Post-exercise facilitation and depression of M wave and motor evoked potentials in healthy subjects

Marianne Lentza, Jørgen Feldbæk Nielsena,b,*

aDepartment of Neurology, Aarhus University Hospital, Aarhus, Denmark
bDepartment of Clinical Neurophysiology, Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C, Denmark

Accepted 23 January 2002

Abstract

Objectives: To characterize so-called central fatigue, the effect of various levels of exercise on central and peripheral motor potentials were compared.

Methods: Thirteen healthy subjects performed 4 levels of exercise following isometric dorsiflexion of the foot. Post-exercise recordings from the anterior tibial muscle of motor evoked potentials (MEP) evoked by transcranial magnetic stimulation (TMS) and M wave evoked by electrical stimulation of the peroneal nerve were performed.

Results: After 5 s the post-exercise MEP amplitude increased. The increase was related to the degree of work performed. Subsequently, there was a gradually decrease of amplitude reaching statistical significance after 15 min. The area of the M wave increased significantly after 10 s and returned to baseline after 2–3 min.

Conclusions: Facilitation and depression of MEP after fatiguing exercise is at least partly a peripheral phenomenon dependent on the level of exercise performed.

Keywords: Fatigue; Postexercise facilitation; Postexercise depression; Transcranial magnetic stimulation

1. Introduction

The cause of muscle fatigue is multifactorial and varies with the intensity and duration of the exercise, the fiber type composition of the muscle and the degree of training. Fatigue can be defined as any reduction in force generating capacity of a muscle and can be separated into peripheral failure at or below the neuromuscular junction or central failure due to progressive reduction of voluntary drive to motoneurons during exercise (Gandevia et al., 1995; Gandevia, 1996). For studies of muscle fatigue M wave measurements have been used extensively as one of the indices of fatigue and recovery in human studies. They provide important information regarding the net effects of ion fluxes, Na-K pump activity and neuromuscular transmission. Several authors have shown potentiation and depression of the M wave during and following exercise or tetanic stimulation, especially high-frequency stimulation (Cupido et al., 1996; Hicks et al., 1989; McComas et al., 1994).

Several authors have used transcranial magnetic stimulation (TMS) to evaluate central fatigue with recording motor evoked potentials (MEP) in relaxed, exercised or fatigued muscles. In 1993 Brasil-Neto et al. described a post-exercise reduction in MEP amplitude (Brasil-Neto et al., 1993). They observed that post-exercise depressions (PED) of MEP did not include the M waves, H reflexes, or MEP elicited by transcranial electrical stimulation (TES). On the contrary MEP to TMS was transiently decreased after exercise, indicating fatigue of motor pathways due to changes of cortical excitability. In 1989 Hicks et al. showed enlargement of the M wave response during series of successive voluntary contractions lasting 3 s of the human thenar and extensor digitorum brevis muscles (Hicks et al., 1989). Hicks also showed that the potentiation was caused by a transient increase in the muscle fiber resting membrane potential which again was caused by enlargement of the fiber action potential. In the present study we recorded EMG activity after 4 different levels of sustained isometric contraction in healthy subjects. Using recordings from the anterior tibial muscle (TA) we compared changes in MEP to TMS with changes of the M wave.
2. Methods

Twenty healthy subjects, 9 men and 11 women, aged 32 ± 10 years with a height of 177 ± 8 cm were included in the first series of experiments. All subjects exercised 1–3 h weekly. In the second series of experiments 5 men and 8 women out of the original 20 subjects participated.

The local ethics committee approved the protocol and all subjects gave their written informed consent to the study. All subjects were asked to refrain from smoking, and drinking coffee, tea or alcohol for at least 3 h prior to the experiment. The room was air-conditioned to keep the room temperature constant at 19–22 °C.

2.1. Experimental setup

The subjects were seated in a chair in semi-supine position, the flexion/extension axis of the ankle being adjusted to the axis of the dynamometer. In order to stabilize the patient Velcro straps were fastened over the pelvis and chest. Two Velcro straps strapped the foot on the dominant side to a foot plate. The foot plate was connected with a dynamometer (LIDO Active Multijoint II, Loredan Biomedical Inc., West Sacramento, CA, USA), to evaluate the isometric muscle strength of ankle dorsal flexion, and during contraction the torque was shown to the patient on a monitor.

