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Modulations of input-output properties of corticospinal tract neurons by repetitive dynamic index finger abductions

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Abstract The goal of this study was to investigate how corticospinal tract neurons (CTNs) are modulated after repetitive dynamic muscle contractions. To address this question, changes of motor evoked potentials (MEPs) to transcranial magnetic stimulation and background EMG (B.EMG) activities were examined. Subjects were instructed to perform an isometric dynamic index finger abduction as accurately as possible under the target-force-matching tasks (10% or 30% MVC), while MEPs of a first dorsal interosseous (FDI) were elicited during performance of the task. After repetitive dynamic FDI contractions (100 trials), the following remarkable phenomena were observed: (1) both B.EMG activities and MEP amplitudes decreased in proportion to the number of trials, (2) these phenomena were most commonly observed in

different conditions, i.e., different force levels and hands (preferred or non-preferred hands), and (3) after repetition of the tasks, the MEP amplitude/B.EMG (MEP/B.EMG) ratio became smaller. Decreases of B.EMG activities with reduction of MEP amplitudes and diminishing MEP/B.EMG ratio might suggest the occurrence of reorganization of input-output properties in CTNs for an efficient performance as a function of motor adaptation. Thus, we conclude that motor adaptation after repetitive dynamic muscle contractions probably occurs less specifically and due to susceptible modulations of spinal motoneurons reflected in the integrative functions of CTNs.

Keywords Motor adaptation · Motor evoked potentials (MEPs) · Corticospinal tract neuron (CTN) · FDI muscle · Repetitive dynamic contraction · Human

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Introduction

In general, a precise dynamic (gradation) muscle contraction is of the utmost importance for human motor control. Thus, one of the main requirements for well-coordinated motor behavior is that the central nervous system (CNS) must be able to produce the correct dynamic force production in all the muscles concerned. The CNS can grade force by two alternative mechanisms used in parallel, i.e., by varying the number of activated motor units (recruitment order) and by varying the discharge rate of already recruited units (rate coding). Additionally, use-dependent changes would be needed for the continuous adjustment of these two mechanisms in well-coordinated motor performance. It has been shown that even single, mechanical degree-of-freedom movements are subject to improvement through practice (Gottlieb et al. 1988; Corcos et al. 1993). However, with the exception of these studies, to our knowledge, there are very few reports and little is still known about how neurophysiological changes dependent on usage occur at cortical and spinal levels in humans (Kernell 1992).

Motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) are supposed to reflect the activated populations of corticospinal tract neurons (CTNs). In human studies, TMS has most often been used in experiments that investigated the properties of CTNs during precise movements. In particular, the input-output properties of CTNs are referred both to the transmission of signals to the motoneuron pool via CTNs and to segmental neural elements that influence the excitability of the motoneuron pool (Devanne et al. 1997). In our daily life, the CNS may be optimizing a combination of background EMG (B.EMG) and CTN activities when the force output must be sustained at a fixed target force level. Recently, our report indicated that there were definitely different CTN activities with different force production modes, for example, isometric (sustained) and isotonic (kinetic), despite the same force level (Yahagi et al. 2003). Then, are there different CTN activities between tonic and dynamic contraction modes at the same force level and the same isometric muscle contraction? In particular, how are CTN activities modulated after repetitive dynamic force productions by a ramp contraction mode?

The present study was, therefore, undertaken to examine excitability changes of MEP related to B.EMG activities after repetitive dynamic muscle contractions in the target-force-matching task. That is, the aim of the present study was to explore how different neural mechanisms are generated between tonic and dynamic muscle contractions, and, in particular, how input-output properties related to dynamic force production are modulated after repetitions of the target-force-matching task.

Materials and methods

Subjects

All 13 subjects participating in the present experimental series were right-handed. The subjects were informed of the purpose of the research and experimental procedures in advance and all gave informed consent as required by the Helsinki Declaration (1964). In the first experiment, ten subjects (seven males and three females; range 22–35 years and mean age 26.5 ± 3.9 years) participated and

