Responses were averaged from 10 tests, during *minutes 6–15* before and *minutes 11–20* after exercise. Means ± SE ($n = 5$ subjects) of the peak response are shown relative to that before exercise (Pre).

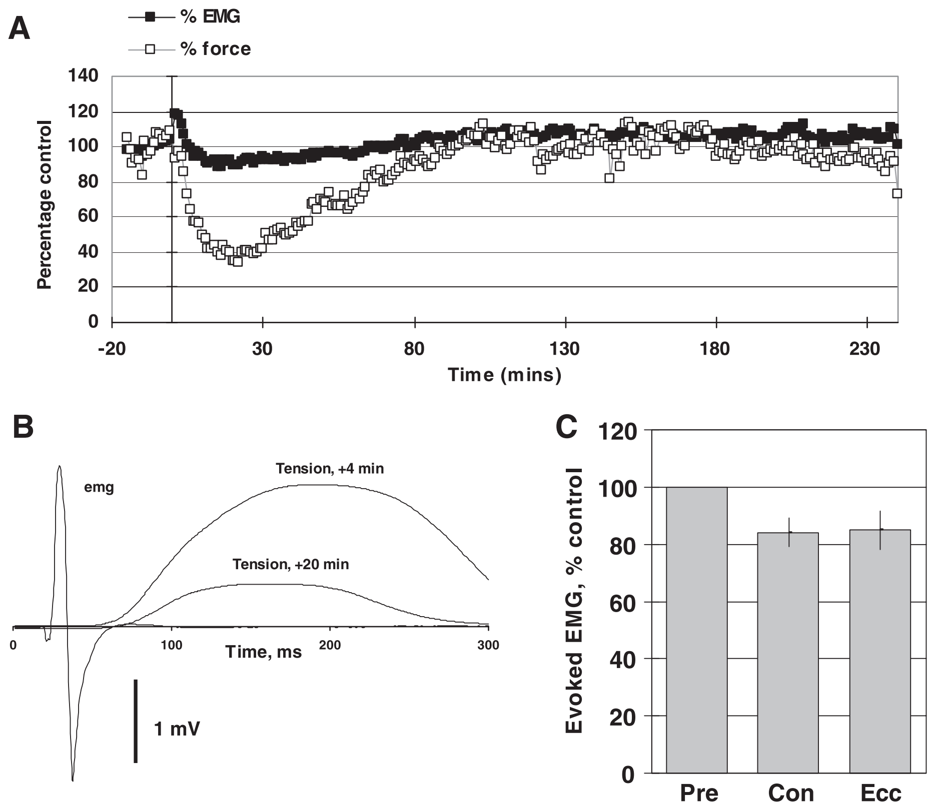

Fig. 3. Neuromuscular changes following fatiguing exercise. *A*: peak surface EMG (M wave) and contractile response to single-shock stimulation following concentric contractions in a single individual. *B*: individual records of the evoked EMG and of twitch 4 min and 20 min after concentric exercise. *C*: means ± SE (n = 7) of the evoked EMG amplitude 20 min after either concentric or eccentric exercise relative to value during the control period (Pre).

exercise protocol (41). A large long-lasting fatigue was indeed observed, with the test response more than halved for both concentric and eccentric fatiguing exercise. However, the time scales of fatigue were quite different for the two types of exercise: there was full recovery from the fatigue due to concentric exercise within 2 h, but with eccentric exercise not only was the recovery less than half complete at 4 h but the onset of fatigue was slower. These recoveries roughly match those observed for quadriceps muscle (30).

The protocol used to monitor long-lasting fatigue in these studies, maximal single-shock electrical stimulation, differs from conventional studies of low-frequency fatigue that use the ratio of responses to 10- and 50-Hz stimulation, with the intention of emphasizing changes related to activation per shock (calcium release or calcium sensitivity). Although this index (see Fig. 2) gave similar degrees of fatigue, there are important differences in twitch force. Peak twitch measurements are affected by postactivation potentiation and by changes in the twitch time scale. Postactivation potentiation can indeed produce large increases in twitch force (15, 32), but there is a rapid recovery largely complete within 3 min. The twitch time scale is well known to be slowed immediately after fatigue, but this also recovers within 3 min and is replaced by a very small speeding of the twitch for the duration of the low-frequency fatigue (6, 11). Finally, the 50-Hz response itself is slightly depressed during long-lasting fatigue (11, 13). Taken together, this suggests that the twitch response is an effective and sensitive index of long-term fatigue (22). One reason for differences in fatigue between concentric and eccentric fatigue is that there is a rightward shift in the ascending force-length relationship following eccentric exercise, probably from the presence of damaged sarcomeres (35). However, this effect enhances the apparent eccentric fatigue, so it cannot explain the differences observed here. It has recently been shown (6) that long-lasting fatigue can be induced by low-force as well as maximal voluntary contractions. The investigators found that 10 min of isometric contractions at 10% maximal induced a 34% reduction in twitch force at 30 min, comparable to the fatigue we saw from the 20, rather than the 40, maximal contractions we used to develop a near maximal long-lasting fatigue.

