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RESEARCH ARTICLE

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Functional demanded excitability changes of human hand motor area

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Abstract The present study was performed to examine if there are functional differences between the first dorsal interosseous (FDI) and the abductor digit minimi (ADM) muscles during different muscle contractions, namely dynamic and static contractions of the index and little finger abductions. It was also examined whether these functional differences occur at the cortical level. The motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) and force curves, during the muscle contractions, were simultaneously recorded. Rest motor thresholds (RMTs) and active motor thresholds (AMTs), during dynamic and static contractions, were determined in the two muscles. In all trials, the background EMGs (B.EMGs) were kept at the same level in each muscle. Results showed that the target matching errors of dynamic contractions were statistically smaller in the FDI muscle than those in the ADM. In the FDI muscle, the AMT during dynamic contractions was significantly lower than during static ones and the MEPs elicited by TMS were larger during dynamic contractions than those during static ones. However, such results were not found in the ADM muscle. In order to investigate whether the differences were caused by the excitability changes that occurred in the cortical level, the responses elicited by subcortical stimulations were recorded using the same procedures as the experiment of TMS. Responses to subcortical stimulations during dynamic contractions were similar to those during static ones in either muscle. It is concluded that there are differences in the task-dependent MEP facilitations between the FDI and ADM muscles. And the differences are due to the functional demanded excitability changes accompanied by the cortical activation.

Keywords Transcranial magnetic stimulation (TMS) · Motor evoked potential (MEP) · First dorsal interosseous (FDI) · Abductor digit minimi (ADM) muscle · Dynamic and static muscle contraction

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Introduction

It is well known that the motor evoked potential (MEP) elicited by transcranial magnetic stimulation (TMS) is task- and muscle-dependent (Datta et al. 1989; Flament et al. 1993; Hasegawa et al. 2001a, b; Kischka et al. 1993). Additionally, different muscle contractions also influence MEP responses. Different facilitory effects of step versus ramp (Kasai and Yahagi 1999) and isometric versus isotonic (Yahagi et al. 2003) muscle contractions on the MEP responses were reported.

Through the study of dynamic versus static muscle contractions (isometric), Arányi et al. (1998) demonstrated that MEP amplitudes in the deltoid muscle were larger during dynamic contractions than those during static contractions. In the ADM muscle, similar differences were not found.

Wu et al. (2002) demonstrated that the different degrees of direct corticomotoneuronal inputs to each muscle and the inherent properties of the spinal motoneruons, probably, generate the differences of finger dexterity. And from daily life, it is obvious that the index

finger can do a motor task more perfectly than the little finger. Thus, the first purpose of the present study is to examine if there are any differences in the task-dependent MEP facilitations between the FDI and the ADM muscles, corresponding to the index and little fingers, when two muscles perform dynamic and static contractions.

The powerful facilitatory effect of voluntary contraction is most pronounced in the small hand muscles, which are mainly involved in finely controlled motor tasks (Lemon et al. 1995). Finger functions related to the small hand muscles are deeply affected by task-dependent cortical control (Lemon et al. 1998). Accordingly, the second purpose of the present study is to examine if the differences in task-dependent MEP facilitations are due to the functional demanded excitability changes accompanied by cortical activation. Although the TMS is more sensitive to changes in excitability occurring in the primary motor cortex (M1), the MEP reflects the overall excitability of the corticospinal system (Abbruzzese and Trompetto 2002). Therefore, we employed subcortical stimulations to make sure whether the differences were due to activation in the cortical level.

Materials and methods

Subjects

Ten right-handed subjects, who did not suffer from any known neuromuscular disorders (two females, eight males; age range 19–37 years), volunteered for the present study. All of them participated in the TMS experiment. Five of them participated in measuring target matching errors, during dynamic contraction, to estimate functional differences between the FDI and ADM muscles. Seven of them also participated in experiments of subcortical stimulations. All subjects were informed of the purpose of the study and the experimental procedures in advance. The ethical committee of Hiroshima University approved the experimental procedures described hereafter.