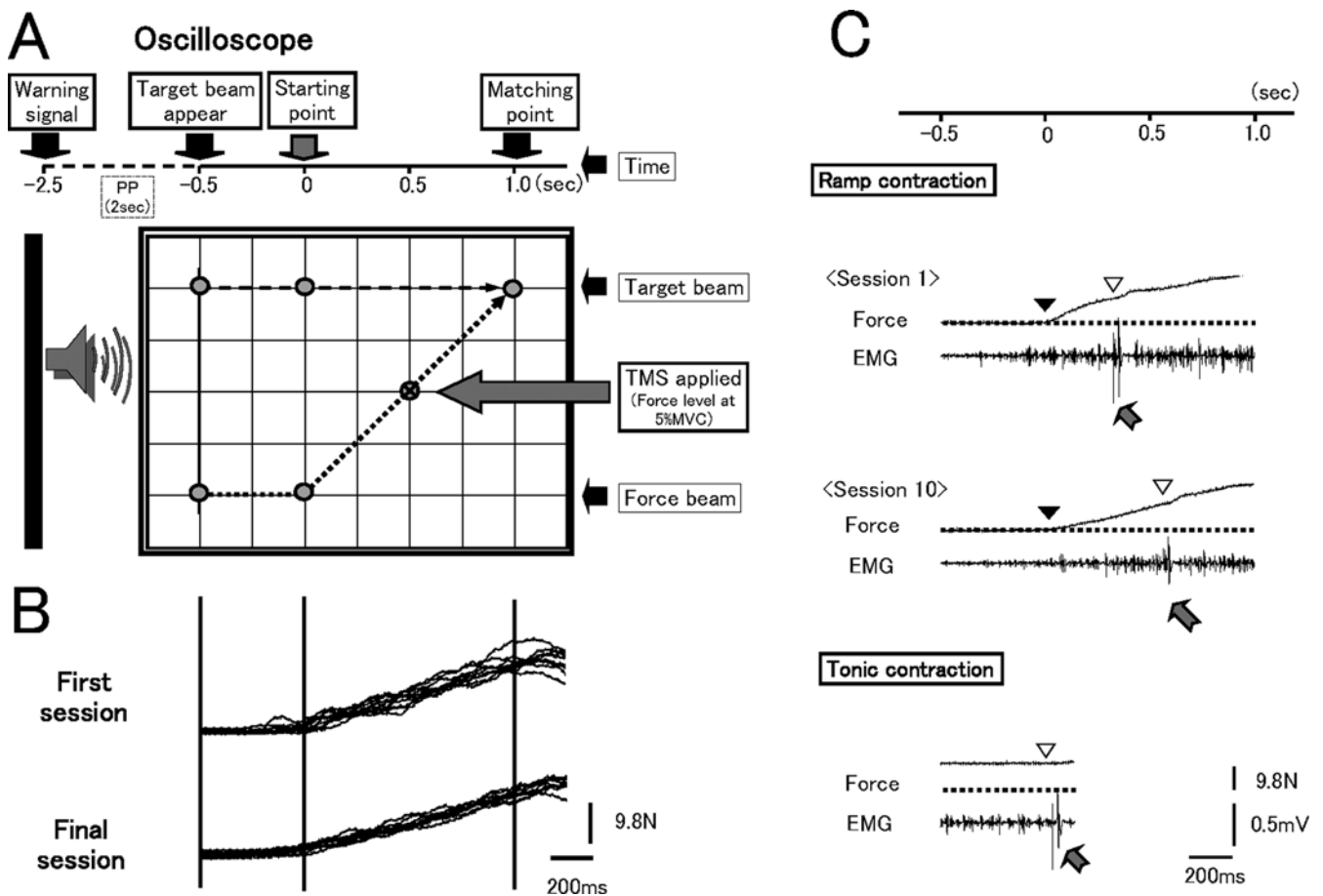


Fig. 1 A The display system used for the target-force-matching task. B Ten superimposed force curves in the first (upper traces) and final (lower traces) sessions. C Upper two traces (force curve, EMG activity and MEP) obtained from a dynamic contraction trial in the first (upper traces) and in the final sessions (lower traces). Bottom

traces show those in tonic (sustained) contraction. Filled triangles indicate starting points and open triangles are 5% maximum voluntary contraction (MVC) force levels at the onsets of transcranial magnetic stimulation (TMS) as shown by the arrows

they were asked to perform the isometric target-force-matching task of a dynamic force production of 10% maximum voluntary contraction (MVC) by abduction of their right (preferred) index finger. Three of the ten subjects also participated in the test for performing the same isometric target-force-matching task by abduction of their left (non-preferred hand) index finger on a different date. In addition, to examine the changes of input-output properties before and after repetitive dynamic muscle contractions, we recorded MEPs from five of the ten subjects using four intensity changes.

In the second experiment, to investigate whether different influences occur at different contraction force levels (30% MVC), five male subjects (two of the ten subjects in the first experiment and three new subjects; range 24–29 years and mean age 27.2 ± 4.1 years) performed the task using their right index finger. All conditions were the same as in the above-mentioned 10% MVC target-force-matching task.

Experimental procedures

The subjects were requested to perform the isometric and dynamic contractions by abduction of their right or left index finger (10% MVC at 1 s; see Fig. 1A). After a verbal “ready” signal was given, the target beam appeared and arrived at the starting point 0.5 s later. The subjects were required to initiate the index finger abduction as soon as the target beam arrived at the starting point and to match it to the target point exactly 1 s later as accurately as possible. The index finger was fixed tightly to an immobile bar that was connected to a strain gauge amplifier. The abduction force signal generated by the first dorsal interosseous (FDI) muscle was fed to a trigger circuit (Signal Processor 7T23S; Nihondenkisanei, Tokyo, Japan). The force signal was used to trigger the application of TMS. In the present study, TMS was delivered at a half of each target force level, i.e., TMSs were applied at 5% for 10% MVC and at 15% for 30% MVC target force levels (see Fig. 1A).

A visual display system similar to that used in a previous report from our laboratory (Kasai and Yahagi 1999) was used to control the dynamic contraction. The beam on the oscilloscope moved from left to right in proportion to the force applied to the bar. The subjects were instructed to abduct the index finger as accurately as possible to match the position of the targeted force level. The subjects were also instructed to perform the dynamic contraction at the same speed as the target, which reached the matching point at 1 s (see Fig. 1A).

