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Further Insights Into Post-exercise Effects on H-Reflexes and Motor Evoked Potentials of the Flexor Carpi Radialis Muscles

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The present study investigated the relative contribution of the cortical and spinal mechanisms for post-exercise excitability changes in human motoneurons. Seven healthy right-handed adults with no known neuromuscular disabilities performed an isometric voluntary wrist flexion at submaximum continuous exertion. After the subjects continued muscle contraction until volitional fatigue, the H-reflexes induced by an electric stimulation and motor evoked potentials (MEPs) induced by a transcranial magnetic stimulation (TMS) from a flexor carpi radialis (FCR) muscle were recorded 7 times every 20 s. The H-reflex was used to assess excitability changes at the spinal level, and the MEP was used to study excitability changes at the cortical level. H-reflexes showed a depression (30% of control value) soon after the cessation of wrist flexion and recovered with time thereafter. On the other hand, an early (short latency) MEP showed facilitation immediately after the cessation of wrist flexion (50% of control value) and thereafter decreased. A possible mechanism for the contradictory results of the 2 tests, in spite of focusing on the same motoneuron pool, might be the different test potential sizes between them. In addition, a late (long latency) MEP response appeared with increasing exercise. With regard to the occurrence of late MEP response, a central mechanism may be proposed to explain the origin—that is, neural pathways with a high threshold that do not participate under normal circumstances might respond to an emergency level of muscle exercise, probably reflecting central effects of fatigue.

Key Words: H-reflex, early and late motor evoked potentials (MEPs), flexor carpi radialis (FCR) muscle, exercise, fatigue

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Introduction

Fatigue of the motor system is characterized by a decrease of the force generated by the neuromuscular system during sustained or repeated voluntary muscle contraction. Although reports on muscle exercise effects are innumerable, the details of the mechanisms concerning the decrease of force are still under open debate (Enoka, Gandevia, McComas, Stuart, & Thomas, 1996; Enoka & Stuart, 1992; Yue, Bilodeau, Hardy, & Enoka, 1997). Especially, in the field of voluntary muscle exercise, the relationship of these changes to the loss of force or fatigue is unclear because of methodological restrictions (Proske, Morgan, & Gregory, 1993). Generally, it is believed that the decrease of force with exercise is a phenomenon of muscle fatigue. In recent years, it has been pointed out that muscle exercise effects are not solely due to biochemical changes that occur within muscle fibers or effectors. That is, muscle exercise effects cannot be explained without changes in the central nervous system (CNS; Taylor & Gandevia, 2001).

Transcranial magnetic stimulation (TMS) of the motor cortex that elicits motor evoked potentials (MEPs) has been used to explore the dynamics of central motor involvement before, during, and following motor activity. The neural mechanisms underlying both facilitation and depression of MEPs following exercise are believed to reside within the motor cortex. That is, central fatigue leads to a post-exercise depression of MEPs and results from reduced neural drive proximal to spinal motoneurons (Brasil-Neto, Cohen & Hallett, 1994; Brasil-Neto, Pascual-Leone, Valla-Sole, Cammarota, Cohen, & Hallett, 1993; Liepert, Kotterba, Tegenthoff, & Malin, 1996; Loscher & Nordlund, 2002; McKay, Tuel, Sherwood, Stoki, & Dimitrijevic, 1995; Mills & Thompson, 1995; Sammi, Wassermann, Ikoma, Mercuri, & Hallett, 1996). Brasil-Neto and colleagues (1993) first reported the changes in MEPs in the flexor carpi radialis (FCR) muscle after fatiguing exercise. They demonstrated a remarkable progressive decrease in the MEP amplitude evoked at 5-s intervals in the post-contraction period, but later studies have not confirmed this evidence (Samii et al., 1996; Zanette, Bonato, Polo, Tinazzi, Manganotti, & Fiaschi, 1995; Zijdewind, Zwarts, & Kernell, 2000). Furthermore, the relative contribution of the cortical and spinal mechanisms to these effects is still uncertain, in particular after muscle contraction (post-exercise effect). Thus, post-contraction depression induced by exercise and the potential difference between the cortical and spinal level remain interesting questions for fatigue study. The purpose of the present study was, therefore, to re-examine the effects of exercise on cortical and spinal excitability changes using H-reflex and TMS methods.

Methods

Seven subjects who suffered from no neurological disorders (all male subjects, aged 21 to 47 years; mean = 32 years) participated. Before the experiment, we gave them sufficient information concerning the study's purpose and all subjects gave their informed consent in accordance with the Declaration of Helsinki (1964) on the use of human subjects in experiments. The local ethics committee of Hiroshima University approved the experimental procedures.

