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# Excitability Changes of Motor Evoked Potentials Dependent on Muscle Properties and Contraction Modes

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Using transcranial magnetic stimulation (TMS), differences in the excitability changes of motor evoked potentials (MEPs) between isometric (force task) and isotonic (movement task) muscle contractions in a distal (first dorsal interosseous; FDI) and a proximal (middle deltoid; MD) muscle were studied. In the FDI muscle, the active threshold of MEP recruitment was significantly lower in the isotonic than that in the isometric muscle contraction in spite of identical background EMG activity levels. Additionally, the dependence of the MEP amplitude on background EMG activity was significantly greater in the isotonic than in the isometric muscle contraction at low EMG activity levels, but the difference disappeared beyond middle EMG activity levels. In the MD muscle, the dependence of the MEP amplitude on background EMG activity was significantly greater in the isotonic than in the isometric muscle contraction, and further this dependence was kept at all muscle contraction levels. These results indicate that the dependence of the MEP amplitude on background EMG activity is modulated not only by the different muscle contraction modes (isotonic and isometric), but also by muscle properties (distal and proximal). Thus, the present findings suggest that the task-specific extra excitation in the proximal muscle is definitely produced corresponding to task differences (task-dependent subliminal fringe), which might be explained by the predominant frequency principle if applied to the proximal muscle. On the other hand, the lack of task-dependent extra excitation in the distal muscle is explained by the predominant recruitment principle for force grading in small hand muscles.

***Key Words:*** MEP, isotonic and isometric muscle contraction, FDI muscle, MD muscle, background EMG activity, human

## Introduction

Over the last several years, more and more evidence has been accumulated to suggest that muscle activation is task-dependent. Evidence has shown that muscle

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activation may change depending upon the type of task being performed. For example, Dettmers et al. (1995) demonstrated that the relationships between transcranial magnetic stimulation (TMS) thresholds and background force are different for distal and proximal muscles. Additionally, it has been suggested that the central activation of alpha and/or gamma motoneuron pools is different for isometric (force task) and the isotonic (slow movement task) muscle contractions (Tax et al., 1989, 1990). From previous reports, the issue of whether there are fundamental differences between isometric and isotonic muscle contraction modes has been a topic of interest. However, neural mechanisms that produce the selective recruitment of isometric or isotonic muscle activity are not well known.

Previous findings from monkeys have indicated that TMS excites the majority of the fast corticomotoneuronal (CM) fibers (Barker et al., 1995), and CM cells modify their discharge rate with force under isotonic, isometric, and auxotonic (spring-like) conditions. Furthermore, TMS to the human motor cortex can produce short-latency facilitation responses (motor evoked potentials: MEPs) with voluntary activation of most target muscles, including distal and proximal arm muscles. Recent findings in cortical activity suggest that, during the performance of various tasks, the corticospinal volleys evoked by TMS may vary in amplitude (Abbruzzese et al., 1994; Aranyi et al., 1998; Datta et al., 1989; Flament et al., 1993; Shieppati et al., 1996; Turton & Lemon, 1999). In particular, it is well known that the MEP amplitude could change as a function of the background EMG activity (Hasegawa et al., 2001a, 2001b; Hess at al., 1987; Kasai & Yahagi, 1999; Lim & Yiannikas, 1992; Ravnborg et al., 1991), and that these responses do not occur in the same way in all muscles (Kischka et al., 1993; Taylor et al., 1997). That is, the quantitative relationship between pre-contraction and MEP amplitudes is complex and probably different between proximal and distal muscles (Kischka et al., 1993; Shieppati et al., 1996; Turton & Lemon, 1999). If that is the case, we hypothesize that in different muscles (distal and proximal) and different muscle contraction modes (isotonic and isometric), the dependence of the MEP amplitude on background EMG activity may differ in spite of identical background EMG activities. That is, two parameters of the corticospinal pathway related to task- and muscle-dependency may be determined by different neural mechanisms (Capaday, 1997; Devanne et al., 1997; Kernell & Hultborn, 1990). From this theoretical point of view, the present study was undertaken to address further insight into the dependence of the MEP amplitude on the background EMG activity in different tasks and in different arm muscles. That is, the present study aimed to extend previous observations more systematically by examining how MEPs are modulated by task- and muscle-dependency—that is, relationships between the MEP amplitude and the background EMG activity of different tasks and muscles.

## Methods

### *Subjects*

Sixteen healthy adult volunteers (ages, 23–50 years; all male subjects) participated in the present experimental series. In the experiment of an index finger flexion by contraction of the first dorsal interosseous (FDI) muscle, 10 of 16 subjects participated. In particular, 2 subjects were retested on a subsequent day to check for reproducibility. The retests confirmed the reproducibility of the present tasks.

