Distinct profiles of neuromuscular fatigue during muscle contractions below and above the critical torque in humans

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Burnley M, Vanhatalo A, Jones AM. Distinct profiles of neuromuscular fatigue during muscle contractions below and above the critical torque in humans, J Appl Physiol 113: 215–223, 2012. First published May 3, 2012; doi:10.1152/japplphysiol.00022.2012.—Whether the transition in fatigue processes between “low-intensity” and “high-intensity” contractions occurs gradually, as the torque requirements are increased, or whether this transition occurs more suddenly at some identifiable “threshold”, is not known. We hypothesized that the critical torque (CT; the asymptote of the torque-duration relationship) would demarcate distinct profiles of central and peripheral fatigue during intermittent isometric quadriceps contractions (3-s contraction, 2-s rest). Nine healthy men performed seven experimental trials to task failure or for up to 60 min, with maximal voluntary contractions (MVCs) performed at the end of each minute. The first five trials were performed to determine CT [35–55% MVC, denoted severe 1 (S1) to severe 5 (S5) in ascending order], while the remaining two trials were performed 10 and 20% below the CT (denoted CT-10% and CT-20%). Dynamometer torque and the electromyogram of the right vastus lateralis were sampled continuously. Peripheral and central fatigue was determined from the fall in potentiated doublet torque and voluntary activation, respectively. Above CT, contractions progressed to task failure in ~3–18 min, at which point the MVC did not differ from the target torque (S1 target, 38.7 ± 4.3 N·m vs. MVC, 89.3 ± 8.8 N·m; P = 0.94). The potentiated doublet fell significantly in all trials, and voluntary activation was reduced in trials S1–S3, but not trials S4 and S5. Below CT, contractions could be sustained for 60 min on 17 of 18 occasions. Both central and peripheral fatigue developed, but there was a substantial reserve in MVC torque at the end of the task. The rate of global and peripheral fatigue development was four to five times greater during S1 than during CT-10% (change in MVC/change in time S1 vs. CT-10%: −7.2 ± 1.4 vs. −1.5 ± 0.4 N·m·min−1). These results demonstrate that CT represents a critical threshold for neuromuscular fatigue development.

Central and peripheral fatigue; maximal voluntary contraction; muscle stimulation; exercise

**Fatigue during exercise** is usually defined as a reversible decline in maximal muscle force or torque-generating capacity (3, 21, 24). During submaximal tasks, fatigue may reduce torque-generating capacity until the subject is unable to achieve the submaximal target torque, despite maximal effort, an event known as task failure or “exhaustion” (10, 31, 53). Fatigue can be attributed to a variety of processes along the motor pathway, and these are typically defined as being of central or peripheral origin. Peripheral fatigue refers to processes that occur at or distal to the neuromuscular junction (i.e., within the contracting muscle), whereas central fatigue refers to processes occurring proximal to the neuromuscular junction [i.e., residing within the central nervous system (CNS) (50)]. Both can be quantified using electrical stimulation of the muscle group(s) of interest using the interpolated twitch technique during a maximal voluntary contraction (MVC) (8, 24). A reduction in torque in response to stimulation at rest following a MVC is representative of peripheral fatigue (10, 13). Central fatigue is commonly quantified as a reduction in voluntary activation (24, 25, 50). The interpolated twitch technique has some important limitations (see Refs. 17, 43, 49 for discussion), and it can only indicate the presence of central fatigue and not its cause or location in the CNS (49). The extent to which central or peripheral mechanisms of fatigue are involved in the reduction in maximal torque-generating capacity depends on a number of factors, including contraction intensity (20, 56), whether the contractions are sustained or intermittent (12), the muscle group used (10), and the age and/or sex of the subjects (26, 32). In short, fatigue is task dependent (22).

During submaximal tasks, it is generally accepted that fatigue processes during “low-intensity” contractions differ from those during “high-intensity” contractions (42). Specifically, during prolonged contractions (sustained or intermittent) at a low fraction of the MVC torque (~5–30% MVC), the extent of central fatigue is substantial (47, 48, 56) and significantly greater than that during contractions at higher fractions of the MVC (20). In contrast, when submaximal contractions are performed at relatively high intensities (greater than ~30% MVC), peripheral fatigue is substantial (10, 25, 45), and central fatigue is either modest (20, 56) or absent (10). However, it is not known whether the transition in fatigue processes between low-intensity and high-intensity contractions occurs gradually as the torque requirements are increased, or whether this transition occurs suddenly at some identifiable “threshold”.

It has long been known that the relationship between power, force, or torque and the time to task failure is hyperbolic (11, 19, 37, 38, 44). The asymptote of this relationship has been termed the critical power or critical torque (CT) (13, 28; for reviews, see Refs. 29, 34, 39). Theoretically, contractions performed below the CT should be fatigueless, and task failure should not occur (37), whereas, above the CT, the mechanisms of fatigue should be common to all trials performed, allowing the time to exhaustion to be predicted precisely (13, 37). The value of CT during isometric contractions is dependent on the duty factor and has been reported to range between ~15% MVC for sustained contractions and ~40% MVC for intermittent contractions, with a duty factor of 0.5 (37). During sustained or repeated contractions, the neuromuscular system maintains the required torque by recruiting additional motor units and/or increasing the firing rate of those units already
METHODS

Ethical Approval

Nine healthy men (mean ± SD: age 28 ± 7 yr, height 1.83 ± 0.07 m, body mass 83.4 ± 19.6 kg) provided written, informed consent to participate in the present study, which was approved by Aberystwyth University’s Ethics Committee for Research Procedures. These experiments conformed to the Declaration of Helsinki.