Cortical stimulation

Since it is well known that the FDI muscle plays an important role in the index finger abduction movement (Kasai and Yahagi 1999; Hasegawa et al. 2001a, b), the excitability changes of CTNs related to the FDI muscle

were assessed by MEP amplitudes elicited by TMS. TMS was performed using a Magstim 200 stimulator (Magstim, Whitland, Dyfed, UK) connected to a figure-of-eight-shaped coil (outside diameter of each loop 135 mm). For stimulation, the coil was positioned tangentially over the skull, centered over the appropriate motor cortex area with the current at the intercept flowing posteriorly (Mills et al. 1992). The optimal coil placement was determined in each of the subjects by searching for the coil position that yielded the lowest stimulation threshold during relaxed or slightly voluntary contraction of the FDI muscle. Surface markings drawn on a swim cap placed on the scalp served as the reference by which the coil was positioned. In most subjects, optimal coil position for the FDI muscle was 4–6 cm lateral to the vertex. Once the optimal coil position was found, the MEP threshold (1.0xth) under the relaxed (at rest) muscle was determined as the intensity of stimulator output with which MEPs were elicited in five out of ten (50%) successive trials. Since mechanical fixation of the coil to the head is not well tolerated by subjects and not reliable, the coil was maintained on the head by the experimenter, and its position and orientation were constantly checked to ensure that no slippage occurred during the experiment.

Concerning MEP recordings before and after performing the repetitive tasks, we used only four TMS stimulus intensity changes in the present experiment, although it is suggested that we must use more different stimulus intensities (at least 8–10 stimuli; cf. Carroll et al. 2001). There are two important reasons why we did not do so. One is that even data obtained from only four TMS intensity changes are enough to reveal differences of input-output properties if these TMS intensities are optimal. In the present experiment the test MEP and B. EMG sizes were controlled and, thus, we could easily focus on and choose optimal TMS intensities to be used. The other reason is that we paid special attention to avoiding effects of extra-task trials on adaptive motor learning processes. Consequently, the two subjects who participated in both experiments were tested on a different date to avoid the above-mentioned effects.

EMG recordings

Surface electrodes (5 mm in diameter) were used for recording MEPs. Paired electrodes for recording were placed 1.5 cm apart over the belly of the FDI muscle and connected to conventional amplifiers (model AB-621G, frequency bands, 5 Hz to 3 kHz; Nihonkohden, Tokyo, Japan). Ten trials were recorded per session and ten sessions were carried out for practice (total 100 trials). Simultaneously, index finger abduction forces were recorded for checking improvement of performance by practice (see Fig. 1B, C). The peak-to-peak amplitudes of MEP responses and EMG activities inside the 100-ms window prior to TMS application were measured and calculated for each trial and each subject (see Fig. 1C). Ten trials of tonic FDI muscle contraction were recorded before

and after practice. To examine changes of input-output properties before and after repetition of the task, the ratio of the MEP amplitude and B.EMG (MEP/B.EMG ratio) was calculated in five subjects at 10% MVC target-force-matching task. That is, we recorded MEP amplitudes at four different TMS intensities (1.11, 1.25, 1.33, and 1.54xth) under the same B.EMG activity.

Statistical analysis

The B.EMG activity was defined as the mean amplitude of the rectified and averaged EMG at 100 ms duration just prior to the TMS stimulus being applied. We have already shown that mean values of B.EMG activities obtained from 100 ms duration is the optimal estimation of B.EMG activities (Kasai and Yahagi 1999; Hasegawa et al. 2001a; Yahagi et al. 2003). Thus, to determine the effects of the repetitive target-force-matching task on MEP amplitudes and B.EMG activities, two-way ANOVAs (trials \times each variable) and post hoc tests for differences were determined by Student's paired *t*-test. The statistical significance level was determined at 5% ($P < 0.05$).

Results

Figure 1B shows the contraction force curves during the first session (upper traces; ten superimposed trials) and the final session (lower traces). After several tens of trials of the task, contraction force curves became smooth and tracing errors were definitely reduced. That is, the subjects acquired the target-force-matching skill after repetitive dynamic contractions. To investigate the neural mechanisms related to the acquisition of the target-force-matching task in more detail, we analyzed each trial in all sessions. Figure 1C shows typical specimen records composed of force curves, B.EMG, and MEP amplitude from the first session and final session (upper traces). The force curve in session 10 becomes as smooth as those in the final session shown in Fig. 1B. Similarly, lower traces in Fig. 1C show a single specimen record of tonic (sustained) contraction. To reveal changes of input-output properties of CTNs as described above, we measured B.EMGs and MEP amplitudes at all trials based on the recordings in Fig. 1C. Figure 2A shows a typical example of scatter plots of the B.EMG (each horizontal line) and MEP amplitudes (each ordinate line) obtained from a single subject. The target-force-matching task (10% MVC level) was performed by the right index finger and the results were ordered from the first to the final session (session 10) compared to those in tonic contraction (T). The central figure shows the same result but represents mean values of each session compared with those of tonic contraction (1–10 and T). Figure 2B uses the same results as shown in the central figure in Fig. 2A, but is a different representation of the results. We calculated the means and standard deviations of the MEP amplitudes and B.EMG (upper and middle figures) and also calculated the MEP/B.EMG ratio