Each subject sat comfortably in the experimental chair. Each forearm was supinated, and a motor task was executed with the subjects' right arm in a fixed position. Based on the results of the preliminary experiment in recording EMG

activities, 6-kg dumbbells were deemed appropriate for the burden and the isometric voluntary muscle contraction as the motor task. The first attempt to generate fatigue involved holding the dumbbells until it became impossible to continue muscle contractions according to the subject's own judgment. Based on EMG recordings of the preliminary experiment as described above, it is reasonable to assume that the FCR muscle plays a major agonist role in this motor task. The reason for picking this motor task is that H-reflexes and MEPs can be recorded under the same conditions in the FCR muscle, which functions as an agonist (Kasai, Toyoda, & Yahagi, 1997). In addition, we judged the appropriate number of exercises for the motor task to be up to seven times (1–7 sessions), because holding times for all subjects in the preliminary experiment showed a plateau from the 5th to the 7th session in spite of different individual values.

The H-reflex and MEP recordings were obtained from Ag-AgCl surface electrodes placed over the FCR muscle. The EMG activity was captured using a 5 Hz–20 kHz band-pass filter (Nihonkohden AB-621G), and then digitized at a sampling rate of 5 kHz and stored. After cessation of muscle contractions, H-reflexes were recorded at 20-s intervals (7 times). Optimal H-reflex sizes (ranging from 15 to 30% of maximum M-wave) were selected as the test H-reflexes for each subject. We paid special attention to keeping the intensity of electrical stimulus constant (1-ms duration) for recording H-reflexes. In order to keep the test H-reflex size consistent through experiments, we monitored the direct M-wave recorded as a simple accessible measure of stimulus strength (Kasai & Komiyama, 1996; Kawanishi, Yahagi, & Kasai, 1999). After the final (7th) recording of the H-reflex, the maximum M-wave (M-max) was recorded for each subject. It is well known that part of the changes in the H-reflex and MEP amplitude may largely reflect changes in the muscle fiber electrophysiological properties; hence, it is important to compare changes in the H-reflex and MEP sizes with those of the maximum M-waves (Boorman, Hoffer, Kollesoe, Viberg, & Mah, 1996; Zijdewind, Zwarts, & Kernell, 1999). Moreover, after a 30-min break following the 7th session of muscle contractions, the H-reflex and M-max were recorded again. This was to assess how long the influence of sustained voluntary muscle contraction continues after a long break.

MEPs were recorded under the same conditions as the H-reflexes on a different day. TMS was performed with a Magstim 200 (Magstim, Dyfed, UK) using a round coil with a 9-cm outside diameter, and we used the maximum output intensity (100%) of TMS to record the MEPs stably. In recording MEPs, using side A of the coil facing up, the left hemisphere was stimulated, and we simultaneously recorded MEPs from two different muscles: the extensor carpi radialis (ECR), which is the antagonist of the FCR muscle, and the biceps brachii (BB) muscle, which is the synergist of the FCR muscle. In recording MEPs from the contralateral (left arm) FCR muscle, using side B of the coil facing up, the right hemisphere was stimulated.

Data were inspected online and stored for subsequent analysis. The responses were analyzed using a computer program that calculated the peak-to-peak amplitude of each response. After the experiment, the amplitude values, area values, and necessary information were derived from the stored data and were displayed on a computer display. The mean values and standard deviations of all subjects' M-waves, H-reflexes, and MEPs were calculated. The size of the H-reflexes and MEPs recorded under the present experiment were compared using two-way analysis of

the variance (ANOVA; fatigue × time). Post hoc comparisons were made using Tukey's post hoc test. The regression lines and Pearson's correlation coefficients were also calculated for consideration of the correlation of the two samples. The significance level was at $p < .05$.

Results

Exercise-Associated Changes of Holding Time

The holding time of the 6-kg dumbbell by the right wrist joint decreased over exercise trials (1st to 7th sessions). Setting the holding time of the first session to be 100% (control values: range, 4 to 6 min) for all subjects tested ($n = 7$), decreased holding times were observed during the 2nd session, which showed approximately a 40% reduction ($F_{6,6} = 5.61, p < .05$; Figure 1). Thereafter, the holding time gradually decreased by a few percentage points over each session. Taken together, this evidence and previous reports (Enoka & Stuart, 1992; Enoka et al., 1996; Proske et al., 1993), we judged the task on which the present experiment was based to be effective in bringing about muscle fatigue.

Exercise-Associated Changes of H-Reflexes

Figure 2 shows an exemplary record of the H-reflex up to 130 s after the cessation of voluntary muscle contractions in each session of the motor task obtained from a single subject. These H-reflex recordings clearly show a depression immediately after the cessation of voluntary muscle contractions, compared to a stable H-reflex before executing the voluntary muscle contractions (pre-exercise in Figure 2). This

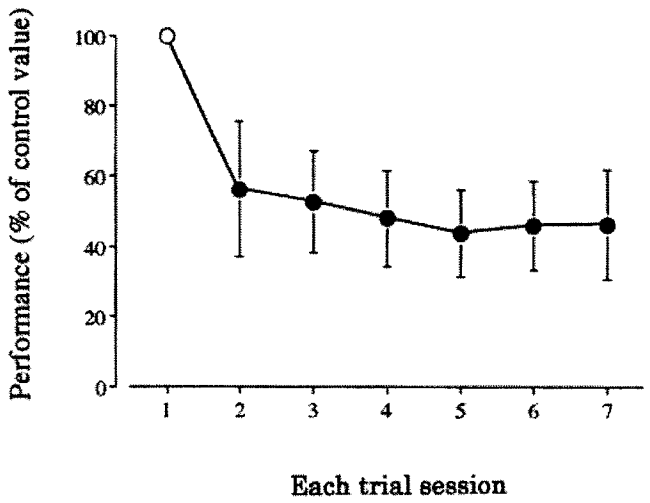

Figure 1 — Decrease of the holding time with increasing practice. The average values and standard deviations of all the subjects tested ($n = 7$). The holding time of session 1 (abscissae) is set as 100% (ordinate; control value). Decrease of the holding time was statistically significant ($F_{6,6} = 5.61, p < .05$).