Experimental Design

Subjects visited the laboratory on eight occasions over a 4- to 6-wk period, with all tests separated by at least 24 h. The first session was used to familiarize the subjects to the measurements and experimental protocol. During this session, the settings for the dynamometer and muscle stimulator were recorded for each subject. Subsequently, subjects performed five intermittent contraction protocols to task failure (“severe” trials; see Experimental Protocol). From these five tests, the CT was calculated, and subjects subsequently performed two further tests at 10 and 20% below the CT (CT-10% and CT-20%, respectively) for 60 min or until task failure, whichever occurred sooner. The severe trials and the sub-CT trials were each presented in a randomized order.

Experimental Protocol

Visit 1: set up and familiarization. During the familiarization session, the isokinetic dynamometer used in all testing (Biodex System 3, Shirley, NY) was adjusted so that the axis of rotation of the lever arm was in line with the lateral epicondyle of the right femur, and subjects were seated with the hip and knee joints at relative angles of 85° and 90°, respectively. The chair settings were then recorded and replicated in all subsequent trials. Electrodes were attached to the anterior aspect of the right thigh for stimulation of the m. quadriceps femoris. Carbon-rubber electrodes (12 × 10 cm, EMS Physio, Oxfordshire, UK) were coated in electrode gel with the anode placed 8 cm proximal to the superior border of the patella over the vastus medialis, and the cathode was placed at 30% of the distance measured from the anterior superior iliac spine to the superior border of the patella. On returning to the chair, the subjects’ position was firmly secured using Velcro straps across the shoulder and waist, while the right leg was secured to the dynamometer using a padded Velcro strap attached above the ankle.

The m. quadriceps femoris was stimulated using a constant-current, variable-voltage stimulator (DSAH7, Digitimer, Welwyn Garden City, UK). Paired stimuli (doublets) were delivered in 100-μs square-wave pulses with 10-ms interpulse interval at 400 V. Doublets were initiated at 100 mA, and stimulator current was increased in steps of 10 mA until the measured torque no longer increased. The current was then increased by a further 11 ± 1% to ensure the stimuli were supramaximal, and this current was recorded (range 330–500 mA). The subjects subsequently performed a series of 3-s MVCs to establish their maximum torque. A minute of rest separated each contraction. Typically, subjects produced five such efforts, with the last two being accompanied by muscle stimulation. In all instances, where MVCs were performed with stimuli, the stimuli were delivered 1.5 s into the contraction to coincide with maximal torque, and 1 s after the cessation of the contraction to provide a resting potentiated doublet.

Following the MVCs, the subjects rested for 10 min before practicing the experimental protocol. This involved producing targeted contractions (as described below) at 20% MVC for 5 min, followed, after 5 min recovery, by 3 min of targeted contractions at 40% MVC. In each case, the subjects were instructed to produce a MVC at the end of each minute before again attempting to achieve the target. These MVCs were accompanied by muscle stimulation. At the conclusion of the 40% MVC contractions, subjects recovered for 5 min, producing a MVC each minute, again with stimulation. Therefore, familiarization required a cumulative total of 18 MVCs, 15 with muscle stimulation, and 88 submaximal targeted contractions. At all stages, subjects were given verbal and visual feedback of their performance.

Visits 2–6: trials performed above CT (severe-intensity trials). All experimental trials followed an identical protocol. Subjects arrived at the laboratory, and the right leg was prepared for the experimental trial by attachment of the stimulating electrodes, followed by the attachment of surface electrodes for the measurement of the EMG of the vastus lateralis. The subjects were then strapped into the chair of the dynamometer and, after reestablishment of the supramaximal stimulation current, performed three 3-s MVCs with a minute of passive rest between each. Electrical stimuli were applied to the second of these MVCs to determine the fresh voluntary activation and potentiated doublet torque. The third MVC was used to determine the fresh average rectified EMG (AREMG) and MVC torque. Collectively, these represented the “preexercise” measures of neuromuscular function. In visit 2, the highest instantaneous measure of voluntary torque was recorded as the peak MVC torque, and the target torque for the submaximal contractions in trials 2–6 was calculated from this value. The targets then rested passively for 10 min, before commencing the submaximal targeted contractions.

The submaximal contractions were performed using a similar trial design to that presented by Bigland-Ritchie et al. (10), in which intermittent submaximal contractions were performed with MVCs regularly interspersed. The target for the submaximal contractions in visit 2 was set at 50% of the peak torque measured in the preceding MVCs. The subjects performed intermittent isometric contractions (3 s on, 2 s off) at this target torque for as long as possible. At the end of each minute, subjects were instructed to produce a MVC, before returning to targeted contractions. The dynamometer torque and the
target torque were presented on a screen, with a visual prompt to “push” and “stop” accompanied by the same verbal instructions from the experimenter. Doubplet stimulation accompanied each MVC, and these contractions were performed with strong verbal encouragement. The trial was terminated when the subject failed to attain the target torque for three consecutive contractions, with the subjects being informed of each miss. Following the third missed contraction, subjects were instructed to produce a final MVC. The duration of the first trial was used to determine the percentage of the MVC used in subsequent trials, which were performed in identical manner, so as to yield trial durations of 2–15 min, which have been recommended for the assessment of CT (29). These trials were performed in a randomized order. For all tests, subjects were told that the submaximal contractions would continue for 60 min or until task failure, whichever occurred sooner. Subjects were not informed of the elapsed time during the trials, nor were they provided any information about the performance of each trial. Visits 2–6 were used to determine the CT and the fatigue processes attending supra-CT contractions. Individual trials were identified as severe 1 (S1) to severe 5 (S5), with S1 being the lowest torque and S5 being the highest torque.