Surface EMG activity was recorded (Ag/AgCl electrodes) from TA and the soleus muscle (SOL). The impedance was kept below 5 kΩ. The electrodes were placed in a belly-tendon montage at SOL and in a bipolar montage at TA. EMG was recorded by an EMG amplifier (Dantec, Copenhagen, Denmark) with a bandpass of 20–1000 Hz. The acquisition software was developed in LabWindows/CVI (National Instruments Corp., Austin, TX, USA). This acquisition system offered a high resolution system with a data sampling frequency of 10 kHz giving a maximal temporal resolution of 100 µs. All signals were stored for analysis. The EMG activity of TA was monitored audio-visually for the examiner and the subject to ensure total relaxation of the muscle at the time the measurements were made. As recommended by Gandevia et al. (1995), we used the term optimal muscle strength of ankle dorsal flexion, and during contraction the torque was shown to the patient on a monitor.

Surface EMG activity was recorded (Ag/AgCl electrodes) from TA and the soleus muscle (SOL). The impedance was kept below 5 kΩ. The electrodes were placed in a belly-tendon montage at SOL and in a bipolar montage at TA. EMG was recorded by an EMG amplifier (Dantec, Copenhagen, Denmark) with a bandpass of 20–1000 Hz. The acquisition software was developed in LabWindows/CVI (National Instruments Corp., Austin, TX, USA). This acquisition system offered a high resolution system with a data sampling frequency of 10 kHz giving a maximal temporal resolution of 100 µs. All signals were stored for analysis. The EMG activity of TA was monitored audio-visually for the examiner and the subject to ensure total relaxation of the muscle at the time the measurements were made. As recommended by Gandevia et al. (1995), we used the term optimal force for maximal voluntary activation of the motoneuron pool. Maximal voluntary contraction (MVC) was the best contraction observed from a number of maximal efforts. Maximal effort was obtained in every contraction the subject considered maximal regardless of the force actually achieved.

2.2. Nerve stimulation

For transcranial magnetic stimulation a Magstim 200 (Magstim Co. Ltd, UK) and a concentric figure-of-8-shaped coil with an outer diameter of 13 cm were used to deliver a maximal output of 1.4 T at a rise time of 100 µs. The coil was localized on the fronto-parietal region contralateral to the target muscle and moved around until the ‘hot spot’ was reached where the threshold was lowest and the latency shortest. This position was maintained throughout the experiment by marking the position on the scalp and securing the coil by a wire in the ceiling. Stimulation usually started at an output of 30% and increased in steps of 5% until the threshold was reached. Threshold was defined as the intensity which elicits 5 or more MEPs out of 10 consecutive stimulations at an amplitude of at least 25 µV recorded from the relaxed muscle. Stimulation intensity was 120% of threshold intensity. Pre-exercise and post-exercise MEPs were recorded from a relaxed target muscle. Peak-to-peak amplitudes and take-off latencies were measured. M waves were evoked by supramaximal biphasic stimulation with a duration of 0.2 ms of the peroneal nerve at the fibular head in the dominant leg. To ensure the stability of the stimulating electrode its position was marked and fixed with a rubber-band. Stimulus strength for M wave recordings was supramaximal, being 150% of the strength used to elicit maximal stimulus response of constant amplitude and area. For evaluation of the M response, areas were registered.