Experimental procedures

Before the experiments, we measured the force levels during maximum voluntary contraction (MVC) of the right FDI (the prime mover of index finger abduction) and ADM (the prime mover of little finger abduction) muscles, when the subject abducted the right index and little finger with maximum effort. In the experiment of dynamic muscle contraction, 50% MVC was set as the target force level for each muscle. Protocols of the FDI and ADM muscles were separately undertaken. The subjects were instructed to abduct their fingers at a speed of generating the target force in 1 s. Concretely, an assumed force generation line was illustrated on a computer monitor, in advance (see Fig. 1a). One division of the illustration represented 250 ms in latitude and 10% MVC in longitude. After the starting signal (‘‘Ready ‘‘) was given, a beam point indicating the real force level of each subject appeared at the left side on the monitor. The point ran from left to right, at the speed of four divisions in 1 s, and arrived at the starting time 0.5 s later. The subject was requested to perform tracking this beam, following the assumed line illustrated. In static muscle contraction, a horizontal line indicating 10% MVC of each subject was illustrated, instead of the assumed line described above. The subject was instructed to abduct the finger and keep the beam point with the line for several seconds. All the subjects were trained to abduct their fingers only at the metacarpophalangeal joint and follow the line as accurately as possible. Distal interphalangeal joint was immobilized by an adhesive tape to a bar, which was connected to a strain gauge amplifier. A custom-built device was used to support and restrict movements of the wrist and other uninterested fingers. The force signals were recorded (Fig. 1b) and fed to a trigger circuit (Nihondenkisansei, Signal Processor 7T23S, Tokyo, Japan). These experimental procedures were controlled by a home-made laboratory computer program.

TMS

A Magstim 200 stimulator (Magstim, Whitland, Dyfed, UK) and a figure-of-eight shaped coil (the outside diameter of each loop was 9.5 cm) were used to provide the TMS. The slightly angulated coil was placed tangentially to the scalp, with the junction region pointing backward, at approximately 30° to the mid-sagittal line (Peinemann et al. 2004). Current induced in the brain was anterior-medially directed, which could activate the corticospinal system trans-synaptically (Di Lazzaro et al. 2001; Kaneko et al. 1996a, b). The optimal positions for the right FDI or ADM muscles were found out by moving the coil in 0.5 cm steps around the presumed hand area in the M1. The position, named the motor hot-spot, at which the stimulation of a slightly superthreshold intensity consistently produced the largest MEP, was marked with a pen (a swimming cap covered the scalp, paper tapes were adhered to the cap in 2 cm steps as a reference). Special attention was paid to the position and orientation of the coil (the coil was maintained on the scalp by an experimenter). The hot-spots of the FDI and ADM muscles were found out separately, because they were not always at the same position.

At the beginning of each experiment, the rest motor thresholds (RMTs) of the FDI and ADM muscles were determined, respectively. The RMT was defined as the minimum output of the stimulator that induced reliable MEPs (above 50 μV in amplitude) in at least five out of ten consecutive trials, when each muscle was completely relaxed. The stimulation intensities were determined according to the RMT.

