Central and peripheral aspects of exercise induced fatigue

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Introduction
In clinical practice, fatigue seems to be a frequent complaint of patients suffering from neuromuscular disorders. This enlarged level of experienced fatigue might both be influenced by psychological and physiological factors. Physiologically, local muscle fatigue, defined as a loss of force producing capacity as a result of exercise (for review, see Gandevia 1998a), can both originate from peripheral and central factors. Peripheral fatigue results from variations in the muscle itself, like changes in the neuromuscular junction and sarcolemmal membrane, accumulation of metabolites and depletion of fuels (for review, see Kirkendall, 1990). Central fatigue can be located in both the central and peripheral nervous system. If central fatigue occurs, muscle force decreases because of a decrease of neural drive (Gandevia et al, 1996 and 1998b, Kent-Braun et al, 1996 and 1999). As yet, the relationship between central and peripheral factors (both qualitatively and quantitatively) are unknown.

The present study tried to determine the quantity of both peripheral and central aspects of fatigue simultaneously in healthy subjects. Therefore, voluntary contraction and responses to electrical stimulation of the biceps brachii were studied by both force and surface EMG.

![Figure 1. Voluntary force during 2 min sustained maximal contraction. Force decreases almost linearly during the first 90 s. The last 30 s voluntary force shows hardly any further decrease.](image-url)
(sEMG) recordings in a fatigue inducing protocol.

Methods
25 healthy subjects (18 men, 7 women, age 19-53) with no history of neuromuscular disorders were included in the experiment. Subjects were set in a chair with their left arm fixed in a strain gauge, their shoulder in abduction, the elbow in an angle of 90° and their forearm supinated.

Subjects were instructed to contract their biceps brachii maximally for two minutes. Before, during and after sustained contraction the muscle received electrical stimulation. Stimulation was applied via two adhesive electrodes attached to the surface of the skin, the cathode above both motor endplates of the biceps brachii, the anode more proximally above the same muscle. A stimulus event consisted of five series of five short (0.1 ms) pulses, the latter given with 10 ms interval (100 Hz). Five twitches (force responses to a series of 5 short pulses) were averaged, resulting in one mean twitch per stimulus event. The appropriate intensity for electrical stimulation was determined for each subject separately before the actual experiment. The level (range between 26.0 and 91.9 mA) was chosen such that stimulation resulted in a maximal force contraction. Before and after two minutes of

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\begin{array}{c|c|c}
\text{Twitch force (N)} & \text{Time (ms)} & \text{Twitch force (N)} \\
\hline
& & \\
0 & 0 & 0 \\
10 & 100 & 10 \\
20 & 200 & 20 \\
30 & 300 & 30 \\
40 & 400 & 40 \\
50 & 500 & 50 \\
\end{array}
\]

Figure 2: Typical example of twitches before (A), during (B) and after (C) two minutes sustained contraction. Notice the difference in both time and force scale between the rest twitches (A and C) and twitches during sustained contraction (B). Rest twitch force after sustained contraction is about half the rest twitch force before contraction. Both force increase and force decrease has been slowed down.

The middle panel (B) shows twitches during MVC, the darkest one resulting from stimulation after 15 s sustained contraction, the lightest one resulting from stimulation after 2 min sustained contraction. Notice the changes in twitch size and in steepness of the relaxation phase. Twitches have been compensated for changes in voluntary force.
sustained contraction a single stimulus event was given in rest (initial and final rest twitch).
During voluntary sustained contraction, every fifteen seconds a stimulus event was applied.
The twitch force curve was corrected for changes in voluntary muscle force. Twitch sizes
were calculated as percentage of an estimated possible rest twitch, composed by linear
interpolation in time between the initial and final rest twitch.
Both force and sEMG recordings were made. SEMG was measured using a device
containing five inline placed small diameter (1.5 mm) electrodes at 3 mm inter electrode
distance. The device was placed on the skin parallel to the muscle fibre direction, also
enabling the detection of muscle fibre conduction velocities.

Results
During two minutes sustained voluntary contraction, force decreases till about a third of the
original maximal voluntary contraction (MVC) (fig. 1). This decline is almost linear during
the first 1.5 min of contraction, but voluntary force stabilises during the last half minute.
Applying electrical endplate stimulation in rest in all subjects resulted in twitch forces
ranging from 5 to 12 % of MVC. Only about half of this twitch force is left after two
minutes sustained maximal contraction (compare fig. 2A with 2C). Rest twitch duration,
expressed as width at half maximum, is about 1.5 times longer after sustained contraction
than before. Both the contraction and relaxation phase of the response contribute to this
response slowing (fig. 2A,C). Twitch forces during sustained contraction are much lower
than in rest (fig. 2B, note vertical scaling) but twitch force increase over time from about 8%
after 15 s until about 25% of estimated maximal twitch size after two minutes (fig. 3).
However, intersubject differences are large. In all subjects, twitch relaxation clearly slows
down during the first minute of contraction (fig. 4).
From the sEMG recordings, muscle fibre conduction velocity (MFCV) was calculated. MFCV shows a clear decrease during the first half period of sustained voluntary contraction. Also the EMG amplitude showed a clear decrease.

**Discussion**
Both force and sEMG measurements showed that a major part of voluntary force loss during sustained maximal contraction of the biceps brachii can be explained by peripheral fatigue. The differences between the initial and final rest twitches and the changes in MFCV and relaxation rates during sustained contraction illustrate this finding. However, the contribution of peripheral fatigue seems to reach a plateau after 1 - 1.5 minutes, since from that moment on MFCV and relaxation rates do not further change. As suggested by Zwarts and Arendt-Nielsen (1988), the influence of peripheral fatigue is large in the beginning of sustained contraction because the muscle pressure is high enough to occlude blood circulation in the muscle. If internal muscle pressure is lowered sufficiently to allow renewed blood flow, peripheral fatigue seems to stabilise.

The change in contribution of central fatigue to loss of voluntary force was measured by the size of the twitches during maximal voluntary contraction. The occurrence of additional force during maximal voluntary contraction showed that central drive was not maximal. For twitch forces showed an increase over time, the amount of central fatigue increased. At the end of voluntary contraction, twitch size showed that in the absence of peripheral fatigue, central fatigue alone could explain a force loss as large as a quarter of initial MVC.

Further research will be done to detect differences in fatiguing healthy subjects and neuromuscular patients. Since muscle force in this patient group will be much lower than in healthy subjects, less blood flow occlusion is expected. Therefore, peripheral fatigue possibly plays a less important role in these patients.

![Figure 4](image_url)  
Figure 4: Relative relaxation rate of twitches during sustained maximal voluntary contraction. Relaxation velocity clearly declines during the first minute, but stays constant during the last. Error bars represent the standard errors of the mean.
Conclusions
The described method allows the detection of several aspects of both peripheral and central fatigue simultaneously. In healthy subjects peripheral fatigue explains most of the force loss during sustained maximal contraction. However, the relative role of central fatigue seems to increase over two minutes sustained contraction.

References


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