for each session (bottom figure). These results showed that both the MEP amplitudes and B.EMGs decreased dependent on the number of trial sessions and finally converged on the tonic contraction level. ANOVA tests of these reductions of MEP amplitudes, B.EMGs, and MEP/B.EMG ratios were statistically significant (MEP amplitude, $F_{(9,9)}=3.359$, $P < 0.05$; B.EMG, $F_{(9,9)}=3.760$, $P < 0.05$; MEP/B.EMG ratio, $F_{(9,9)}=3.531$, $P < 0.05$). Similar results were obtained from all subjects although trial sessions across subjects were different. In Fig. 3 we show means and standard deviations of all subjects tested ($n=10$) only at the first and final sessions. Comparing the first with the final sessions, the reductions in each of the three variables were statistically significant (MEP amplitude, $t=4.978$, $P < 0.01$; B.EMG, $t=2.971$, $P < 0.05$; MEP/B.EMG ratio, $t=3.059$, $P < 0.05$).

A typical example of the performance by the left (non-preferred) hand doing the same target-force-matching task is shown in Fig. 4. Also, a typical example of the target-force-matching level at 30% MVC performed by the right (preferred) hand is shown in Fig. 5. Very similar results were obtained in both tasks despite the different conditions. Results obtained from all subjects tested (three and five subjects, respectively) were similar, as shown in Figs. 4 and 5, although trial sessions across subjects were different. Considering these present results, it is suggested that there are common basic neural mechanisms related to acquire associative motor skills by repetition of the dynamic target-force-matching task.

In addition, to investigate the above-mentioned neural mechanisms in more details, we calculated the changes of the MEP/B.EMG ratio dependent on different TMS intensities before and after repetitive dynamic muscle contractions. Figure 6A shows specimen MEP and B.EMG records (three superimposed trials) obtained from a single subject at four TMS intensity changes before and after repetitive dynamic contractions. The MEP amplitudes after the repetition task became smaller than before despite the same B.EMG (TMS intensity at 45% in Fig. 6A). Figure 6B shows means and standard deviations of the MEP/B.EMG ratio obtained from all subjects tested ($n=5$). MEP/B.EMG ratios decreased after repetitive dynamic contractions. The difference in this ratio between before and after the repetition task was statistically significant at the optimal TMS intensity (1.25xth; $t=3.204$, $P < 0.01$).

Discussion

The present experimental paradigm aimed to reveal relationships between B.EMG activities and MEP amplitudes as functional changes of motor adaptation learning of the target-force-matching task. The novel finding reported here was that both B.EMG activities and MEP amplitudes were modulated after repetitive dynamic force productions, i.e., the amount of B.EMG activities and MEP amplitudes gradually decreased dependent on the number of task trials. Surprisingly, in the final session of

Fig. 2 A Relationships between motor evoked potential (MEP) amplitudes (vertical line) and background EMGs (B. EMGs; horizontal line) are shown by ten trials plotted at each session and tonic contraction (T) performed by the right (preferred) hand. *Central figure* shows means of MEP amplitudes and B.EMGs of ten trials at each session. *Numbers in each circle* show its trial session and T is tonic muscle contraction. **B** Means and standards deviations of MEP amplitudes (upper figure), B.EMGs (middle figure), and MEP/B.EMG ratio (lower figure) at each trial session (circles) and tonic muscle contractions (filled squares). These variables decrease dependent on trial number