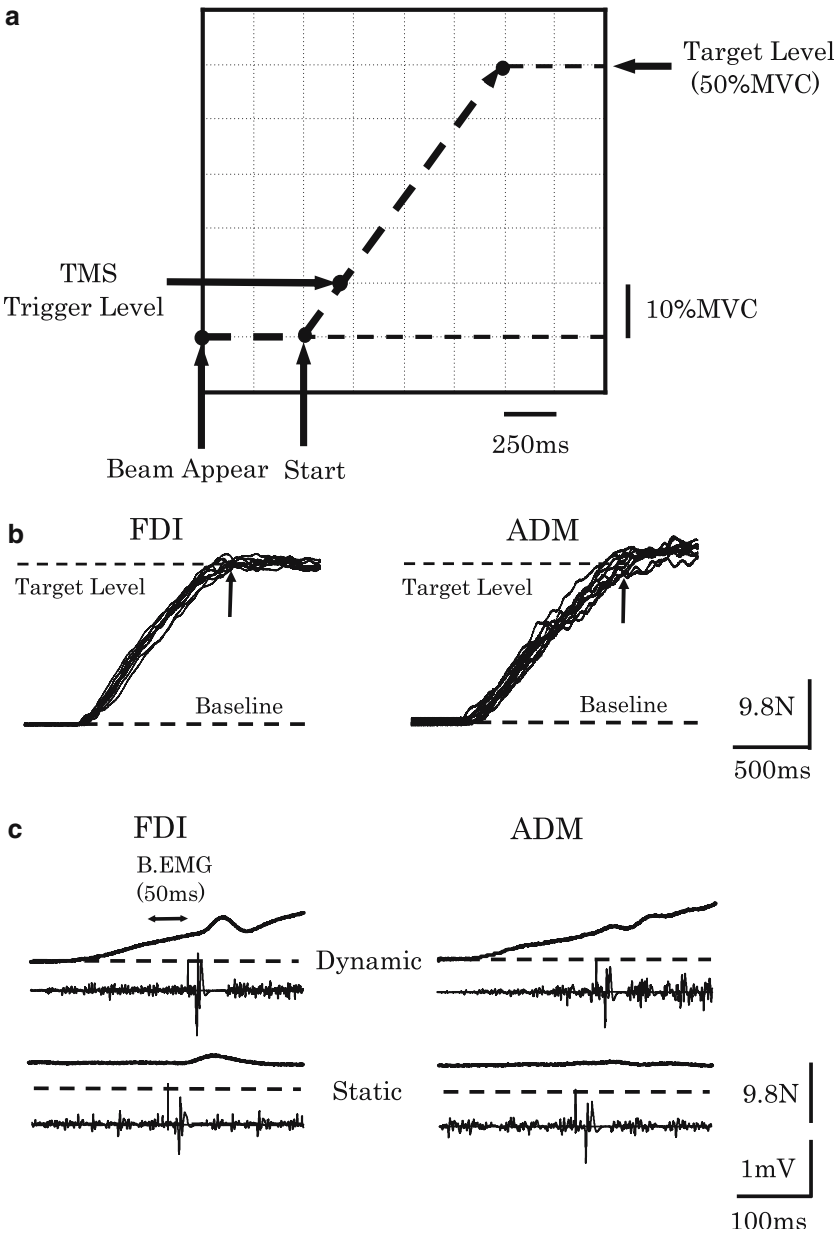

Fig. 1 **a** Shown of the experimental setup of dynamic contraction. The *bottom dashed line* is a baseline and the *top dashed line* is a target (50% MVC). The *middle leaning* one shows the assumed force generation. The TMS was applied at 10% MVC, automatically. **b** Typical force curves (superimposed ten trials) of the FDI (*left traces*) and the ADM muscles (*right traces*), during dynamic contractions, in tracking the assumed force generation line. *Top dashed lines* show the target force levels. *Arrows* are the best timing for matching the target (1 s after starting). **c** Typical recordings of the MEP, B.EMG and the force curve during dynamic (*upper traces*) and static (*lower traces*) contractions in the FDI (*left traces*) and the ADM (*right traces*) muscles, obtained from one subject. The B.EMG was calculated as an integrated value of the EMG activities, 50 ms prior to the TMS artifact

After several sessions of training trials of dynamic contraction in each muscle (the performances during training are showed in Fig. 1b as an insight to the present study), all the subjects could do the performances accurately. During the data collections of dynamic (Fig. 1c, upper traces) and static contractions (Fig. 1c, lower traces), the TMSs were automatically applied at the 10% MVC level, using the above-mentioned trigger circuit. These data collections were repeated at five TMS intensity steps, according to the RMT (0.7–1.1 times RMT), until 20 trials for every condition were recorded. To avoid fatigue effects, the order of the trials was randomly arranged and adequate rest was taken between trials.

Additionally, we determined the active motor threshold (AMT) of each muscle contraction by off-line analysis. The AMT was defined as the minimum output of the stimulator that could induce MEP responses in at least five out of ten consecutive trials. The amplitude qualification was set above 200 μV so that it could be distinguished reliably from the background EMG (B.EMG).

Subcortical stimulations

To make sure whether the extra task-dependent facilitation of MEP was affected by cortical activation, we employed subcortical stimulations of F-wave study and brainstem magnetic stimulation (BMS). For each condition (muscles cross contractions), ten successful responses were recorded using the same procedures as the TMS experiment.

F-waves were recorded in three subjects. Excitability of the spinal motoneuron pool can be partly assessed by

testing the magnitude of the F-wave, which is generated by a recurrent discharge of antidromically activated spinal motoneuron pool (Meyer and Feldman 1967). Supra-maximum electric stimulations on the ulnar nerve were delivered to elicit F-waves.