In the experiment of the middle deltoid (MD) muscle, 6 of 16 subjects participated. All subjects were informed as to the purpose of the research and experimental procedures in advance, and the research was approved by the Ethics Committee of Hiroshima University.

## Experimental Designs

Subjects were seated comfortably on a chair, with their entire dominant (right) upper limb pointing forward, the forearm stabilized on a board; the index finger was free to move (see upper panels in Figure 1). All subjects were asked to perform two different tasks. One was an isometric muscle contraction using their right index finger flexion (upper left panel in Figure 1). In this task, joint angles were fixed, and the subjects were required to match targeted forces. Another was an isotonic muscle contraction, starting from a fully extended position and reaching 50 of the right index finger flexion (upper right panel in Figure 1). In this task, movement velocity was about 8 /s (ramp muscle contraction) and displayed on an oscilloscope in front of the subject to allow visual feedback using a homemade background EMG activity feedback system. In addition, a pulley system was imposed across the subject s index finger joint for adjusting the same background EMG activity during the matching of a target position as the isometric task condition. In the present study, rather weak muscle contraction forces (within 30% maximum voluntary contraction; MVC) were chosen to keep small the number of voluntarily activated motoneurons to avoid saturation.

In the second step of the experiment, subjects were asked to perform both isometric and isotonic shoulder abduction tasks with their dominant (right) upper limb. In isometric shoulder abduction, both limbs were fastened for immobility, and EMG discharges were measured during isometric shoulder abduction. The experimental conditions of the homemade visual feedback system, as described above, and EMG recordings were the same as with the FDI muscle. In this experiment, we did not use the pulley system, because background EMG activities increase depending upon shoulder abduction angles in isotonic muscle contractions. In isotonic shoulder muscle contractions, we kept background EMG activity similar to isometric contraction level. To keep similar background EMG activities in isometric contraction, the subjects were allowed to use the visual feedback system, and EMG and MEP amplitudes were recorded.

Finally, in the present experiment, the following three studies were performed. In the first study, to examine the threshold intensity and dependence of MEP amplitude on background EMG activity, TMS intensities were varied, and MEPs were recorded during isotonic and isometric contractions of the FDI muscle with background EMG. In the second study, a single stimulus intensity was used to evoke MEPs in the FDI muscle during isotonic and isometric muscle contractions of two different strengths (low: 5~10%MVC and middle:15~20%MVC). In the third study, to ascertain whether evidence for the FDI muscle is similar to that for the MD muscle, the second study was repeated in the MD muscle.

## Stimulation and Recording

TMS was delivered through a Magstim 200 stimulator (Magstim Co., Dyfeed, UK). A standard round coil was used, with an inner diameter of 10 cm, generating a magnetic field of 1.5T. The coil was placed over the vertex and oriented (A-facing

up) to activate optimally the left motor cortex being tested in each subject. The position of the vertex was marked on the scalp to enable monitoring of the relative position of the coil during the course of the experiment. After coil-adjustment, the threshold for the MEP (motor threshold; MT) was determined with a relaxed (at rest) muscle. The motor threshold was determined by the method of limits and