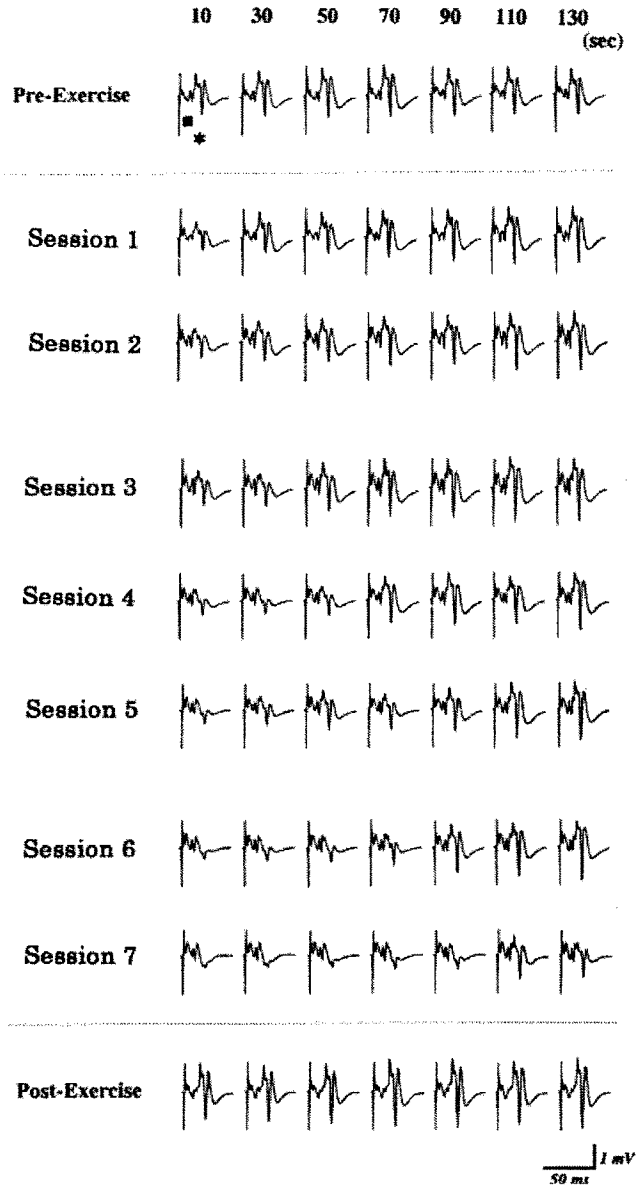

Figure 2 — An example recording of FCR H-reflexes (asterisk) and small M-waves (filled square) obtained from a single subject after the cessation of voluntary muscle contractions. The time (10–130 s) shows the process of time after the cessation of muscle contractions, and also shows the H-reflex recording time at each trial session. Pre-exercise shows the H-reflex records before the start of voluntary muscle contraction, and post-exercise shows those after a 30-min break (after session 7). The FCR H-reflex was strongly depressed immediately after the cessation of voluntary muscle contractions and thereafter recovered gradually.

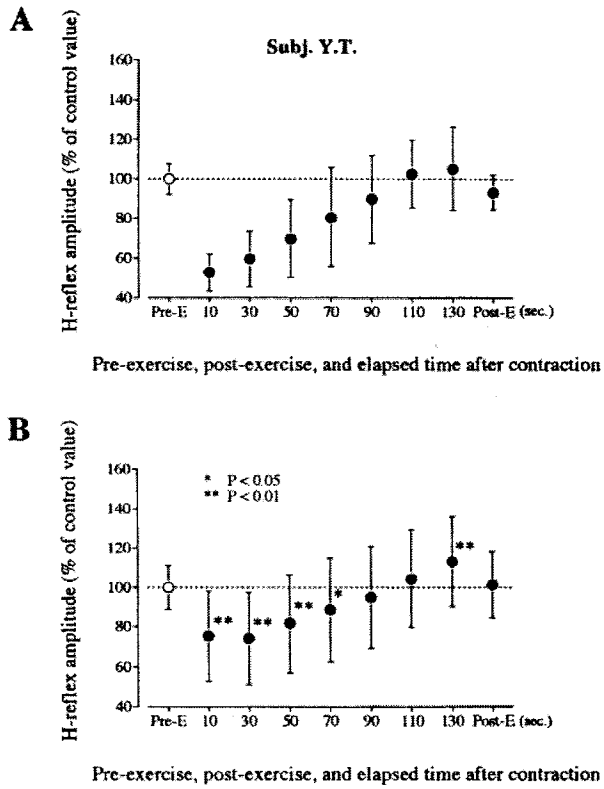

Figure 3 — The quantitative change of the FCR H-reflex after the cessation of voluntary muscle contractions. A: A typical example of subject Y.T. B: Average values and standard deviations of all subjects tested (n = 7). The depression of the H-reflex continues for approximately 70 s after the cessation of muscle contractions. Mean of pre-exercise H-reflex values is control (100%).