Since there is a general agreement that the F-wave is only due to the activation of larger motor units, it is limited when motoneuron pools are evaluated at a relatively low force level. In compensation for this, the BMS was used. The BMS was given by a Magstim 200 stimulator (mentioned above) through a 110° double cone coil (each cone was 9 cm in diameter). The coil was placed with the center of the junction region near the inion. The current flowed downward at the junction region of the coil, so that the maximum current induced in the head flowed upward. This current direction has the lowest threshold for activation (Ugawa et al. 1994; Taylor and Gandevia 2004). The BMS intensity was set at 80% of the maximum output of the stimulator. Under this intensity, we could record MEPs of 0.5–1.0 mV in amplitudes, which showed an extra task-dependent MEP facilitation in the TMS experiment (see part of the result). Four subjects were tested in this experiment.

EMG and force recordings

Surface EMGs were recorded from the FDI and ADM muscles with 9 mm diameter Ag-AgCl surface cup electrodes. The active electrodes were placed over the belly of the right FDI and ADM muscles and the reference electrodes over the ipsilateral metacarpophalangeal joints. The EMG responses were amplified by a conventional amplifier (model AB-621G, frequency bands, 5 Hz–3 kHz; Nihonkohden, Tokyo, Japan) and then recorded by a computer for later off-line analysis. Force curves were also recorded by the same experimental setup. Specific attention was paid to keep the same B.EMG for dynamic and static contractions in each muscle. Recordings with different proceeding B.EMGs were excluded from the final data.

Data analysis

In each trial there was a recording of the MEP or F-wave, preceded by successive EMG activity. In most subjects, the latencies of MEPs elicited by the BMS were 2 ms shorter than those elicited by the TMS. We integrated the EMG activity, just 50 ms prior to stimulation, as the value of B.EMG. Each value was normalized as a percentage of B.EMG under MVC contraction (B.EMGmax). The MEP and F-wave amplitudes were measured as the peak-to-peak value. In addition, we also recorded the maximum M wave (Mmax), both before and after the experiment, for checking the amount of motoneuron pools. The MEP and F-wave amplitudes were normalized as percentage values of Mmax.

A two-way repeated measures ANOVA (muscle contractions cross TMS intensities) was used for statistic analysis in the TMS experiment. The Greenhouse-Geisser ε correction was used to evaluate the F-ratios for repeated measures. A paired t-test, with Bonferroni correction for multiple comparisons, was used to determine differences as a post hoc test. A common paired t-test was used for comparing MEP thresholds (RMT and AMT). All the significant levels were set at a criterion of $p < 0.05$.

Results

Target matching errors during dynamic muscle contraction

Figure 1b showed ten superimposed force curves of dynamic contractions by the FDI and ADM muscles, obtained from the training sessions. There was a definite difference in the force curves of the two muscles. The error to the target force was measured as a simple index of it. The absolute difference between the generated force and the target, when the dynamic contraction had ended (1 s after starting), was calculated. It is named target matching error and was normalized as a percentage of the force value during the MVC. The errors produced by the FDI muscles were $1.72 \pm 0.19\%$ MVC, and those by the ADM were $2.20 \pm 0.39\%$ MVC ($N = 5$). The differences between the two muscles were statistically significant ($t = 3.75$, $df = 4$, $p < 0.05$).

MEP threshold

Table 1 showed the MEP thresholds in different muscles and their contractions. There was no difference in the RMT between the FDI and the ADM muscles. In the FDI muscle, the AMT was significantly lower during dynamic contractions than during static ones ($t = 3.61$, $df = 9$, $p < 0.01$). However, similar results were not obtained in the ADM muscle. During dynamic contraction, the AMT was significantly lower in the FDI muscle than in the ADM ($t = 2.41$, $df = 9$, $p < 0.05$). However, the AMT was the same for both muscles during static contractions.

MEP (elicited by TMS) amplitude

Figure 1c showed the example recordings of MEP, B.EMG and the force curve obtained from one subject. In the FDI muscle, the MEP amplitude during dynamic contraction was definitely larger than during the static one, in spite of the same force level and the B.EMG, but such a difference was not observed in the ADM muscle.