2.3. Experiment 1

For baseline recordings, 5 MEPs were recorded from the relaxed TA and SOL at a frequency of 0.2 Hz. For subjects with identical motor threshold for eliciting MEPs from SOL and TA recordings were made from SOL in order to study MEPs in an antagonistic muscle. MVC was determined from the best of 3 attempts of maximal effort before the exercise. Following definition of MVC patients were fatigued in randomized order to each of the following maximum volitional contraction levels: from 100 to 75%, from 100 to 50%, from 100 to 25% and from 50 to 25%. The interval between each of the 4 fatigue experiments was 15 min. Before the two last trials MVC was again determined to secure its level in comparison to the starting value. During the breaks the subject was asked to leave the chair and move around. Five seconds after the last stimulus of the experiments the subject was asked to perform a sustained isometric contraction starting at maximal strength (100%). Efforts were made to motivate the subjects maximally. During the contraction subjects were vigorously encouraged to sustain the contraction level as long as possible. In addition, the monitor displayed on-line to the subject the gradual decrease of torque. The contraction was maintained until the maximal effort was less than 50/75% of the starting value (cut-off level). Five seconds following the end of the fatigue experiment subjects had TMS at times 5, 10, 15, 20, 25 s and at 1, 2, 3, 4, 5, 10, 15 min including 5 MEP recordings at each interval. During the post-fatigue registration period subjects were asked to maintain their position and to be quiet.

2.4. Experiment 2

For baseline, 5 M waves from TA were recorded at a frequency of 0.1 Hz. After a rest of 10 s the subject
performed a maximal effort of TA. As in Expt. 1, the order of the various isometric contractions was random, and the tests of fatigue were also identical. After a further 10 s the peroneal nerve was stimulated at a frequency of 0.1 Hz for 15 min.

2.5. Data analysis

All values are given as mean ± 1 SD. Regarding TMS, 5 evoked potentials obtained each minute were averaged. The amplitude varied considerably and normal probability plots revealed a skewness of distribution. Data was therefore logarithmically transformed resulting in normal data distribution (Nielsen, 1996). In addition, we recorded the latency of MEP (onset) in Expt. 1. In Expt. 2 the area under the M wave curve was the response parameter. Unpaired and paired t tests were applied with a significance level of 0.05.

3. Results

MVC was 45.7 ± 11.7 Nm and 47.2 ± 12.2 Nm at start in Expts. 1 and 2, respectively (P > 0.05). There was no observed any significant changes of maximal effort during the experimental periods. Table 1 shows time until predefined contraction level occurred and torque of the muscle contraction for each period in both studies. No differences in Expts 1 and 2 were present in contraction time or in performed torque before the contraction level was achieved. Fig. 1 shows a typical torque-curve for one subject at all 4 work loads.

3.1. Experiment 1

The mean latency of MEP was 31.63 ± 3.03 and 32.09 ± 2.6 ms, before and after exercise, respectively (P > 0.05). Magnetic stimulation intensity was 55.1 ± 8.6% of maximal output. The baseline amplitude values for the 4 contraction levels were gradually reduced during the experiments from 5.3 lnμV at the first experiment to 4.7 lnμV at the 4th experiment (P < 0.001).

Examples of post-exercise recordings are given in Fig. 2. Post-exercise changes of MEP amplitudes of TA are shown in Fig. 3A. At time 5 s, the post-exercise amplitude was increased statistically significantly at all 4 fatigue levels. The increase gradually declined during the first post-exercise minute, and at 2, 5, 10 min the amplitude was decreased significantly at all 4 fatigue levels. In the soleus muscle the post-exercise amplitude was increased at all 4 levels, but the change was only statistically significant (P < 0.05) at level 100–75%. No significant decrease of the SOL amplitude occurred at levels 100–75%, 100–50% and 100–25%. At contraction level 50–25% the decrease was statistically significantly at 2, 3, 4 and 5 min (Fig. 3B).

Post-exercise increase of TA amplitude was largest for the two most exhaustive exercise experiments (100–25% and 50–25%, Fig. 4). A similar relation did not appear at the following post-exercise decrease as shown in Fig. 3.