depression recovered to the control size within 90 to 110 s after the cessation of muscle contractions. After that, H-reflexes showed a tendency to increase to beyond the control size. During the 30-min break, H-reflexes recovered to their control size (post-exercise in Figure 2). Since the M-max directly reflects the functional changes of the neuromuscular junction as described above, the change naturally influences the H-reflex. Therefore, we recorded the M-max of all the subjects tested and in each session. Then, we calculated the ratio between the amplitude of the H-reflex and that of M-max that was recorded in each session. Figure 3 shows the changes of the H-reflex standardized by the method as mentioned above and calculated seven H-reflexes recorded at each session (1–7 sessions) as time went by. Figure 3A shows a typical example of average values of H-reflex amplitude obtained from another single subject. Since there was a similar tendency in the examined subjects even though there were quantitative differences among the subjects, we calculated the average values and standard deviations of all the subjects tested (n = 7) and shown in Figure 3B. The amount of H-reflex

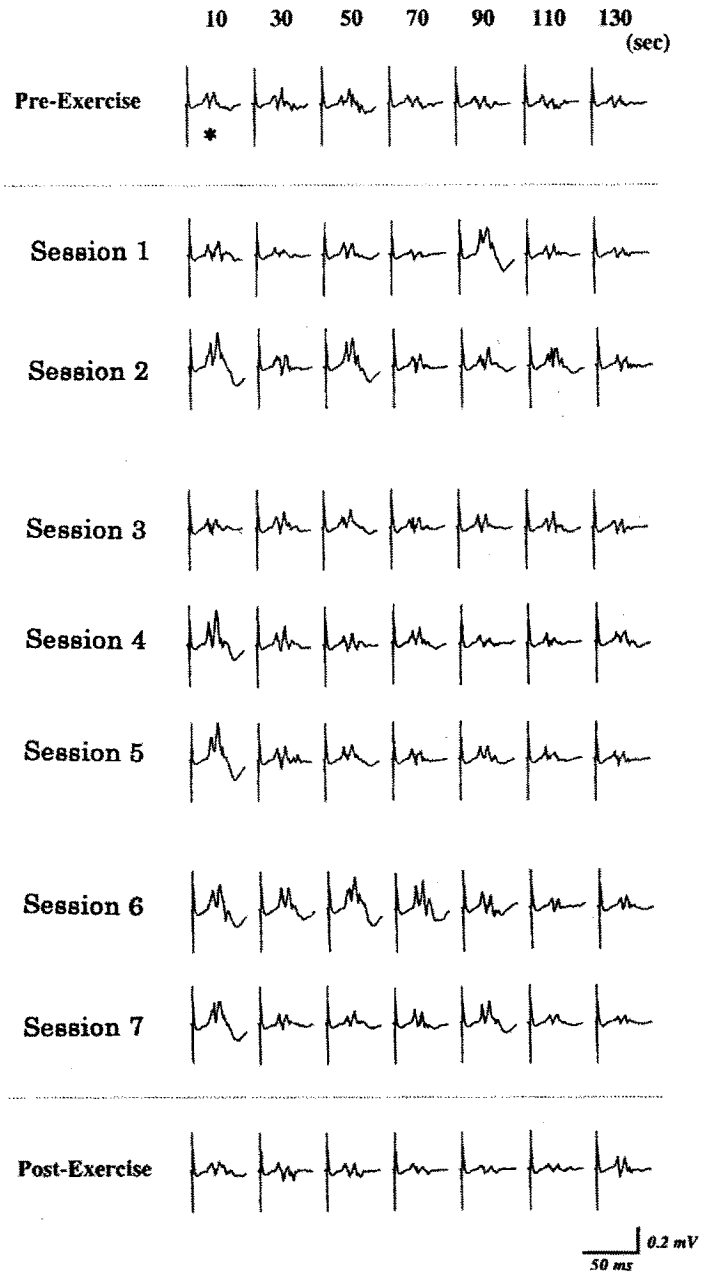

Figure 4 — An example recording of early MEP responses (asterisk) from a single subject after the cessation of voluntary muscle contractions. Representations are the same as Figure 2. Note that the gain of MEP amplitude is one fifth of that of the H-reflex. The MEP amplitude increases just after the cessation of muscle contractions and decreased later on.

depression was statistically significant soon after the cessation of voluntary muscle contractions as shown in Figure 2 ($F_{1,6} = 9.68$, $p < .05$). Thereafter, the H-reflex recovered in 90 s and showed facilitation in 130 s.