Visits 7 and 8: trials performed below CT. The final two trials were used to determine the fatigue processes during exercise performed at target torques 10 and 20% below the CT (identified as CT-10% and CT-20%). These trials again required the subjects to perform intermittent contractions (3 s on, 2 s off) to perform MVCs at the end of each minute. The order of these two trials was determined by the toss of a coin. Subjects were not given feedback of elapsed time for the first 30 min of the trials, but were informed of the time remaining after 30, 45, and 50 min to maintain motivation during the latter stages of the trial. Subjects continued for 60 min or until task failure.

Measurements

Torque. Knee-extensor torque from the Biodex dynamometer was sampled at 1,000 Hz and low-pass filtered at 40 Hz, before being displayed on a large screen 3 m in front of the subject using LabVIEW 8.5 (National Instruments, Austin, TX). The torque required during submaximal contractions was indicated using a target bar superimposed on the torque display. The subjects were instructed to match the torque to this bar when instructed to push for each 3-s contraction.

Surface EMG. Following the cleaning and shaving of the skin, two Ag-AgCl electrodes (10-mm diameter, 30-mm center-to-center distance) were attached to the belly of the vastus lateralis of the right leg. A reference electrode was attached to the medial aspect of the right tibial tuberosity. The EMG was sampled at 1,000 Hz, amplified (gain 1000, Dual Bioamp, ADI Instruments, Colorado Springs, CO), and band-pass filtered (13–500 Hz) using a fourth-order Butterworth filter (LabVIEW 8.5, National Instruments, Austin, TX) and displayed alongside the dynamometer torque.

Data Analysis

Torque. The torque in all experimental trials was processed using MATLAB R2009B (the Mathworks, Natick, MA). Each contraction was identified, and the peak torque (the highest instantaneous torque), mean torque (the arithmetic mean torque produced during the 3-s contraction), as well as the torque impulse (the integral of torque and time during the 3-s contraction; N·m·s) were calculated. The resting potentiated doublet torque was calculated as the highest torque measured following the resting stimuli delivered 1 s following a MVC, while voluntary activation was calculated using twitch interpolation (8, 9):

Voluntary activation (%) = 1 − (superimposed doublet/resting potentiated doublet) · 100.

where the superimposed doublet refers to the increment in torque measured following stimulation during a MVC.

Determination of time to task failure and the CT. The first five experimental trials (visits 2–6) were used to establish the CT. The time to task failure was determined as follows. First, the mean torque produced in the first minute of the trial was calculated. Then task failure was deemed to have occurred when three consecutive contractions each produced a mean torque of 5 N·m below the mean of the first minute. The first of these contractions was used to indicate time of task failure. Subsequently, the total torque impulse produced until task failure was calculated. To complete the analysis, the total contraction time during each individual trial was calculated. The CT was then determined by plotting the torque impulse against contraction time (Fig. 1B). The parameters of the torque-duration relationship were then estimated using linear regression of the torque impulse vs. contraction time:

\[ \text{Torque impulse} = W' + CT \cdot t \]

where \( W' \) represents the curvature constant parameter and \( t \) is the time to task failure.

EMG analysis. The filtered EMG signal from the vastus lateralis was processed using MATLAB to provide the AREMG during each 3-s contraction. The AREMG was normalized by expressing the data as a percentage of the AREMG during the last of the three pretest
MVCs within each trial. The AREMG in the last 30 s of each trial was also expressed as a percentage of the AREMG during the first MVC following task failure (to express the AREMG during submaximal targeted contractions as a percentage of that attainable during a maximal contraction at task failure).

**Parameters of neuromuscular fatigue.** The changes in voluntary torque, potentiated doublet, and voluntary activation measured from the onset of the contractions to the first MVC following task failure (or the MVC at 60 min during trials < CT) were used to quantify global, peripheral, and central fatigue, respectively. These responses were also expressed as the rate of change per unit time (Δ/Δt) to provide a measure of the respective rates of fatigue development during the experimental trials. Similarly, the normalized AREMG during a 30-s time bin before task failure (or task end) was taken as the measure of the degree of change in EMG amplitude produced by the trial. The maximal EMG at task failure was taken from the first MVC following task failure.

**Statistical Analysis**

Two-way ANOVAs with repeated measures (trial × time) were used to compare main effects for torque, potentiated doublet, voluntary activation, and AREMG across experimental conditions. The rates of change in these parameters were determined by one-way ANOVAs with repeated measures. Results were considered statistically significant when \( P < 0.05 \). When main effects were observed, specific differences within conditions were determined using Bonferroni-adjusted paired-samples 95% confidence intervals (95% CIs).