Previous studies (e.g., Refs. 6, 13, 30, 25, 31, 32 but not 11) have not shown the delayed onset of long-lasting fatigue observed here. This may be related to a difference in protocols. In the present study, the fatiguing exercise was completed within 2 min, whereas exercise periods ~20 min are common in other studies, thus masking the early decline. However, one recent study (11), which had an isometric exercise period of 1 min and measurements at 3, 9, 15, 21, and 27 min afterward, showed a delayed decline in force with a time scale not dissimilar from those here. The time scale of onset differed for eccentric and concentric exercise; both showed an early rapid decline in force but a continued and slower decline with eccentric exercise. The much smaller rapid decline following eccentric contractions (~30%) compared with following concentric contractions (~70%) may be related to the much smaller energy use with eccentric contractions (1, 33, 32). If so, the time scale for the development of long-lasting fatigue (half-time 6 min) should be linked to the presence of metabolic changes following intense short-term exercise, such as inorganic phosphate (2). There have been no convincing explanations of what governs the time scale of recovery from long-lasting fatigue following nondamaging (concentric) contractions, although the implicit suggestion (3, 12) remains that it

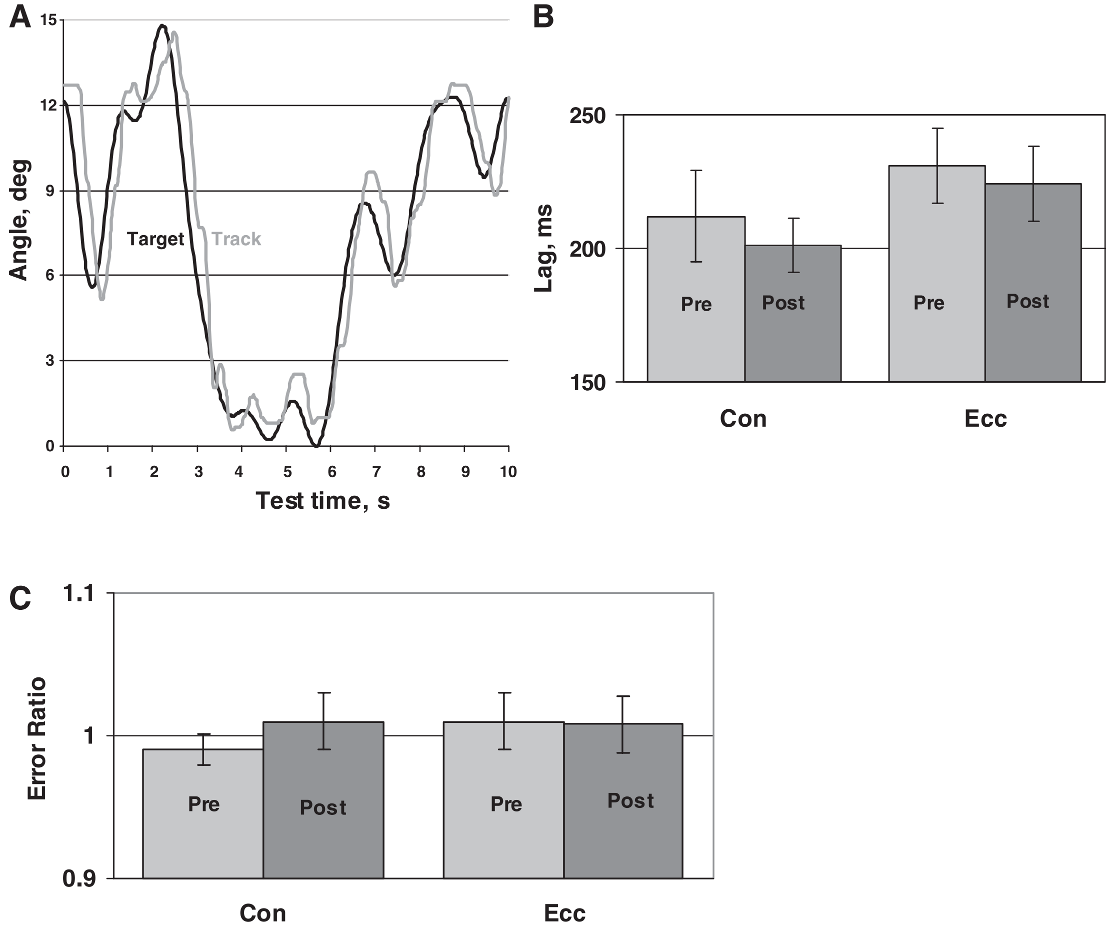

Fig. 4. Motor tracking skill following fatigue. *A*: trace of the vertically moving target (black line) during the 10-s skill test and the observed tracking response (gray line) using a laser beam attached to the forearm to point to the target. *B*: means ± SE ($n = 6$) of overall lag in tracking before (Pre) and 20 min after (Post) concentric or eccentric exercise. *C*: ratios of errors in tracking, after correction for overall lag, between upward and downward accelerations of the arm. The target path was randomized for each measurement, and the overall lag was measured by searching for the maximal coherence between the target trace and the shifted track trace. deg, Degrees.