Exercise-Associated Changes of MEPs

Figure 4 shows the change of the early MEPs of the right FCR muscle obtained from a single subject. The amplitude of the MEPs increased soon after the cessation of the voluntary muscle contractions unlike the behavior of the H-reflex. Figure 5A shows the average values and standard deviations of all subjects tested ($n = 7$), similar to H-reflex data shown in Figure 3B. Changes in the MEP amplitude were also seen in other muscles—ECR muscle (Figure 5B), BB muscle (Figure 5C), and contralateral FCR muscle (Figure 5D). We observed that MEP amplitude changes of these muscles became larger immediately after the cessation of voluntary muscle contraction and then faded with time. The changes of MEP amplitude between the agonist FCR muscle and the other muscles were also observed to show similar tendencies—that is, a quick return to the control level of excitability within 30 s after the cessation of voluntary muscle contractions.

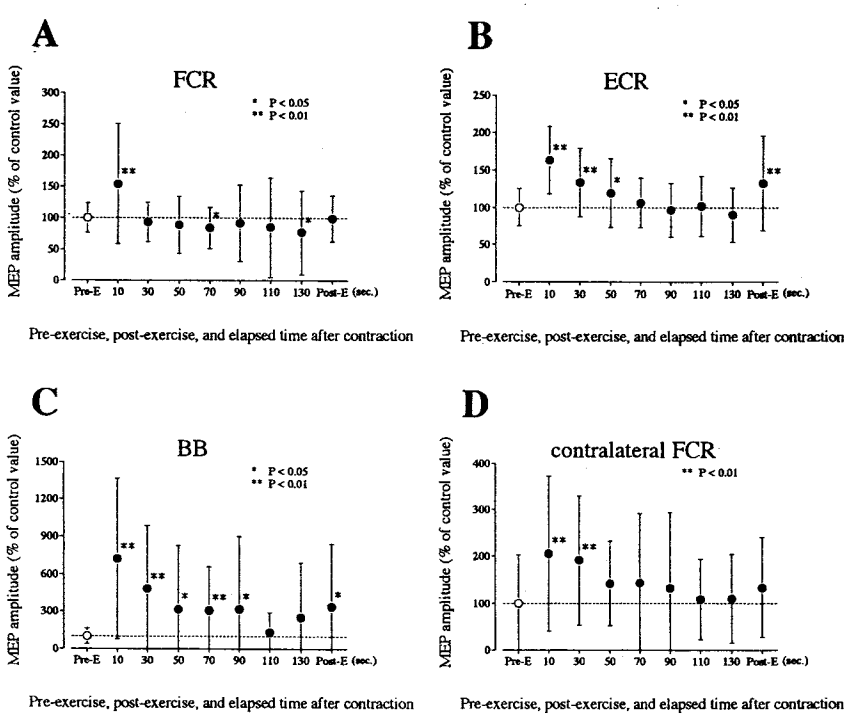

Figure 5 — A: The means and standard deviations of the MEP amplitude of the agonist (A; FCR), extensor carpi radialis (B; ECR), biceps brachii (C; BB), and contralateral FCR (D). Representations are the same as Figure 3. The MEP changes of B, C, and D are similar to those of the agonist FCR (A) with regard to a temporary increase immediately after the cessation of muscle contractions, while in B, C, and D, the increase of MEPs did not decrease rapidly and rather continued for approximately 10–30 s.