Linear regression was used to describe the rates of change in the mean MVC torque, doublet torque, and voluntary activation across trials. Similarly, the normalized AREMG rates of change in these parameters were determined by one-way ANOVAs with repeated measures. Results were considered statistically significant when \( P = 0.001 \), and the MVC torque at task failure was not different from the mean torque produced during the submaximal trials (Table 1). All trials above CT resulted in a significant reduction in the doublet torque (\( F = 62.43, P < 0.001 \); Table 1, Fig. 3A), indicating the presence of peripheral fatigue. The voluntary activation also declined in S1, S2, and S3 (\( F = 12.75, P = 0.007 \); Table 1, Fig. 3B), indicating the development of central fatigue, but the fall in voluntary activation in

**RESULTS**

**Preliminary Measures and the CT**

The peak instantaneous torque measured during a MVC in visit 2 was 237.0 ± 15.7 N·m, and this was used to set the target torques for the five tests performed above CT. These torques ranged from 88.7 ± 4.3 to 127.7 ± 6.1 N·m, or 38 ± 2 to 55 ± 2% MVC (Table 1). The CT was calculated to be 79.6 ± 4.2 N·m (34 ± 2% MVC), and the W' 5,444 ± 561 N·m·s. The 95% CI for the estimation of CT was 5.2 ± 0.8 N·m (range, 1.3–8.6 N·m). The two trials below CT (CT-20% and CT-10%) were performed at 66.4 ± 3.3 and 71.8 ± 3.6 N·m, or 29 ± 2 and 31 ± 2% MVC, respectively (Table 1).

**Trials Performed Above the CT (S1–S5)**

Figure 1 shows the typical torque profile during a trial performed to task failure above the CT. Task failure occurred when the subject was not able to achieve the target torque, despite a maximal effort, as shown by the declining MVCs as the trial progressed (Fig. 1A). This pattern is also evident in the mean MVC torque data presented in Fig. 2A. All trials above CT resulted in a significant decrease in the MVC torque (\( F = 58.77, P < 0.001 \)), and the MVC torque at task failure was not different from the mean torque produced during the submaximal trials (Table 1). All trials above CT resulted in a significant reduction in the doublet torque (\( F = 62.43, P < 0.001 \); Table 1, Fig. 3A), indicating the presence of peripheral fatigue. The voluntary activation also declined in S1, S2, and S3 (\( F = 12.75, P = 0.007 \); Table 1, Fig. 3B), indicating the development of central fatigue, but the fall in voluntary activation in