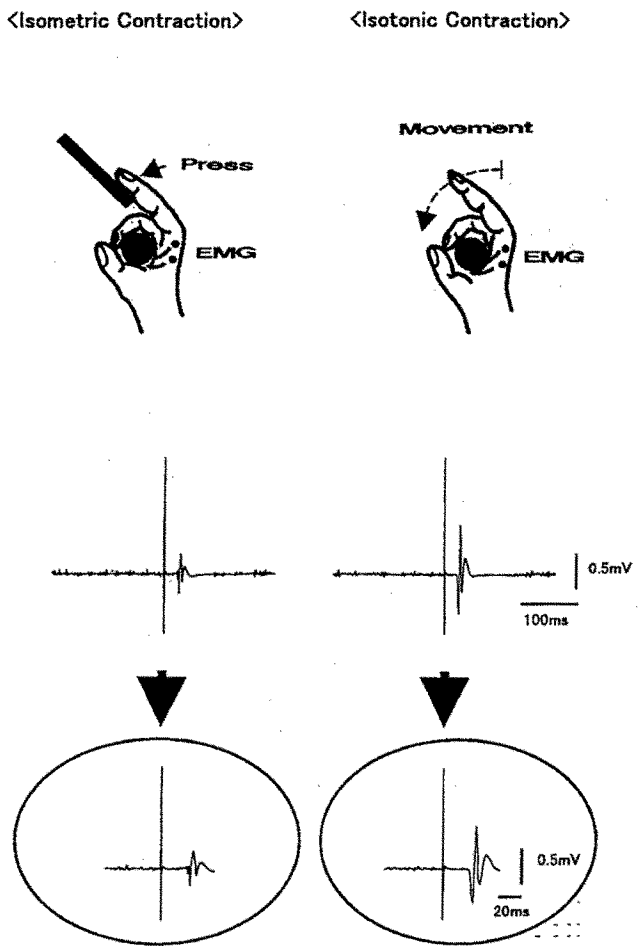


**Figure 1 — Diagrams of the tasks performed and EMG specimen recordings. The upper left-hand figure shows an isometric index finger flexion (force task) and the upper right-hand figure, an isotonic one (movement task). The lower EMG traces show weak background EMG activities (10% MVC, lower muscle contraction) and motor evoked potentials (MEPs) induced by an appropriate intensity of focal transcranial magnetic stimulation (TMS) to the M1 obtained from the first dorsal interosseous (FDI) muscle of a single subject during a force task (left) and movement task (right).**

was defined as the lowest stimulation intensity capable of inducing 50% MEPs in muscles at levels of 50 μV in a series of several magnetic stimuli (8 to 10 stimuli), with the coil centered over the appropriate scalp position. The stimulus intensity was referred to as the motor threshold at rest (1.0 × MT). The active threshold was determined using the same methods as the motor threshold at rest.

When performing isotonic muscle contractions, the trigger pulse for delivering TMS was obtained when the index finger went through a photoelectric beam. When performing isometric muscle contractions, TMS was voluntarily delivered according to the experimenter's inspection by a homemade EMG level-meter when the same amount of EMG discharge could be activated, with the identical background EMG activities as in the isotonic muscle contraction (lower EMG traces in Figure 1). Using the appropriate stimulus intensity (0.9–1.0 × MT) for MEP amplitude (1.0~1.5 mV) for each subject, we recorded MEPs separately from the FDI and MD muscle while the subject generated lighter isometric or isotonic muscle contractions against a load. Under the fixed TMS intensity, 30 to 40 MEP records were made unilaterally (right hand) from one muscle at a time. To objectively evaluate the effect of increasing voluntary muscle contractions on MEP amplitude, muscle forces were indirectly assessed in general (Kischka et al., 1993; Taylor et al., 1997; Turton & Lemon, 1999). The reason why we chose rectified background EMG activity instead of force in this study is that we could precisely evaluate the dependence of MEP recruitment on increasing voluntary muscle contractions (Kasai & Yahagi, 1999). In order to allow a direct comparison, the MEPs and background EMG activity level were simultaneously recorded (lower EMG traces in Figure 1).

The raw EMGs and MEPs were converted by an analog-to-digital interface at a sampling rate of 5 kHz using high-pass filtering to overcome some of the movement related to artifacts and stored on a computer for further analysis. Each recording lasted 1 s, starting 500 ms preceding the stimulus. The amount of background EMG, which began 100 ms just before the brain stimulation, was taken as the area (in an arbitrary unit) substituted by the envelopes of the off-line rectified EMGs. The MEP size was expressed as peak-to-peak amplitude potential (mV).

### *Statistical Analysis*

By comparing the task-dependent differences of MEP threshold and amplitude at each TMS intensity, we could obtain at least 30 trials for each subject to enable the best matching of the amplitude characteristics of the rectified surface EMG between isometric and isotonic muscle contractions. All statistical analysis of MEP amplitudes was performed on these trials. Since the EMG changes as a function of the task, and also the MEP is known to change as a function of the background EMG as described above, in each subject the mean amplitude of the MEPs was compared among conditions within a range of background EMG activities common to the tasks. Thus, a two-way ANOVA for each muscle and for each condition (background EMG level × muscle contraction level, muscle contraction mode × muscle contraction level) was performed. Within these couples, the mean background EMG was not significantly different and was actually very close, as were the variations. Thus, a paired Student $t$ test was performed to compare the pooled data from all subjects. Correlations were examined with Spearman's rank correlation. Statistical significance was set at a 5% level.