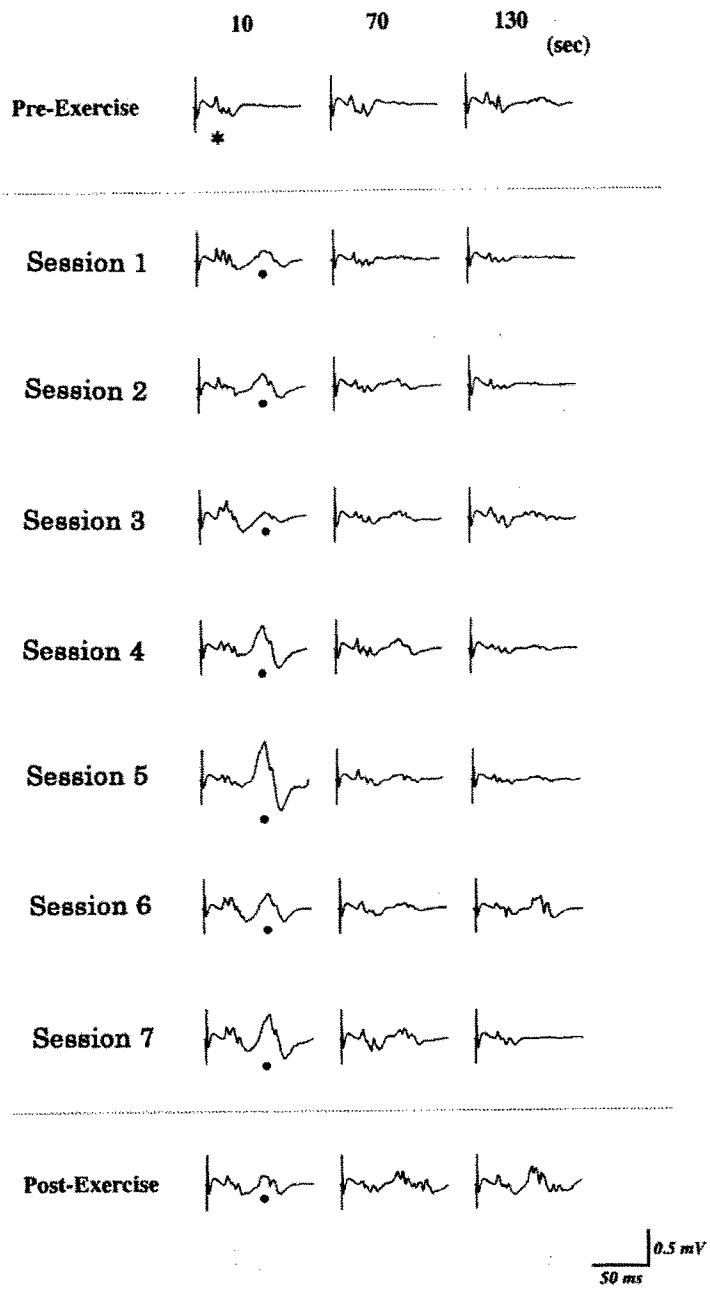

Figure 6 — An example recording of late MEP response appeared in post-exercise. In particular, amplitudes of late MEP responses (filled circles) increased just after cessation of muscle contractions as well as the early MEP responses (asterisk).

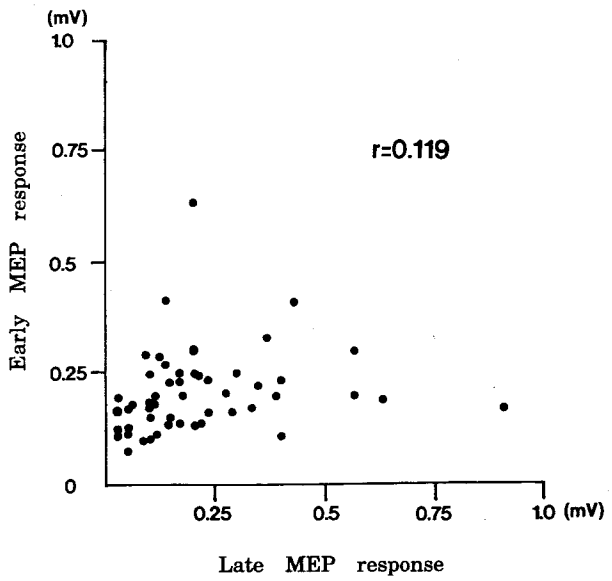

Figure 7 — An example of relationship between early and late MEP responses. There is no statistically significant correlation between them. (See Figure 6 for plots of early and late MEP responses recorded in a single trial.)

We observed late MEP responses (latency about 50–60 ms), which did not appear before executing voluntary muscle contractions (5 out of 7 subjects). Typical records are shown in Figure 6. These late MEP responses are especially recognizable immediately after the cessation of a muscle contraction similar to facilitation of early MEPs as mentioned above (filled circles in Figure 6). Therefore, to investigate the relationships between early and late MEP responses, we calculated the correlation coefficients between the magnitudes of these two MEP potentials. A typical plot obtained from a single subject is shown in Figure 7. There were no significant correlations between the two MEPs in all subjects, as shown in Figure 7 (n = 5, range of correlation coefficients; r = –0.11 to 0.21).

Discussion

To re-examine the post-exercise changes of neural mechanisms acting upon human motoneurons, the subjects sustained an isometric voluntary wrist contraction at a submaximum continuous exertion, and the H-reflexes and MEPs of the FCR muscle were recorded from soon after to 130 s after the cessation of muscle contractions. In analyzing these changes, FCR H-reflexes showed a depression soon after the cessation of wrist contractions and recovered over time. On the other hand, early MEP responses showed facilitation immediately after the cessation of muscle contractions and thereafter decreased. Late MEP responses appeared after the muscle exercise, an unexpected phenomenon. What do these changes mean to post-exercise changes of neural mechanisms related to human fatigue?

Exercise-Associated Changes of H-Reflexes

Several neurophysiological mechanisms concerning phenomena of H-reflex depression have been considered (Windhorst & Boorman, 1995). One possible neurophysiological change occurring in the motoneuron pool is that the threshold change of motor units varies selectively in muscle fatigue (Bigland-Ritchie, Dawson, Johansson, & Lippold, 1986; Bigland-Ritchie, Johansson, Lippold, Smith, & Woods, 1983; Bigland-Ritchie, Thomas, Rice, Howarth, & Woods, 1992; Bongiovanni & Hagbarth, 1990; Grimby, Hannerz, & Hedman, 1981; Woods, Furbush, & Bigland-Ritchie, 1987). A continuing excitatory input to the motoneuron pool associated with a voluntary muscle contraction changes the membrane resistance of the motoneurons (Kernell & Monster, 1982a, 1982b). Indeed, it was proved by model experiments that the recruitment gain of a motoneuron pool depends on the change of the synaptic connectivity that responds to the input (Kernell & Hultoborn, 1990). Therefore, there might be threshold changes in the spinal motoneuron pool as a result of muscle fatigue.