**Table 1. Voluntary torque, potentiated doublet, voluntary activation, and EMG responses to contractions below (CT-20%, CT-10%) and above (severe 1–5) the critical torque**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CT-20%</th>
<th>CT-10%</th>
<th>Severe 1</th>
<th>Severe 2</th>
<th>Severe 3</th>
<th>Severe 4</th>
<th>Severe 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean test torque, N·m</td>
<td>66.4 ± 3.3</td>
<td>71.8 ± 3.6</td>
<td>88.7 ± 4.3</td>
<td>96.9 ± 4.8</td>
<td>106.3 ± 5.3</td>
<td>115.8 ± 5.7</td>
<td>127.7 ± 6.1</td>
</tr>
<tr>
<td>Mean test torque,%MVC</td>
<td>29 ± 2</td>
<td>31 ± 2</td>
<td>38 ± 2</td>
<td>42 ± 2</td>
<td>46 ± 2</td>
<td>50 ± 2</td>
<td>55 ± 2</td>
</tr>
<tr>
<td>Time to task end/failure, min</td>
<td>60.0 ± 9.0</td>
<td>57.1 ± 2.9</td>
<td>17.6 ± 2.2</td>
<td>9.1 ± 1.1</td>
<td>6.4 ± 0.8</td>
<td>4.3 ± 0.4</td>
<td>2.8 ± 0.3</td>
</tr>
<tr>
<td>Global fatigue</td>
<td>Preexercise MVC, N·m</td>
<td>212.5 ± 16.1</td>
<td>213.4 ± 16.9</td>
<td>201.3 ± 18.2</td>
<td>192.9 ± 17.0</td>
<td>196.8 ± 16.4</td>
<td>191.6 ± 14.3</td>
</tr>
<tr>
<td>MVC at task end/failure, N·m</td>
<td>148.3 ± 11.5±</td>
<td>139.5 ± 17.9±</td>
<td>89.3 ± 8.2</td>
<td>96.8 ± 6.1</td>
<td>98.6 ± 7.0</td>
<td>107.8 ± 6.3</td>
<td>115.3 ± 4.4±</td>
</tr>
<tr>
<td>ΔMVC/Δt, N·m·min⁻¹</td>
<td>−1.1 ± 0.2</td>
<td>−1.5 ± 0.4</td>
<td>−7.2 ± 1.4</td>
<td>−11.8 ± 2.1</td>
<td>−17.3 ± 2.8</td>
<td>−21.4 ± 3.4</td>
<td>−27.3 ± 5.5</td>
</tr>
<tr>
<td>Peripheral fatigue</td>
<td>Preexercise doublet, N·m</td>
<td>99.7 ± 1.6</td>
<td>99.0 ± 5.2</td>
<td>96.5 ± 6.0</td>
<td>97.8 ± 5.3</td>
<td>96.6 ± 5.5</td>
<td>95.5 ± 4.5</td>
</tr>
<tr>
<td>Doublet at task end/failure, N·m</td>
<td>73.4 ± 4.6±</td>
<td>70.1 ± 5.0</td>
<td>59.3 ± 5.7</td>
<td>63.4 ± 4.1</td>
<td>61.7 ± 5.3</td>
<td>63.2 ± 3.5</td>
<td>64.6 ± 3.9±</td>
</tr>
<tr>
<td>%Change at task end/failure</td>
<td>9 ± 3</td>
<td>24 ± 10</td>
<td>29 ± 6</td>
<td>20 ± 5</td>
<td>12 ± 4</td>
<td>7 ± 5</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>ΔDoublet/Δt, N·m·min⁻¹</td>
<td>−0.4 ± 0.1</td>
<td>−0.5 ± 0.1</td>
<td>−2.2 ± 0.5</td>
<td>−3.9 ± 0.7</td>
<td>−5.6 ± 1.0</td>
<td>−7.7 ± 1.0</td>
<td>−9.9 ± 1.3±</td>
</tr>
<tr>
<td>Central fatigue</td>
<td>Preexercise VA, %</td>
<td>90 ± 2</td>
<td>90 ± 3</td>
<td>87 ± 4</td>
<td>88 ± 5</td>
<td>87 ± 4</td>
<td>87 ± 4</td>
</tr>
<tr>
<td>VA at task end/failure, %</td>
<td>82 ± 3</td>
<td>70 ± 10</td>
<td>62 ± 6</td>
<td>70 ± 5</td>
<td>77 ± 4</td>
<td>80 ± 3</td>
<td>85 ± 3</td>
</tr>
<tr>
<td>%Change at task end/failure</td>
<td>9 ± 3</td>
<td>24 ± 10</td>
<td>29 ± 6</td>
<td>20 ± 5</td>
<td>12 ± 4</td>
<td>7 ± 5</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>ΔVA/Δt, %/min</td>
<td>−0.1 ± 0.1</td>
<td>−0.4 ± 0.2</td>
<td>−1.3 ± 0.5</td>
<td>−2.2 ± 0.7</td>
<td>−1.9 ± 0.8</td>
<td>−2.5 ± 1.0</td>
<td>−3.2 ± 1.8</td>
</tr>
<tr>
<td>Surface EMG</td>
<td>AREMG at 1 min, %MVC</td>
<td>39 ± 4</td>
<td>43 ± 4</td>
<td>55 ± 7</td>
<td>60 ± 6</td>
<td>64 ± 6</td>
<td>72 ± 6</td>
</tr>
<tr>
<td>Submaximal AREMG at task end/failure, %MVC</td>
<td>46 ± 5</td>
<td>54 ± 6</td>
<td>76 ± 9</td>
<td>88 ± 8</td>
<td>88 ± 7</td>
<td>94 ± 6</td>
<td>96 ± 7</td>
</tr>
<tr>
<td>Maximal AREMG at task end/failure, %MVC</td>
<td>80 ± 3</td>
<td>82 ± 6</td>
<td>76 ± 8</td>
<td>88 ± 5</td>
<td>80 ± 4</td>
<td>86 ± 6</td>
<td>96 ± 6</td>
</tr>
<tr>
<td>Submaximal AREMG at task end/failure</td>
<td>57 ± 6</td>
<td>69 ± 8</td>
<td>100 ± 6</td>
<td>99 ± 6</td>
<td>110 ± 5</td>
<td>108 ± 5</td>
<td>101 ± 3</td>
</tr>
<tr>
<td>ΔAREMG/Δt, %MVC/min</td>
<td>0.1 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>1.4 ± 0.3</td>
<td>3.0 ± 0.5</td>
<td>3.8 ± 0.8</td>
<td>5.3 ± 0.8</td>
<td>5.7 ± 0.9±</td>
</tr>
</tbody>
</table>

Values are means ± SE. EMG, electromyogram; CT-10% and CT-20%, 10 and 20% below the critical torque, respectively; MVC, maximal voluntary contraction; Δ change; t, time; VA, voluntary activation; AREMG, average rectified EMG of the m. vastus lateralis. Mean test torque is expressed as a percentage of the peak torque measured during the MVCs in visit 2. Eight subjects completed 60 min of contractions during CT-10%, and one subject reached task failure after 34 min. Letters indicate a statistically significant difference compared to the following: *mean test torque, *preexercise value/AREMG at 1 min, *CT-20%, and *submaximal AREMG at task end/failure (Bonferroni-adjusted 95% paired-samples confidence intervals do not include the null value).
S4 and S5 was not statistically significant (95% CIs: S4, −17.4, 3.3%; S5, −13.0, 2.7%).