3.2. Experiment 2

Baseline values of area and amplitude of M wave were 56.5 ± 20.5 μVs. and 3.0 ± 1.1 mV, respectively. Initial post-exercise increase of the TA amplitude was present at all contraction levels (Fig. 5) but a significant decrease of the amplitude at 2, 3, 4, 5, 10 and 15 min was only seen after a exercise level of 50–25%. The maximal increase of the post-exercise M wave response was to some degree related to the fatigue level. After the least exhaustive exercise (100–75%) maximal increase was 1.20 ± 0.15 (% of baseline value) compared with 1.42 ± 0.29 after the most exhaustive exercise (100–25%), P = 0.03. Values from the two other work loads (100–50% and 50–25%) lay in between and did

Table 1

<table>
<thead>
<tr>
<th>Fatigue level</th>
<th>Experiment 1</th>
<th></th>
<th>Experiment 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duration (s)</td>
<td>Performed torque (%)</td>
<td>Duration (s)</td>
<td>Performed torque (%)</td>
</tr>
<tr>
<td>100–75</td>
<td>21.39 ± 5.78</td>
<td>21 ± 5.3</td>
<td>21.47 ± 7.63</td>
<td>23 ± 5.4</td>
</tr>
<tr>
<td>100–50</td>
<td>56.82 ± 19.03</td>
<td>45 ± 3.5</td>
<td>55.69 ± 25.59</td>
<td>47 ± 3.9</td>
</tr>
<tr>
<td>100–25</td>
<td>147.12 ± 49.02</td>
<td>65 ± 7.5</td>
<td>159.22 ± 57.37</td>
<td>73 ± 6.6</td>
</tr>
<tr>
<td>50–25</td>
<td>204.49 ± 53.11</td>
<td>51 ± 11.7</td>
<td>221.35 ± 66.61</td>
<td>55 ± 9.4</td>
</tr>
</tbody>
</table>

*Duration of muscle contraction and performed torque (% of baseline) in both experiments at 4 fatiguing exercises. No significant differences between the two experiments were present. Data are given as mean values ± 1 SD.
not differ significantly from the least exhaustive exercise. Fig. 6 shows the M wave area and the MEP amplitude for the 4 fatigue levels. It appears that post-exercise changes of the M wave response follows the initial increase of MEP amplitudes, whereas the subsequent decrease of MEP amplitudes only for an exercise level of 50–25% was accompanied by a reduction in M wave area. In addition, the post-exercise increase of M wave response was present for a longer period compared with MEP amplitude.

4. Discussion

In the present study, PEF of MEP amplitudes was to some degree related to the level of exercise performed. The increase gradually declined and reached baseline after approximately 25 s at all 4 fatigue levels (Fig. 4). In addition, after peripheral nerve stimulation a similar facilitation of M wave following the various contraction levels was found. However, the increase of M wave area was present for minutes and disappeared after approximately 5 min at 3 out of 4 fatigue levels. Since the increase of MEP declined to baseline in approximately 25 s there seems to be two or more mechanisms involved, including changes in the muscle itself and/or more central events. In addition, we observed a subsequent decline of the M wave to about

Fig. 2. MEPs and M waves recorded from the tibial muscle following a fatiguing exercise (100–25% of MVC).

Fig. 3. Amplitude (lnμV) of motor evoked potentials (mean ± 1 SEM) at 4 fatiguing exercises recorded from tibial muscle (A) and soleus muscle (B). *P < 0.05.

Fig. 4. Amplitude (lnμV) of MEPs recorded from tibial muscle (mean ± 1 SEM) in the first 25 s after 4 fatigu ing exercises.
90% of baseline value at exercise level 50–25%, but no decline at the 3 other levels. Following TMS, MEP was decreased to 90% at all 4 levels for at least 10 min (Fig. 3).

Both PEF and PED of MEP probably primarily reflect changes at a cortical level (Rothwell et al., 1991; Samii et al., 1996). The underlying mechanisms behind changes within the motor cortex after exercise as recorded by TMS are unknown but the possibilities include alteration of membrane properties of the pyramidal cells, changes in syntactic efficacy due to changes in neurotransmitters, and alteration of the response to stimulation of other neurons within the motor cortex and thus of their input to pyramidal cells. In addition, muscle afferent input to the cerebral cortex appears to play a major role in motor control (Wiesendanger and Miles, 1982) and facilitation from muscle afferent may contribute up to 30% of central motor drive (Macefield et al., 1993). At the same time, motor firing is inhibited by afferent feedback from the muscle probably, to prevent high-frequency (peripheral) fatigue. This inhibitory input could be subject to supraspinal control.