Figure 2a showed the MEP specimen recordings of the FDI and ADM muscles, which were elicited by three

Table 1 MEP threshold (% maximum stimulator output) in the FDI and the ADM muscles during relaxed condition and contractions

	FDI	ADM
RMT (relaxed)	50.9 ± 9.6	52.1 ± 10.0
Dynamic	41.9 ± 5.8*,**	43.2 ± 6.0*
Static	44.3 ± 7.0**	43.6 ± 5.9

*$p < 0.05$
**$p < 0.01$

steps of TMS intensity during dynamic and static muscle contractions (superimposed three trials), obtained from the same subject.

The results of all the subjects were summarized in Fig. 2b. In the FDI muscle, there were statistically significant differences of MEP amplitudes, between dynamic and static contractions ($F_{1,9} = 16.19$, $\varepsilon = 1$, $p < 0.01$), and for the various intensities ($F_{4,36} = 33.32$, $\varepsilon = 0.347$, $p < 0.001$). A post hoc test indicated that larger MEPs during dynamic contractions than those during static contractions in the FDI muscle could be found at four lower TMS intensities (0.7, 0.8, 0.9 and 1.0 times RMT, $p < 0.05$). However, in the ADM muscle, there was no significant difference at any step of TMS intensity. These mean results confirmed the above findings for a single subject.

Responses to subcortical stimulations

Figure 3 showed the typical recordings as well as the means and standard deviations (three subjects) of the F-waves during dynamic and static contractions of the FDI and the ADM muscles.

Figure 4a showed the typical MEPs elicited by the BMS during dynamic and static muscle contractions in the FDI and ADM muscles. Since the latency was shorter than the MEP elicited by the TMS, it was impossible that the responses were due to the influence of strong stimulations spreading to M1. Figure 4b showed the means and standard deviations, which were obtained from all four subjects.

No extra facilitation at the subcortical level between the two contractions, in either small hand muscle, was found when the B.EMGs were the same.

Discussion

Task performances during dynamic contractions of the FDI and the ADM muscles, which corresponded to the index and little fingers, were evaluated to give an insight into the functional differences between them. The result that the target matching errors were smaller in the FDI muscle, during the training sessions, was no wonder.