The AREMG responses to contractions performed below and above the CT are presented in Fig. 2A. In contrast to contractions performed above CT, all subjects managed to complete 60 min of contractions in the CT-20% condition, and eight of nine subjects managed to complete 60 min of contractions in the CT-10% condition (Table 1). The subject who reached task failure in this condition did so after 34 min. At the end of the trials, the mean MVC torque was significantly greater than the submaximal torque requirements (95% CIs: CT-20%, 53.3, 110.5 N·m; CT-10%, 25.1, 110.4 N·m; Table 1), in direct contrast to the responses above CT (Fig. 2A). There was a significant reduction in the resting doublet torque in both trials below CT (Table 1, Fig. 3A), and at the end of the task the doublet responses were similar to, although slightly higher than, those of the trials performed above CT. The voluntary activation in both trials below CT fell from ~90% to reach 81.8 ± 3.1 and 70.1 ± 9.9% in CT-20% and CT-10%, respectively (Table 1). The voluntary activation at task end in

Trials Performed Below the CT (CT-10% and CT-20%)

The mean MVC torque responses to contractions performed below CT are presented in Fig. 2A. In contrast to contractions performed above CT, all subjects managed to complete 60 min of contractions in the CT-20% condition, and eight of nine subjects managed to complete 60 min of contractions in the CT-10% condition (Table 1). The subject who reached task failure in this condition did so after 34 min. At the end of the trials, the mean MVC torque was significantly greater than the submaximal torque requirements (95% CIs: CT-20%, 53.3, 110.5 N·m; CT-10%, 25.1, 110.4 N·m; Table 1), in direct contrast to the responses above CT (Fig. 2A). There was a significant reduction in the resting doublet torque in both trials below CT (Table 1, Fig. 3A), and at the end of the task the doublet responses were similar to, although slightly higher than, those of the trials performed above CT. The voluntary activation in both trials below CT fell from ~90% to reach 81.8 ± 3.1 and 70.1 ± 9.9% in CT-20% and CT-10%, respectively (Table 1). The voluntary activation at task end in

S4 and S5 was not statistically significant (95% CIs: S4, −17.4, 3.3%; S5, −13.0, 2.7%).

The AREMG responses to contractions above CT are presented in Fig. 2B. The mean AREMG in the first minute increased with increasing torque requirements ($F = 37.33, P < 0.001$; Table 1), and AREMG amplitude increased over time in all trials, reaching ~76–96% of the pretest MVC value at task failure ($F = 44.39, P = 0.001$). The AREMG at task failure was not different from the AREMG measured during the subsequent MVC in each trial (Table 1, Fig. 2B).

Fig. 2. Maximal voluntary contraction (MVC) torque and electromyogram (EMG) responses to contractions performed below and above the CT. A: MVC responses to the conditions 20% below the CT (CT-20%; ●) and 10% below the CT (CT-10%; ○) compared with the responses in severe 1 (S1; ▲) and severe 2 (S2; △). For clarity, trials S3–S5 not shown. Error bars represent the SE and are only presented at task failure for clarity. The first data point at task failure represents the mean test torque during the submaximal contractions, and the second represents the torque response to the MVC following task failure. B: EMG responses to contractions below and above the CT; conditions are as shown in A. The first data point at task failure represents the final 30-s time bin of submaximal contractions before task failure, whereas the second data point represents the EMG response to a MVC. Note that contractions below CT were associated with quasi-steady-state responses in AREMG and a substantial reserve in MVC torque and EMG at the end of the task. In direct contrast, above CT, the MVC falls until the mean test torque is achieved, and a maximal EMG amplitude is attained.

Fig. 3. Minute-by-minute potentiated doublet torque (A) and voluntary activation responses (B) to contractions performed below (CT-20; ●; CT-10 ○) and above (S1; ▲; S2; △; S3; ■; S4; ○; S5; ●) the CT. Responses at task end/failure are represented by data points with error bars (SE).
the CT-20% trial was significantly higher than that measured at task failure in the S1 trial (95% CIs: 2.3, 37.7%).

Contractions below CT resulted in only modest increases in AREMG as the contractions progressed (Table 1, Fig. 2B). Indeed, the difference between the 1-min AREMG and that at the end of the trial was not statistically significant for the CT-20% trial (95% CIs, \(-2.3, 16.7\%\) MVC), and, as shown in Fig. 2B, in both trials the submaximal AREMG at the end of the trial was significantly lower than the AREMG produced during a MVC (95% CIs: CT-20%, \(-47.3, -20.3\%\) MVC; CT-10%, \(-45.6, -9.3\%\) MVC). In other words, contractions performed below the CT were ended with substantial reserves in maximal torque and muscle activity (Table 1).

Rates of Global, Peripheral, and Central Fatigue Development

The rates of decrease in the MVC torque (Fig. 4A) and the doublet torque (Fig. 4B) were not different between the CT-10% and the CT-20% trials, but were significantly greater above CT compared with the CT-20% trial (\(F = 25.38, P < 0.001\)). Linear regression was used to predict the rate of fatigue development below CT from the responses above CT (dashed lines in each plot of Fig. 4). Both the rate of decrease in MVC and doublet torque above CT increased as the torque requirements increased (\(\Delta\text{MVC}/\Delta t \ r^2 = 0.997, P < 0.001\), Fig. 4A; \(\Delta\text{doublet}/\Delta t \ r^2 = 0.999, P < 0.001\), Fig. 4B; Table 1), and backward extrapolation of these relationships predicted no change in these parameters (i.e., no fatigue) at or below \(-32\) and \(-34\%\) MVC, respectively (that is, close to the estimated CT). The responses in the trials below CT deviated from the relationship established above CT (open circles in Fig. 4, A and B).