PEF of MEP occurs in both submaximal exercise (50–25%, Fig. 3), in which force loss is disguised by progressive recruitment of motor units and increased firing rate, and with maximal contraction, in which force loss develops after only a few seconds (Figs. 1 and 3) during which motor neurons firing rates fall. One would expect that an increase in excitability of motor neurons will contribute to PEF of MEP during submaximal exercise but not during maximal exercise. Following submaximal exercise there is evidence for a decrease in excitability of motor neurons (Norgaard et al., 2000; Schieppati and Crenna, 1984; Ljubisavljevic et al., 1996; McKay et al., 1995; McFadden and McComas, 1996).

At the cortical level, fatigue during maximal contraction could be due to increased inhibition within the cortex. Studies have demonstrated that the silent period following TMS lengthens as fatigue develops during a maximal contraction. Consequently, output from the motor cortex could be insufficient to excite all motor neurons at a high enough rate to tetanize all fibers in the muscle (Gandevia et al., 1996; Woods et al., 1987). For elbow flexors, stimulation at the motor point of biceps brachii muscle during a...
sustained MVC elicits an increment in force. The muscle is not driven maximally by the motoneurons despite MVC. The progressive increase of this increment is evidence of central fatigue.

Several authors have studied fatigue by TMS in healthy subjects (Gandevia, 1996; Brasil-Neto et al., 1993; Samii et al., 1996, 1997; Mills and Thomson, 1995; McKay et al., 1995; Zanette et al., 1995) but only a few have combined this with M wave studies. Brasil-Neto et al. (1993) found PEF and PED of MEP after exercise but an unchanged M wave response. This is in conflict with the previous results and findings in other studies. Hicks et al. (1989) showed increase of the M wave responses interposed between successive 3 s voluntary contractions of the human thenar and extensor digitorum brevis muscles. It was expected that this phenomenon would be caused by increased synchronization of muscle fiber action potentials during the super-normal period after previous discharges, but Hicks et al. (1989) showed that the potentiation was caused by a transient increase of muscle fiber resting membrane potentials resulting from enlargement of the fiber action potentials. Also, McComas et al. (1994) found potentiation of the M wave after exercise, and showed that the enlargement of the M wave was significantly greater at 10 Hz stimulation than at 3 Hz stimulation. This is in agreement with our findings where the smallest increase followed the briefest contraction (100–75%) and the largest potentiation the most sustained contraction (100–25%). McComas et al. (1994) showed in the biceps brachii muscle (BB) that the amplitude increased to 160% before it declined and almost disappeared. In accordance with our findings, Cupido et al. (1996) showed that during 3 Hz stimulation there was only small potentiation of the M wave (amplitude only) while 10, 20 and 20 Hz ischemia resulted in large potentiation of the M wave in BB. In the study by McCadden and McComas (1996), changes in muscle excitation and isometric twitch force was evaluated until 8 s after fatigue stimulation of BB. The exercise was 20 Hz tetanus maintained until the tetanic force had dropped to 50%. They found an initial potentiation of the M wave amplitude lasting for approximately 30 s followed by a decrease lasting 3 h. Decreased excitability of the muscle fiber plasmalemma was suggested as the possible mechanism of the depression. Only minor changes were seen in the soleus muscle, probably reflecting unintended contraction of the antagonist muscle.

In conclusion, the initial PEF of MEP after fatiguing exercise could be explained by both peripheral and cortical mechanisms. However, during the following PED of MEP the cortical inhibition could be counteracted by increased peripheral excitability. After submaximal fatiguing exercise (50–25%) both peripheral and central inhibition occurs. However, major differences in populations of neurons excited by TMS and peripheral nerve stimulation (MEP amplitudes were about 1/10 the size of M wave amplitude) suggests that conclusions should be drawn with caution.

Acknowledgements

This study was supported by The Danish Society of Multiple Sclerosis, The Warvara Larsens Foundation, Karen A. Tolstrup's Foundation and Haslev Municipality/ Horse-dealer Ole Jacobsens Memorial Foundation. We wish to thank research assistant Holger Kiliarich for technical support and Professor Johannes Jakobsen for advice and critical comments.

References