More recently, an increase in the threshold of axon response to electrical stimulation or voluntary contraction has been demonstrated, and this effect could alter the afferent volley of the H-reflex and reduce its efficacy (Vagg, Magyoros, Kierman, & Burke, 1998; Burke & Gandevia, 1999; Kuwabara, Coppelen-Smith, Lin, Mogyoros, & Burke, 2002). Furthermore, Sacco et al. (2000) recently indicated that a decrease in the excitability at the spinal level contributes to the reduced corticomotoneuronal excitability observed after fatiguing exercise using MEP responses of the BB muscle during recovery from two different exercise regimens. If that is the case, the H-reflex amplitude decrease after exercise in the present experiment can be explained in line with the above-mentioned neural mechanisms. That is, depression of H-reflex is considered to follow the reduced cortical excitability and the changed synaptic efficacy occurring as a result of fatigue.

According to reports that consider a possibility of another mechanism known as "after-effects" (Gregory, Mark, Morgan, Patak, Polus, & Proske, 1990; Gregory, Morgan, & Proske, 1987, 1988; Hagbath & Nordin, 1998; Hagbarth, Nordin, & Bongiovanni, 1995; Nordin & Hagbarth, 1996; Ribot-Ciscar, Tardy-Gervet, Vedel, & Roll, 1991; Wilson, Gandevia, & Burke, 1995; Wilson, Gracies, Burke, & Gandevia, 1999; Woods, Gregory, & Proske, 1996), the susceptibility change of motoneuron pool after voluntary muscle contraction more largely depends on sensory inputs than in a normal situation. The central actions of group III and IV nerve afferents involves direct inhibition of the activity of human motoneurons because muscles are richly innervated by these nerve afferents (Balestra, Duchateau, & Hainaut, 1992; Duchateau & Hainaut, 1993; Garland, 1991; Garland & Kaufman, 1995; Garland & McComas, 1990). Based on the present results, it is likely that the afferent inputs from small group III and IV fibers, as an after-effect of fatigue, caused depression of H-reflex after the cessation of muscle contraction, because depression of H-reflexes in the present results showed immediately after the cessation of voluntary muscle contractions, and this depression recovered to the control size within 90 to 110 s. That is, H-reflex changes with time were similar to inhibitory after-effects of group III and IV nerve afferents on human motoneurons (Gregory et al., 1987, 1988, 1990).

Other neural mechanisms are thought to change the response of motoneurons as a result of strong muscle contractions. For example, several spinal reflex

circuits concerning the H-reflex depression are also considered: post-activation depression, recurrent inhibition, Ib inhibition, and so on. It remains an interesting question for further experiments to study how these spinal reflex mechanisms bring about fatigue.

Exercise-Associated Changes of MEPs

According to reports that examined the excitability change of the motor cortex using magnetic and electric stimulation (McKay et al., 1995, 1996; Sacco, Thickbroom, Thompson, & Mastaglia, 1997; Samii et al., 1996), excitability changes of MEP were evoked only by magnetic stimulation but did not occur in electric stimulation. Taken together with recent reports (Gandevia, Allen, Butler, & Taylor, 1996; Gandevia, Patersen, Butler, & Taylor, 1999; Liepert et al., 1996; Ljubisavljevic, Mailanovic, Radovanovic, Vukcevic, Kostic, & Anastasijevic, 1996; Taylor, Butler, Allen, & Gandevia, 1996), these neurophysiological changes with fatigue occur not at the spinal level but at the cortical level. Based on the results of MEP amplitude that the subjects performed to sustain MVC of the elbow flexors for 2 min, Taylor et al. (1999) have suggested that the central mechanisms contributed significantly to the increase of the MEP responses. Hence, the increased MEP amplitude during fatigue in the recent results must be reflected on excitability changes in the CNS. Thus, an increased response from the motor cortex to the magnetic stimulation remains a likely contributor to the increase in the size of the MEPs under fatigue. In addition, similar tests with neurological patients have shown that their motor commands decreased with fatigue because of a lack of motivation (Sammi, Wassermann, Ikoma, Mercuri, George, O'Fallon, Dale, Straus, & Hallett, 1996; Sheean, Murray, Rothwell, Miller, & Thompson, 1997) or increasing perception of effort (Sacco, Hope, Thickbroom, Byrnes, & Mastaglia, 1999).