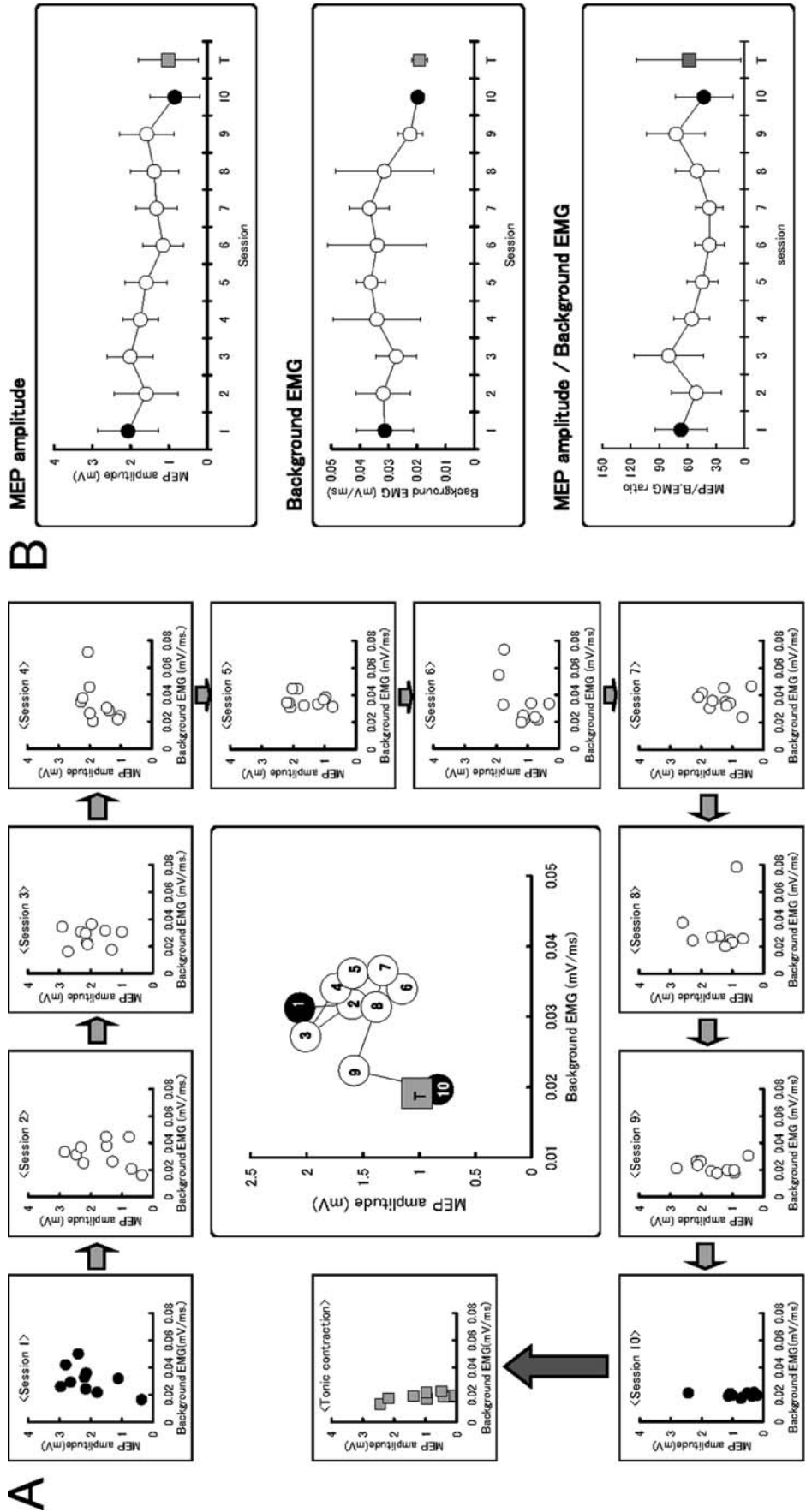
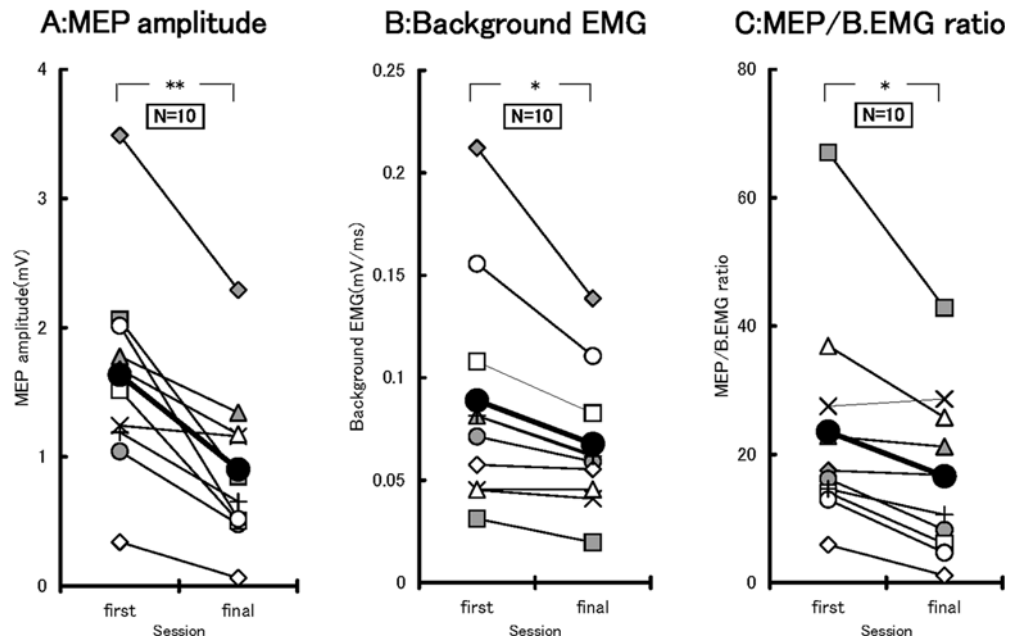


Fig. 3 A Means and standard deviations of MEP amplitudes at first and final sessions of all subjects tested ($n=10$) in target-force-matching task at 10% MVC performed by the right hand. Ground mean (filled circles) of MEP amplitudes at the final session was statistically significantly less than those at the first session. Similar representations of B.EMG and MEP/B.EMG ratio are shown in **B** and **C**, respectively. ** $P<0.01$, * $P<0.05$



all subjects, the B.EMG activity and MEP amplitude levels converged on the similar activity level of the sustained (tonic) contraction. Furthermore, the MEP/B.EMG ratio induced by optimal TMS intensity after the final session became smaller than the first session despite the same force production level. In other words, neural responses decrease over repeated exposure to identical motor tasks. This repetition depression is thought to reflect a progressive optimization of neural responses to the elicited task. These plastic changes contributed to individual learning performance level, suggesting interactions in M1 associative motor learning (Buchel et al. 1999).