The rate of change in voluntary activation across conditions did not differ significantly between trials (\(F = 2.483, P = 0.126\)), but post hoc 95% CIs revealed trends between CT-20% and S1 (\(-0.4, 2.6\%\)) and S2 (\(-0.3, 4.5\%\)). Figure 4C shows that the rate at which central fatigue developed increased with increasing torque (\(r^2 = 0.852, P = 0.025\)) and predicted a similar, although slightly greater, diminution in voluntary activation to that actually observed during the trials below CT. The rate of increase in the AREMG during the trials shows a similar pattern to the changes in MVC and doublet torque, with there being no difference between CT-20% and CT-10% (95% CI, \(-0.3, 0.1\%\) MVC), but a significant increase in the rate of change in AREMG above CT (Table 1).

DISCUSSION

The findings of this investigation provide the first evidence, using comprehensive methods of assessment, for the existence of a critical threshold in fatigue development during submaximal contractions. The key evidence supporting this interpretation is the following. 1) During contractions below CT, MVC torque declined modestly, and, at task end (60 min in all but one trial), the MVC torque was substantially higher than the target torque. In all trials above CT, in contrast, MVC torque fell progressively until task failure, at which point a maximal contraction was required to attain the target torque. In all trials above CT, in contrast, MVC torque fell progressively until task failure, at which point a maximal contraction was required to attain the target torque. 2) Below CT, AREMG increased modestly, and there was a substantial muscle activity reserve at the end of the task, whereas, above CT, AREMG increased inexorably to reach a value not different from that produced during a MVC at task failure. 3) Importantly, the rates of change in the MVC torque and potentiated doublet torque were disproportionately larger above compared with below the CT, indicating that the rate of
fatigue development below CT could not be predicted from the same indexes measured above CT. The main implication of these findings is that the rate of fatigue development does not increase proportionally as the torque requirements as a fraction of MVC are increased, but increases suddenly when CT is exceeded.

The relationship between contraction torque and the time to task failure was accurately described by a two-parameter hyperbolic function, consistent with previous observations (13, 28, 37). The asymptote of this relationship provides the CT, and above CT a fixed impulse (or amount of work in the case of cycle ergometry; Ref. 44) can be performed before task failure (13). The curvature constant parameter, $W'$, is thought to reflect a finite energy store that is utilized at a rate proportional to the difference between the target torque and the CT (for review, see Refs. 29, 34, 39). Recent evidence demonstrates that, during knee extensor exercise performed above the critical power, muscle metabolites associated with peripheral fatigue change progressively until task failure (33), at a rate proportional to the difference between the prevailing work rate and the critical power (52). The present study utilized a protocol similar to that of Bigland-Ritchie et al. (10) to quantify the MVC torque and central and peripheral fatigue on a minute-by-minute basis. The present results demonstrated that peripheral fatigue developed at a progressively faster rate as the torque requirements increased above CT (Fig. 4B), but with the potentiated doublet torque declining to a similar level in each trial (Fig. 3A). These results are consistent with previous data, which showed a consistent level of metabolic disturbance or peripheral fatigue at task failure when inspired $O_2$ concentrations were varied (6, 30, 52). It has been suggested that intramuscular metabolites increase the firing frequency of group III/IV afferents, reducing central drive and thus limiting the development of further peripheral fatigue (5). The similarity of the potentiated doublet responses at task failure in the present study, and in our previous work (13), is consistent with this proposal. In addition, the MVC torque declined (Fig. 2A), and the AREMG increased (Fig. 2B), at rates proportional to the difference between the target torque and the CT. At task failure, a MVC was required to achieve the target torque in all trials, and this was achieved with a maximal AREMG amplitude (relative to that which was possible to achieve, Table 1). During contractions above CT, therefore, muscle metabolites cannot be stabilized (14, 33, 52), and peripheral fatigue progressively develops. This, in turn, requires additional motor unit activation to maintain the target torque (1, 10, 18). The conclusion of this process is presumably the point at which the $W'$ has been expended, and a maximal contraction is required to attain the target torque.

Because CT represents the asymptote of the torque-duration relationship, the model predicts that, below CT, fatigue and, by extension, exhaustion should not occur (37, 39). Indeed, from the trials above CT presented in Fig. 4, A and B, the MVC and potentiated doublet torque data predicted that these variables would not decline below $\sim 33\%$ MVC, in close proximity to the actual CT. Nevertheless, peripheral fatigue did develop in response to contractions below CT (Figs. 2A and 4A). The present data cannot identify the origin of this peripheral impairment, but it is unlikely that fatigue mediated by muscle metabolites (such as $H^+$, $P_i$, and $H_2PO_4^-$) was responsible. This is due to recent evidence showing that, during dynamic contractions just below the critical power, $[PCr]$ (where brackets denote concentration), $[P_i]$, and pH all stabilized within 6 min of a 20-min exercise bout (33). In the present study, the potentiated doublet torque declined little in the first 10 min of the trials below CT (Fig. 3A) and then declined steadily throughout the remainder of the trial when muscle metabolic responses would presumably have been in a steady state (e.g., Refs. 33, 53). The mechanism responsible for peripheral fatigue below CT is obscure, but may be related to the depletion of muscle glycogen, since reduced Ca$^{2+}$ transients and hence lower force development have been observed in glycogen-depleted single fibers (16) and whole muscle (27) in the mouse. At the end of these trials, the potentiated doublet torque was not different from trials performed above the CT (Table 1, Fig. 3A). However, the rate of peripheral fatigue development was substantially lower below the CT, and, at the end of the task (60 min for all but one trial), there was a significant reserve in both the MVC torque and AREMG amplitude (Table 1, Fig. 2). This further indicates that the mechanisms of peripheral fatigue were different below the CT. The present data, therefore, strongly suggest that CT represents a critical threshold for peripheral fatigue development, rather than a threshold separating fatigueless and fatiguing contraction intensities.