The change of early MEP responses in the FCR (agonist) muscle is a facilitation phenomenon just after the cessation of muscle contractions. Bonato et al. (1994), Brasil-Neto et al. (1993, 1994), and Zanette et al. (1995) have reported that these phenomena reflect temporary increases in the excitability of the CNS with the execution of voluntary muscle contractions and fatigue within the CNS associated with that excitability. In particular, Brasil-Netto et al. (1993, 1994) called the facilitation phenomenon "post-exercise facilitation (PEF)" and called the following depression "post-exercise depression (PED)". The results of the present experiment confirmed the conclusions of these previous reports that the temporary facilitation and depression appear in MEPs after the cessation of voluntary muscle contractions with maximum effort. With regard to PEFs in the present experiment, it also occurred in the antagonist (ECR) and the synergist (BB) muscles as well as in the agonist (FCR) muscle (see Figure 5B–C). Thus, it seems that central fatigue occurs not only in the target (agonist) muscle but also in neighboring muscles related to the exercise task. This evidence indicates that the excitability change of the CNS varies depending on the extent of participation in correspondence with the exercise situation (Sammi, Wassermann, & Hallett, 1997).

In addition, Brasil-Neto et al. (1999) have recently demonstrated that PEFs of the first dorsal interosseous MEPs occurred even after simple, ipsilateral, and unilateral finger movements of the dominant hand. This was not seen in a similar paradigm reported by Samii et al. (1997) with the opposite arrangement—that is, TMS was delivered to the left hemisphere, and movements were performed with

the left hand or forearm. In the present study, we observed the contralateral PEFs (see Figure 5D). Based on the explanation of the transfer phenomenon of PEF-related neural activity by Brazil-Neto et al. (1999), our results could be understood as follows: contralateral PEFs are not due to a direct involvement of the non-dominant hemisphere but rather to transcallosal transfer of excitability from the dominant to the non-dominant hemisphere. Studies of callosotomy patients suggest a transcallosal transfer of excitability from the dominant to the non-dominant cerebral hemisphere, perhaps related to mechanisms involved in bimanual motor coordination (Geffen, Jones, & Geffen, 1994).

As described above, PEFs simultaneously occurred in some other muscles in the exercised hand. Thus, one can expect the excitability changes to diffuse widely under fatigue brought about by maximum effort (Gandevia, 1998). Using two monkeys, Belhaj-Saif et al. (1996) examined how the firing pattern of motor cortex cells shows changes under fatigue and demonstrated the existence of a change of firing frequency under fatigue. These findings suggest that the activity of motor cortex cells may change as a compensation for a change in a peripheral organ. Therefore, the changes of the MEP amplitude with fatigue in the present study may be viewed as compensatory phenomena due to mobilized neighboring brain regions.

With regard to the appearance of late MEP responses with fatigue, several studies reported that late MEP responses were mostly elicited in the lower limbs (mainly soleus muscle), and the rubro-spinal tract and reticulo-spinal tract are listed as candidate neural pathways (Dimitrijevic, Kofler, McKay, Sherwood, Van der Linden, & Lissens, 1992; Ertekin, Ertas, Efendi, Larsson, Sirin, Arac, Toygar, & Demir, 1995; Holmgren, Kadanka, & Larsson, 1992; Holmgren, Larsson, & Pedersen, 1990; Masur, Althoff, Kurlemann, Strater, & Oberwittker, 1995; Tarkka, McKay, Sherwood, & Dimitrijevic, 1995; Wilson, Thickbroom, & Mastaglia, 1995). Therefore, the present results obtained in the upper limb muscles using TMS come to prove for the first time that these mechanisms may also exist in the upper limb muscles. This means that CM cells, which did not participate before the exercise, came to participate in the activity with the central fatigue. Some high threshold neural pathways, which did not participate under normal circumstances, might cooperate with each other in an emergency. As for the details of this role of the nervous system, further investigations are needed.

Differences of Exercise-Associated Neural Mechanisms Between H-Reflex and MEP

Finally, why did the excitability change just after the cessation of muscle contractions show opposite excitability changes between H-reflexes and MEPs in spite of focusing on the same motoneuronal pool? A possible reason for this contradictory result is different-sized test potentials between the two tests. That is, the potential size of the H-reflex was 1.5–3.0 mV (about 10–30% of the maximum M-wave). On the other hand, the potential size of the MEP was only 0.2–0.6 mV (3–8%; see actual recording examples in Figures 2 and 4, and the potential scale). That is, the size of the motoneurons that formed the H-reflex potential was likely larger than that of the MEPs. This evidence suggests that the neurophysiological background related to excitability changes might be different depending on the potential size differences within the same motoneuron pool (Crone, Hultoborn, & Jespersen, 1985; see also Kasai et al., 1997).

More recently, Taylor et al. (2000) elegantly tested whether the post-contraction depression of a response to corticospinal or motor cortical stimulation could be maintained by continued firing of ischemically sensitive group III and IV nerve afferents. Based on their results, ischemically sensitive group III and IV nerve afferents do not mediate depression of responses to motor cortical or cortical stimulation. They also suggest that the firing of such afferents does not directly inhibit motoneurons or cortical output cells (Taylor & Gandevia, 2001; see also Zijdewind et al., 2001). This is a fundamentally hypothetical argument, so the accumulation of further experiments for all these mechanisms is necessary.

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