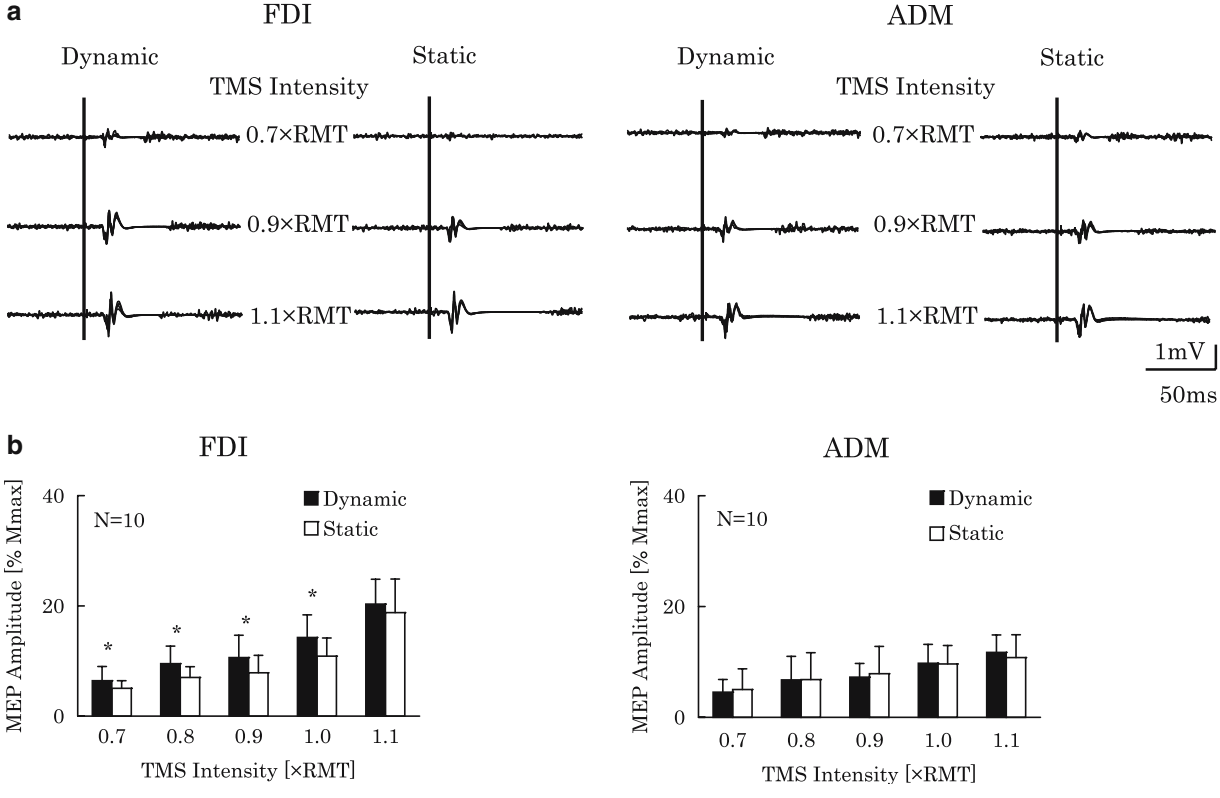

Fig. 2 **a** Typical MEP recordings (superimposed three trials) during dynamic (*left traces*) and static (*right traces*) contractions in the FDI (*left panel*) and the ADM (*right panel*) muscles, elicited by three TMS intensities. *Vertical lines* show the TMS artifacts. **b** Means and standard deviations ($N = 10$) of the MEP amplitudes. The TMS intensity was varied in five steps, from 0.7 to 1.1 times RMT. *Filled* and *open columns* show the data of dynamic and static contractions, respectively. *$p < 0.05$