reflects the time scale to dissolve the calcium phosphate precipitation in the sarcoplasmic reticulum. One important, but not previously stated, prediction of this hypothesis depends on the much higher solubility of calcium phosphate under acid conditions. Thus recovery from long-lasting fatigue should be considerably faster during anaerobic exercise than in equally intense but aerobic exercise. This might underlie why the intermittent contractions (whether concentric or eccentric) used in this study gave a more profound fatigue than those seen in studies using continuous isometric (and thus more ischemic) contractions.

The use of electrical stimulation during the test contractions in these studies defines the fatigue investigated as peripheral. Two tests were used to see whether the fatigue depended on changes in neuromuscular or in excitation-contraction coupling. First, the size of the M wave was measured, and second stimulus-responses curves were measured hourly during the fatigue: the small changes in both suggest that the fatigue measured here is largely of muscular origin. Coupled with the observation that the fatigue was overcome by using 50-Hz stimulation, it is reasonable to conclude that the fatigue we observed was dominated by low-frequency muscle fatigue. However, it should be noted that substantial decreases of the M wave, reaching a minimum of 42% of control levels with almost full recovery by 8 h, have been reported (25). A slower recovery following eccentric compared with concentric contractions has also been seen (32). Although our measurements confirm a long-lasting depression, the M wave fell only to 84% of control and was preceded by a short period of potentiation (Fig. 3*A*), which may be due to electrogenic hyperpolarization (16).

There have been a variety of suggestions for the mechanisms involved in long-lasting fatigue, linked to the central observation of decreased calcium release. In their review, Allen and Westerblad (3) propose elevated inorganic phosphate to be the key factor by leading to the precipitation of calcium phosphate. Alternatively excitation coupling may be disrupted by calcium-activated proteases (40). Our experimental findings provide some evidence for supporting the former because both the concentric and eccentric exercises can be expected to result in roughly similar profiles of activation (24) and calcium release (there is a moderate decrease of EMG activity in eccentric contractions) (21) but with very different use of metabolic energy. Thus the first phase of long-lasting fatigue (20-min peak and much larger in concentric contractions) is unlikely to be due to activation alone but to depend on the amount of metabolic activity. This gives support for the calcium phosphate hypothesis in this phase of fatigue. In contrast, the second phase of long-lasting fatigue (2-h peak and largely limited to eccentric exercise) was associated with greater mechanical forces, supporting the model of a response to muscle damage induced by the stretch (26, 39). Eccentric contractions are well documented to cause physical damage (10, 28), but the early time course and mechanisms involved remain uncertain. A prevalent model suggests that calcium entry leads to protease activation (35), although a reduction in calcium entry and protease action does not lead to a reduced fatigue (5). Gross cellular damage, measured as lactate dehydrogenase release from isolated rat muscle, occurs within 60 min following eccentric contractions, and increases with the number of eccentric contractions (44) and it might thus be related to the progressive decline in force seen 20–90 min after the eccentric exercise.

It has been suggested (30) that the subjective sense of weakness and instability that immediately follows intense eccentric exercise might reflect the intense long-lasting fatigue. The ability of subjects to make judgments of force decreases with muscle fatigue (14), with the sensation of force closely matching the fractional effort rather than the actual outcome (7). One might thus expect motor performance to be substantially altered in fatigue. However, it has been argued (7) that the concurrent increases in EMG activities (11) imply a premotor awareness of fatigue that functionally resets sensation so as to allow proportionate use of motor groups. The observation here of no decrement in skilled performance supports this hypothesis of an accurate knowledge of fatigue in the premotor regions. It is not easy to predict what functional tasks would be affected by low-frequency fatigue (19, 35). The fatigue observed here was dominated by large-force motor units with incomplete (i.e., low frequency) activation. In this study, a rapidly but randomly moving visual target was chosen as the task as this required only brief activation. A further issue is that damage induced by eccentric contractions disturbs proprioception (35), although in our studies the use of visual feedback lessens this factor. The motor task in our study required only moderate forces to be used to accelerate the limb mass: further studies requiring larger forces but of brief duration remain to be undertaken.

In summary, we have shown that short bursts of maximal exercise cause a delayed, insensible, and long-lasting decline in muscle force that is more profound after concentric exercise but more long-lasting after eccentric exercise. The decline is compensated for in low-force motor tasks. This compounds the lack of personal knowledge of the fatigue and may thus lead to motor instability using large-force movements.

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