The decreasing EMG activities, despite the same dynamic muscle contraction, might be associated with a decline in the number of motor units (MUs) that contributed to the interference pattern and a decrease in the discharge rate of the voluntarily activated MUs (De Luca et al. 1996). These adaptations after the task repetition may result from an alteration of the pattern of synaptic input that impinges on the MU pool (Garland and Miles 1997). That is, reduction of B.EMG activity could be due to synchronous activity in MUs and is termed synchrony effects, i.e., a small increase in the synaptic drive can produce a large increase in firing “a common synaptic drive”. The common drive onto pairs of motoneurons is a strong coupling and indicative of a strong common presynaptic drive (De Luca and Erim 2002; Semmler 2002; Semmler et al. 2003). Indeed, based on findings of MU synchronization during isometric force production in the precision grip performing a visually guided motor task with three different force levels, most MUs displayed a positive correlation between firing rate and grip force (Huesler et al. 2000). In addition, synchronization occurred preferentially at the lower force levels and the recruitment threshold appeared to play a determining role in synchronization; the more similar thresholds of the

MUs, the greater the possibility of their being synchronized at this force level (Huesler et al. 2000). If that is the case, the decrease in B.EMG activity dependent on repetition of motor tasks in the present study could be explained in line with the above-mentioned neural mechanisms.

Since it is well known that the dynamic muscle contraction depends on both the recruitment of MUs and the increases in the firing frequency of MUs already active, both mechanisms in the present isometric contractions are involved either when different levels of force are maintained or when ramp contractions are performed. Recently, Kamen and Du (1999) demonstrated that the MU discharge rate may limit force production and be improved through exercise training. Changes in descending cerebral outflow may mediate rapid changes in the MU discharge rate, i.e., repeated activation produced by repetitive muscle contractions might be highly amenable to rapid, task-specific alteration. Rapid alterations in the firing rate, therefore, are clearly associated with changes in the neural strategy used to produce force. Such a cortical adaptation could be responsible for the EMG activities and MEP amplitudes of the present dynamic contraction converging on those of the tonic-force contraction, because the tonic contraction is a more efficient muscle contraction mode than the dynamic one. These neural adaptations may be important mechanisms responsible for motor adaptation learning, such as in the present task.

To quantify the training effect in the present study, we assessed the functional changes of the motor system using the MEP/B.EMG ratio. In particular, the MEP/B.EMG ratio dependent on the stimulus-response relationship reflects the pattern of neural recruitment, the number of descending volleys, and the density of excitable motoneurons. In other words, variations of the MEP/B.EMG ratio indicate changes in the corticospinal excitability (Ridding and Rothwell 1997) and the amount of change of

Fig. 4A, B Relationships between MEP amplitudes and B. EMGs of the target-force-matching task (10% MVC level) performed by the left (non-preferred) hand are shown in the same way as in Fig. 2