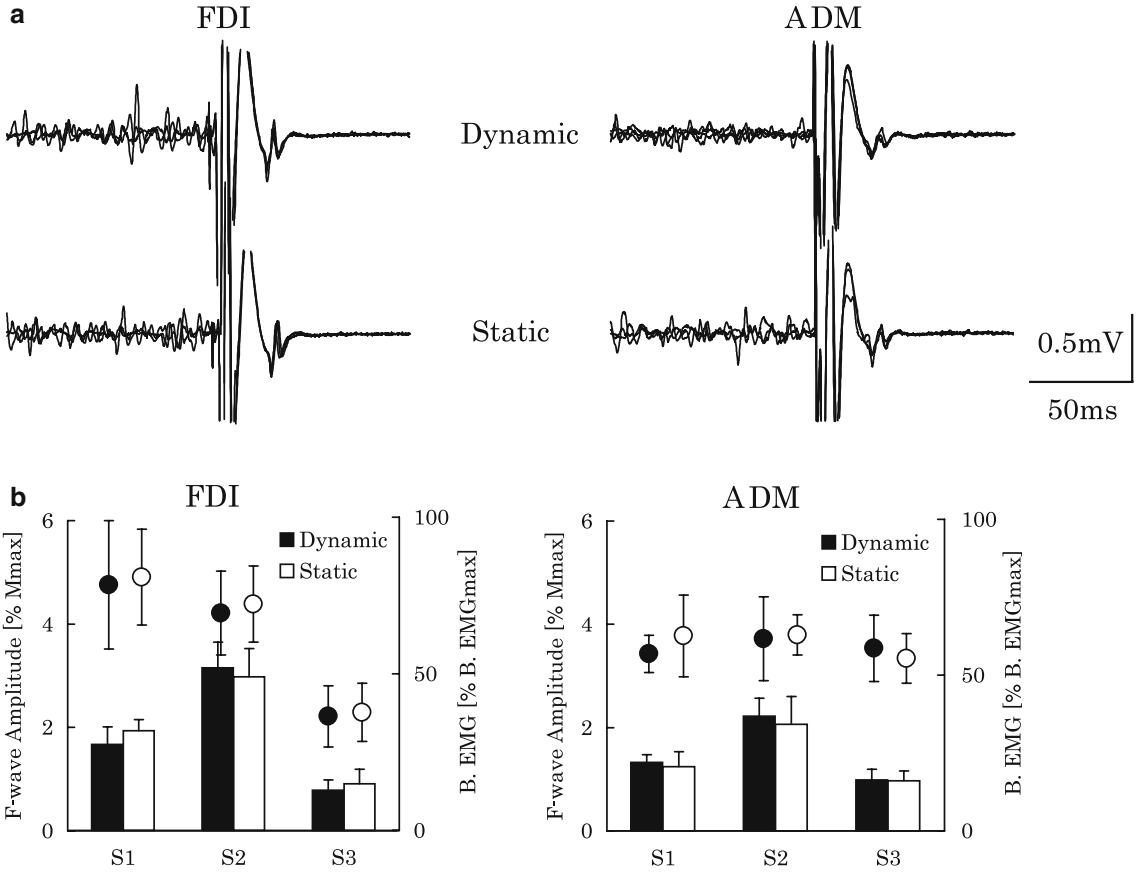

Fig. 3 **a** Typical F-wave recordings from one subject. Upper traces are during dynamic contractions and lower ones during static contractions. Recordings of the FDI muscle are at the left side and of the ADM muscle at the right side. Each trace superimposed three trials. **b** Means and standard deviations of F-wave amplitudes and the B.EMGs were calculated in subject S1, S2 and S3. *Columns* indicate the B.EMGs, circles above the *columns* indicate the F-wave amplitudes

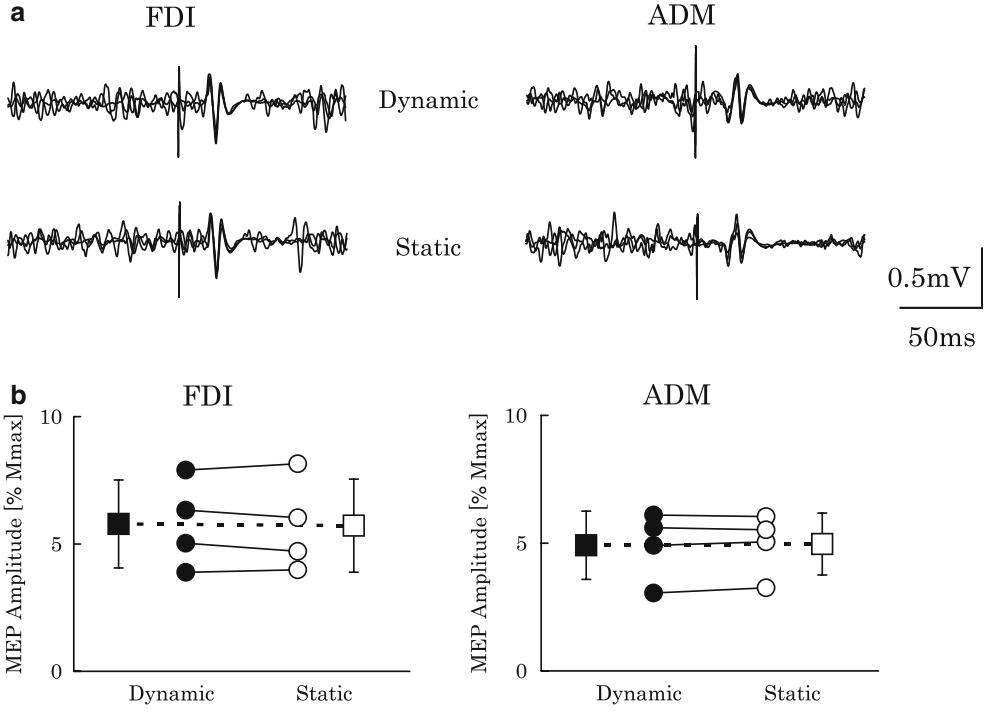

Fig. 4 a Typical MEP recordings (superimposed three trials) during dynamic (*left traces*) and static (*right traces*) contractions in the FDI (*left panel*) and the ADM (*right panel*) muscles, elicited by the BMS. b The mean MEP amplitudes of each subject were calculated and are indicated by *filled* (*dynamic*) and *open* (*static*) *circles*. The squares laid aside with *bars* show the means and deviations of all subjects ($N = 4$) tested

Therefore, although the FDI and the ADM muscles are the same small hand muscles, there are different functional demanded excitability changes between them. Our major findings can be recapitulated as follows: (1) During dynamic contraction, the AMT was lower in the FDI muscle than in the ADM. In addition, when the FDI muscle performed a dynamic contraction, the AMT became lower and the MEP (elicited by the TMS) became larger than when it performed a static contraction. In the ADM muscle, such a difference was not found. (2) Responses to subcortical stimulations remained stable in each muscle, not varying with the kinds of contractions. In the following sections, we will try to interpret these findings.