Central fatigue was present in trials performed both below and above the CT (measured as a reduction in voluntary activation and maximal AREMG), which suggests that, as a result of repetitive contractions, the subjects were unable to voluntarily drive the knee extensors to the same extent at the end of the trials as they were at the beginning (50). The present data cannot identify the location(s) of this impairment within the CNS, but a number of spinal and supraspinal mechanisms have been suggested (for review, see Ref. 24). At the two highest target torques performed above the CT, the reduction in voluntary activation was not statistically significant (Table 1), but central fatigue was evident in the remaining trials (Fig. 3B). These results would suggest that reaching the aforementioned peripheral fatigue threshold (5) may not have been centrally mediated in these trials. We had hypothesized a greater degree of central fatigue during contractions performed below CT, on the basis of previous evidence demonstrating prominent central fatigue during prolonged low-intensity contractions (47, 48) and due to the relative lack of metabolic stress observed during contractions below the CT (33). Our results did not support this hypothesis, as the difference in voluntary activation at task failure/task end between trials below and above CT was statistically significant only for the comparison between CT-20% and the S1 trial, with the reduction in voluntary activation being significantly greater during the S1 trial (Table 1, Fig. 3B). Therefore, these data do not support the hypothesis that central fatigue is more pronounced during intermittent quadriceps contractions performed below CT than above CT.

A key finding of the present study is that the rate of neuromuscular fatigue development does not increase as a simple linear function of the target torque or fraction of MVC required, but is substantially accelerated above the CT. The distinct fatigue profiles observed in this study extend earlier work showing similarly stark transitions below vs. above the critical power in pulmonary gas exchange and blood acid-base responses during cycle ergometry (44) and muscle metabolic profile during knee-extension exercise (33). Specifically, pulmonary oxygen uptake, blood [lactate], and arterial and muscle...
pH can attain steady-state values below the critical power, but not above it (44), reflecting the fact that muscle metabolic homeostasis cannot be achieved during contractions performed above critical power (33). Similarly, the AREMG responses stabilized below but not above the CT (Fig. 2B), and the maximal attainable AREMG was reached at task failure above CT. What remains unclear is the mechanistic origin of this bioenergetic and neuromuscular threshold. Below we outline a plausible working hypothesis to explain it.

In the present study, the demand placed on the neuromuscular system was to achieve the submaximal target torque and, each minute, perform a MVC. We believe the results of the present study, alongside previous bioenergetic data (33, 44, 52), suggest that the distinct responses below and above the CT represent a “phase transition” in neuromuscular function. From this perspective, we propose that, much as the cardiovascular system appears to be structured to achieve the required flow for the lowest mechanical work (40, 46), the neuromuscular system has evolved to produce the required torque at the lowest possible metabolic rate. Below the CT, this is achieved by recruiting relatively low-threshold, fatigue-resistant motor units (1, 36). As the contractions progress, only small additional increases in motor unit recruitment are necessary to maintain the target torque (Fig. 2B). The metabolic disturbance this elicits is also small (33), and the torque-generating capacity of the muscle, although reduced, remains relatively high (Fig. 2A). A phase transition occurs when the target torque exceeds the CT: here, metabolic perturbations cannot be stabilized (14, 33, 52), most likely owing to the recruitment of higher threshold and inherently more fatigable motor units to satisfy the increased torque demands (1, 15). This, in turn, requires the progressive recruitment of additional motor units to maintain submaximal torque (1, 10, 18). As a result, AREMG (Fig. 2B) gradually increases, and, in a similar exercise model, muscle oxygen uptake has been shown to gradually increase during repeated contractions performed until task failure (54). These responses are both accompanied by a gradual reduction in the torque-generating capacity of the muscle until task failure inevitably occurs (Fig. 2A). It should also be considered that the AREMG data may reflect increased rate coding in response to muscle fatigue (2), although the surface EMG measurements used in this study cannot detect changes in the firing rate or recruitment of specific motor units (cf. Refs. 1, 2).

In summary, this study has demonstrated that the CT is a critical threshold for neuromuscular fatigue development during intermittent isometric contractions. Below the CT, peripheral fatigue developed slowly, and the neuromuscular adjustments required to maintain the target torque were modest. Subjects sustained exercise for up to 60 min, and there was a substantial maximal torque and muscle activity reserve present at the end of the task; the fall in voluntary activation was also modest. Above the CT, the MVC and potentiated doublet torque declined progressively and at a disproportionately faster rate than below CT until task failure occurred, at which point a maximal contraction was required to attain the target torque. The CT, therefore, separates domains of contraction intensity in which distinct neuromuscular fatigue profiles are observed.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
M.B. conception and design of research; M.B. performed experiments; M.B. analyzed data; M.B., A.V., and A.M.J. interpreted results of experiments; M.B. prepared figures; M.B. drafted manuscript; M.B., A.V., and A.M.J. edited and revised manuscript; M.B., A.V., and A.M.J. approved final version of manuscript.

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