## Results

### *Task-Dependent Differences of Active MEP Thresholds and Amplitudes in FDI Muscles*

Figure 2 showed MEP specimen records (left hand traces) obtained from a single subject. There were definitely different active threshold intensities between isometric and isotonic muscle contractions—that is, the active threshold intensities were lower in isotonic than in isometric muscle contractions, in spite of identical background EMG activity levels just prior to the stimulation (upper rectified EMG traces of the left hand side; see also Figure 1). These differences in the active MEP threshold intensity were statistically significant in all subjects tested (Figure 3A, $t = 5.61$, $df = 9, p < .001$). Furthermore, differences in the MEP amplitude between muscle contractive modes were also observed when appropriate TMS intensities were delivered (right side columns obtained from a single subject in Figure 2). Figure 3B showed, therefore, differences in the MEP amplitude produced in all subjects tested ($n = 10$). Differences in the MEP amplitude were statistically significant from 0.8 × MT to 1.1 × MT except at 1.0 × MT in TMS intensity.

### *The Dependence of MEP Amplitude on Background EMG Activity in FDI and MD Muscles*

Upper superimposed EMG traces in Figure 4 show the MEP specimen records of the FDI muscle obtained from a single subject under the two different muscle contraction levels during isometric and isotonic contraction modes. Different MEP amplitudes between isometric (Figure 4A) and isotonic (Figure 4B) muscle contractions were definitely observed at the lower muscle contraction level; these differences then disappeared at the middle muscle contraction level (Figure 4D) in spite of identical background EMG activity levels (Figure 4C). These phenomena related to changes of the dependence of the MEP amplitude on background EMG activity were consistently observed across all subjects in spite of individual differences in absolute values. Then, the grand averages of the background EMG activity and the MEP amplitudes produced in all subjects tested ($n = 10$) were calculated and are shown in Figures 6A–B. The results in Figures 6A–B indicated that interactions (background EMG level × muscle contraction level and background EMG activity level × muscle contraction mode) were statistically significant ($F_{3,27} = 29.720$, $p < .01$ and $F_{3,27} = 16.051$, $p < .01$, respectively). That is, in lower EMG activity levels, the MEP amplitudes of the isotonic contraction mode were larger than those of the isometric contraction mode ($t = 5.23$, $df = 9$, $p < .001$) in spite of identical background EMG activity level, whereas this was not true at a middle EMG activity level. To investigate the cause of the above-mentioned different dependence of the MEP amplitude on background EMG activity in the FDI muscle, we calculated the correlations between the MEP amplitudes and the background EMG activities (Figure 4E). The results showed that there were definitely different regression lines between isometric and isotonic muscle contractions—that is, the regression line was steeper for the isotonic muscle contraction than that for the isometric. These relationships between MEP amplitudes and background EMG activities were consistently observed across all subjects in spite of individual differences in regression coefficients.

To ascertain if this evidence was similar to that of the MD muscle, we investigated the dependence of the MEP amplitude on the background EMG activity in the MD muscle. Figures 5A–B show the MEP specimen records for the MD muscle obtained from a single subject in the same way as the FDI muscle shown in Figures 4A–B. Although in all subjects tested ($n = 6$), no differences of threshold intensity between isometric and isotonic muscle contractions were observed (not illustrated), the MD muscle definitely displayed different MEP amplitudes in both muscle contraction modes, in spite of identical background EMG activity levels (Figures 5C–D). Then, the grand averages of MEP amplitudes and background EMG activities produced in all subjects were calculated and are shown in Figures 6C–D. The results in Figure 6D indicated that interactions were statistically significant ($F_{3,15} = 31.087$, $p < .01$ and $F_{3,15} = 19.055$, $p < .01$). That is, MEP amplitudes of isotonic muscle contraction were larger than those of isometric muscle contraction in both EMG activity levels (Lower: $t = 4.13$, $df = 5$, $p < .01$;