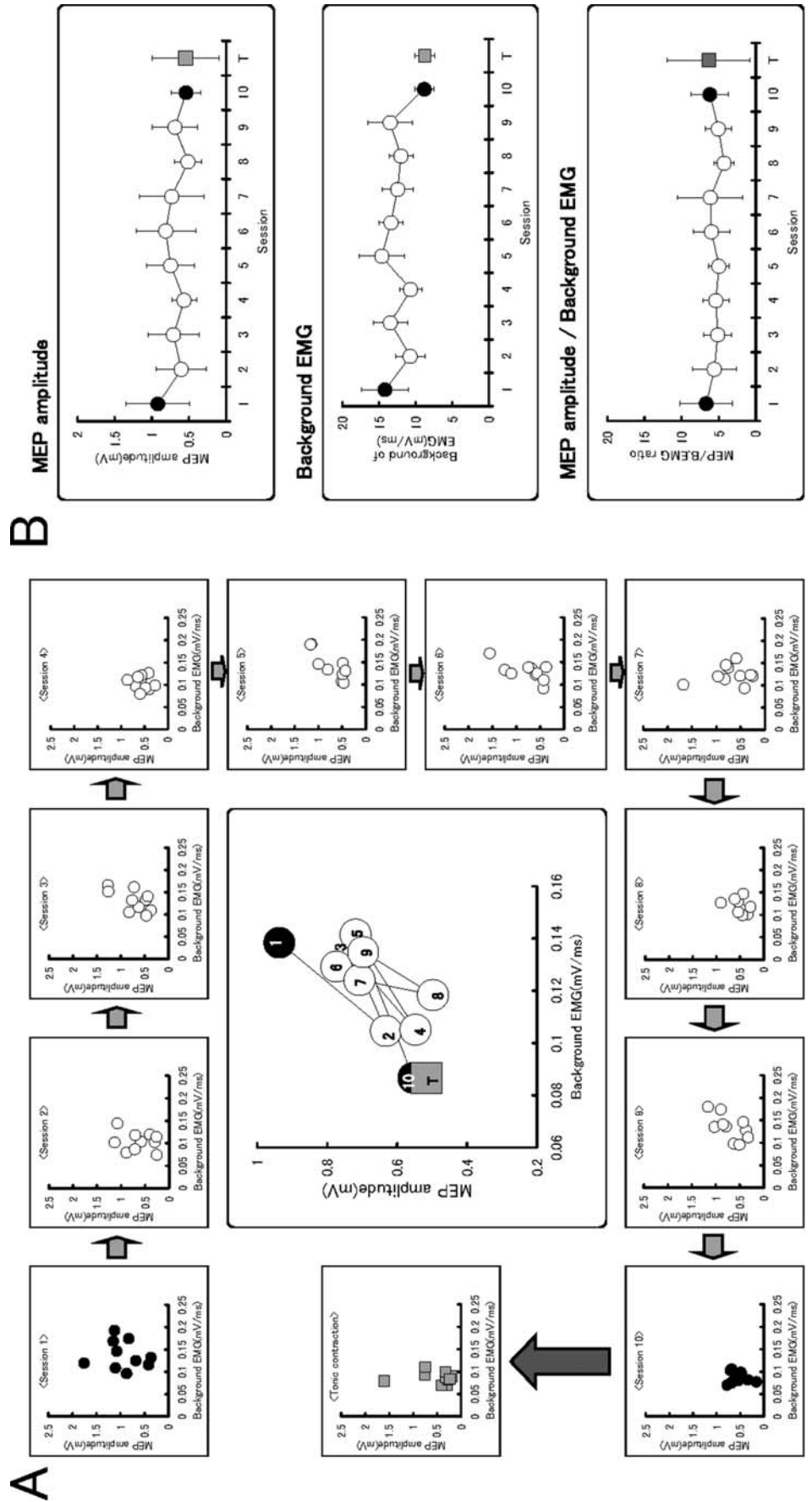
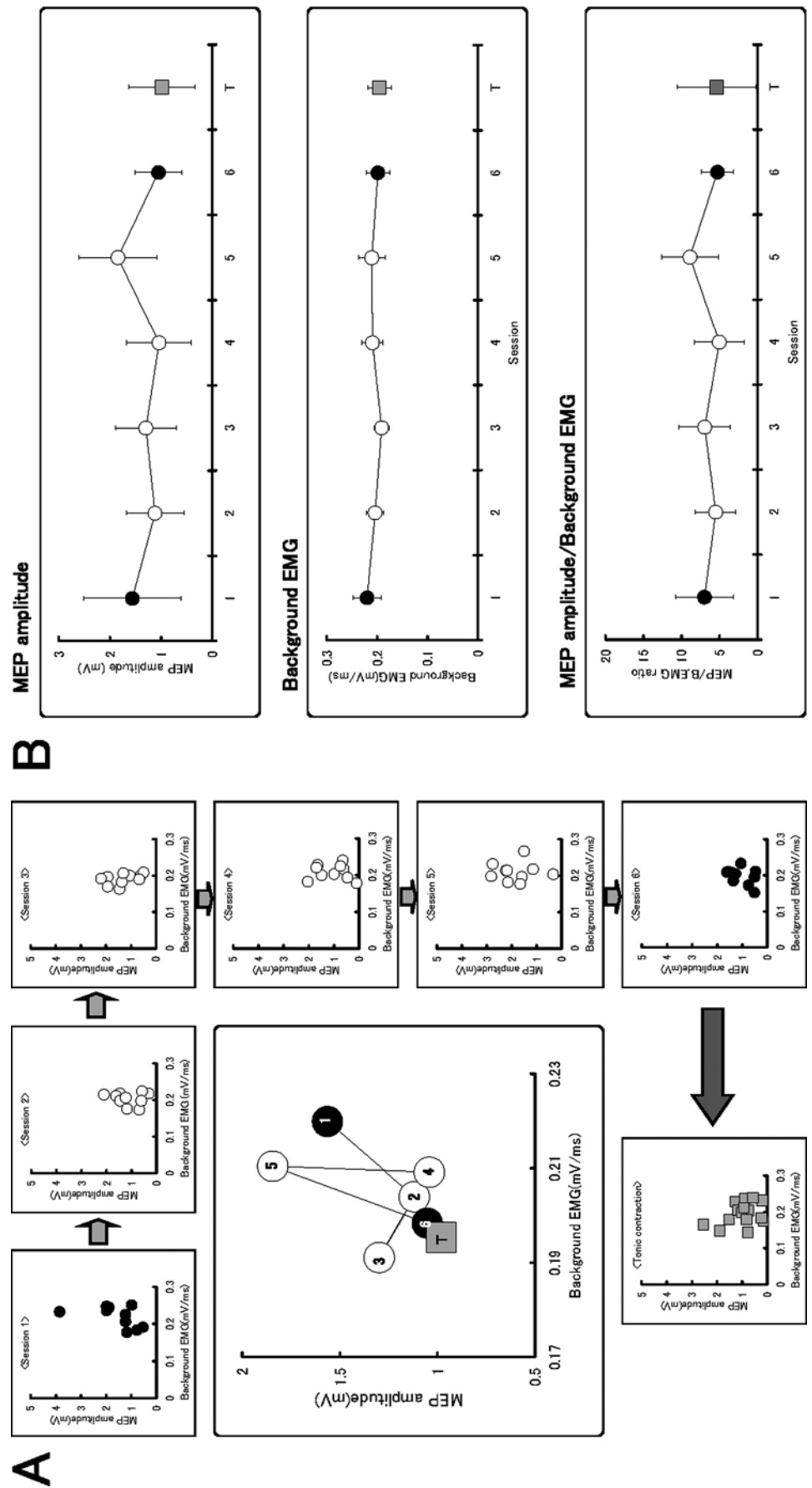


Fig. 5A, B Relationships between MEP amplitudes and B. EMG of the target-force-matching task at 30% MVC by the right (preferred) hand are shown in the same way as in Fig. 2