Extra task-dependent MEP facilitation

It was reported that, in the M1 of primate species, the large pyramidal cell bodies and high proportion of mono-synaptic connections to spinal motoneurons were correlated with the control of the musculature of the fingers, hand and wrist (Lemon et al. 1998; Maier et al. 1997; Bortoff and Strick 1993). If that was the case in the human M1, then these specializations are likely to explain the MEP threshold differences between the FDI and the ADM muscles. The MEP threshold could be affected by large pyramidal cells, cortical excitatory and inhibitory interneurons, and spinal motoneurons, i.e., the global excitability and sum of the motor pathways determine the MEP threshold in small hand muscles. There was no different MEP threshold between the FDI and the ADM muscles in a relaxed condition and during the static contraction. However, when the muscles generated a force dynamically, the AMT became lower in the FDI muscle than in the ADM. It may be explained that in a relaxed condition or a static contraction, the extra part of motor pathways, which induces a lower MEP threshold in the FDI muscle than in the ADM, has a relatively small proportion in M1 or in motoneuron pools, since the two muscles share the same nerve innervations. However, during dynamic contractions, as the B.EMG increases, the relatively small part may be magnified by branched-axon inputs from the M1 to motoneuron pools, and by synchronizations in the pools, which can produce larger groups of subliminal fringe in the pools.

Background EMG is a good estimate of the activity level of motoneuron pools, and the MEP can assess this level together with the activity level of subliminal fringe in the M1 and motoneuron pools (Capaday 1997). Therefore, when the MEP becomes larger and the B.EMG remains stable, it can be explained that there is a more active or larger subliminal fringe existing in the M1 and in the pools. Such a mechanism may have worked in the present study because the result showed that there were different MEPs between dynamic and static contractions in the FDI muscle, when the B.EMGs were the same. In addition, we should point out that at a higher TMS intensity (1.1 times RMT) the MEP became saturated, which was similar to our previous report (Kasai and Yahagi 1999). It was not caused by the functional mechanisms of muscle contractions.

Site of the facilitation

Using a familiar experiment paradigm, Arányi et al. (1998) reported that there is an extra task-dependent MEP facilitation existing in the deltoid muscle and that this facilitation is mainly due to subcortical activation (motoneuron pool).

To make clear which site (cortical or subcortical level) activation causes the extra task-dependent MEP facilitation showed in the present result, subcortical stimulations were used. Modulation of the MEPs is likely to depend on changes in cortical activation if the spinal excitability, tested simultaneously by means of the F-wave, is not modified (Abbruzzese and Trompetto 2002). BMS is a method that activates motor pathways at a subcortical level and allows a good interpretation of the MEP elicited by the TMS (Ugawa et al. 1994; Taylor and Gandevia 2004). The results showed that responses to subcortical stimulations (the F-wave and the MEP elicited by the BMS) remained stable. It suggested the notion that the extra task-dependent facilitation in the FDI muscle was due to cortical excitability changes. Compared with the limb muscles (such as the deltoid), small hand muscles, especially the FDI, are more skillful and own a larger territory for corticospinal projections in the M1 (Bortoff and Strick 1993). Therefore, stronger control to the FDI muscle in the cortical level is possible and reasonable.

Combining the results of Arányi et al. (1998), it may be inferred that there are two types of extra task-dependent facilitations in motor pathways. One is in the motoneuron pools, which has an impact on the proximal muscles, and the other is in the M1, which is more sensitive in the small hand muscles.

Other factors

Other possible factors to the present results might not be ignored. They are anatomical conditions, including the number, construction and location of involved musculatures, which may allow different degrees of movement freedom for the index and little fingers (Enoka and Fuglevand 2001; Schieber 1999). Consequently, the index finger becomes a more independently structured muscular apparatus and performs individuated finger movement more frequently than the little finger.

Conclusion

More recently, using a penta-stimulation technique, Ziemann et al. (2004) demonstrated that cortical

activation differs between small hand muscles and it is stronger in the FDI muscle than in the ADM. This paper can strongly support our data.

It can be concluded that there are differences in the task-dependent MEP facilitations between the FDI and the ADM muscles when they perform dynamic and static contractions and the differences are due to the functional demanded excitability changes accompanied by cortical activation.

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