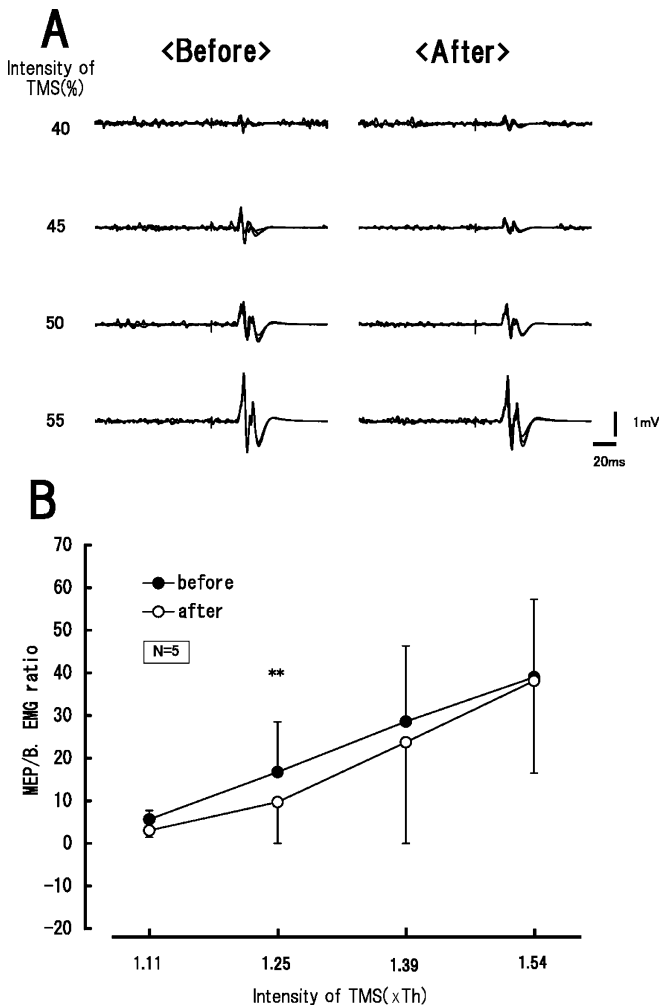


Fig. 6 **A** Specimen records (three superimposed trials) of MEPs with B.EMG activities obtained from a single subject evoked by four TMS intensity changes before and after repetitive target-force-matching tasks. **B** Means and standard deviations of MEP amplitude/B.EMG ratio (vertical line) obtained from five subjects tested induced by each TMS intensity (horizontal line) before (filled circles) and after (open circles) repetitive target-force-matching tasks. ** $P < 0.01$

B.EMG activities reflects a strategy intended to produce a force gradient with each subsequent movement. Thus, changes of the MEP/B.EMG ratio after practice in the present result might reflect changes of the CTN systems. That is, the present findings indicate changes of the CTNs related to the reorganization for a more efficient performance as a function of motor adaptation induced by practice. Indeed, based on the findings of Carolan and Cafarelli (1992), the trained CNS may be able to more effectively remove or reduce inhibitory input to the motoneuron pool of the muscle, resulting in an increase in motoneuron output. That is, training-induced neural adaptations may include improvements in muscle coordination, such as reductions in the activity of other muscles when performing the task efficiently.

Another possible explanation of the present results is that motoneuronal plateau potentials provide a mechanism for a short-term memory that could reduce the need for

steady ongoing synaptic drive during maintained muscle contraction (Kiehn and Eken 1997, 1998; see also Hultborn 1999; Kernell 1999, for review). In other words, activation of self-sustained firing, via the plateau currents, adds to the depolarization of the motoneurons and contributes to firing at a lower force level, i.e., the force at graded recruitment might usually be higher than the force at a sustained recruitment. Firing can thus be intrinsically maintained and would assist in maintaining contractions during dynamic muscle contraction tasks (Gorassini et al. 1998, 2002; Collins et al. 2002). Thus, from the view point of motoneuron performance and behavior, the essential neural mechanism of motor adaptation is a reduction in the upper limit of motoneuron recruitment dependent on the exploration and shaping in proportion to task specificity, i.e., the ultimate adaptation of motoneurons. However, such a mechanism in humans is demonstrated only in postural muscles (for example, soleus and pretibialis muscles). If that is the case in upper muscles, this mechanism might be useful when part of the continuous descending synaptic drive could be replaced by self-supporting intrinsic membrane properties, as in the present motor task. The decrease of B.EMG activity dependent on repetition of the target-force-matching task in the present results could be explained in line with the above-mentioned neural mechanisms, i.e., after repetition of producing, grading changes of plateau-like potential in FDI motoneurons might occur

The present study was undertaken to explore what kind of strategies could be used in dynamic force generation after repetitive muscle contractions (motor adaptation), i.e., to investigate how much and what type of plasticity could occur in the brain, and how much it could be used or how it could be enhanced (cf. Boniface and Ziemann 2003). Although the present results provided a foundation for understanding how corticospinal structures participated and changed in repetition of dynamic isometric muscle contraction, it remains still unclear what and how visual information contributes to on-line control of these finger movements (Eliassen et al. 2003; Saunders and Knill 2004). Thus, further investigations need to examine neural mechanisms related to visual-motor association learning.

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