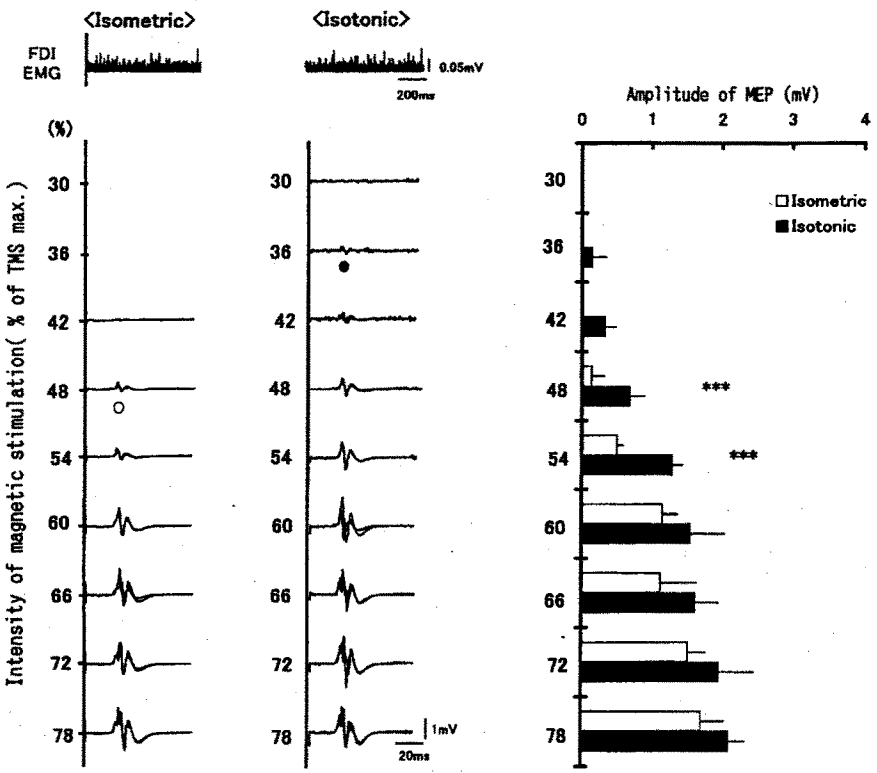


**Figure 2 — A: Specimen records of background EMG activities (upper EMG traces) and MEPs (superimposed three trials) obtained from various TMS intensities (ordinate: % of maximum intensity = 100%) applied to the M1. Filled circles show active MEP threshold intensity levels at each task. B: Mean MEP amplitudes of isometric (open bars) and isotonic (filled bars) at various TMS intensities obtained from a single subject. ***$p < .001$.**

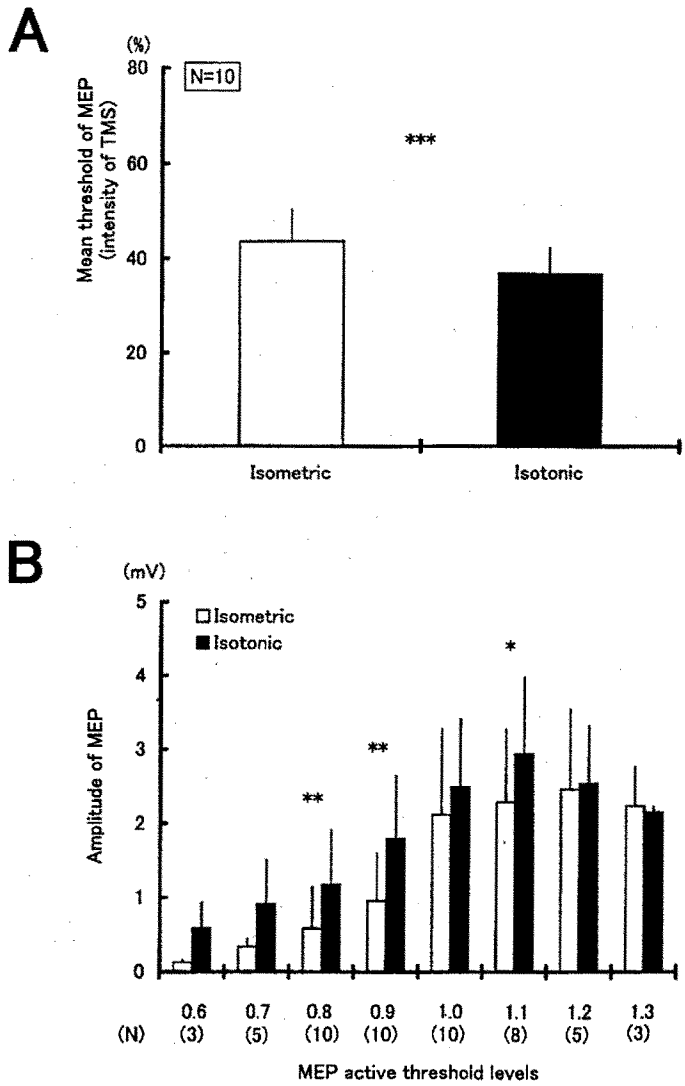


**Figure 3—A: Grand averages of active MEP threshold intensities in all subjects tested ($n$ = 10). The bars represent the grand means of active MEP threshold intensity with standard deviations. Differences of active MEP threshold intensity between isometric (open bars) and isotonic (filled bars) tasks were statistically significant ($p < .001$). B: Grand averages of MEP amplitude in all subjects tested ($n$ = 10) at each TMS intensity (xMT). Differences of MEP amplitude between isometric (open bars) and isotonic (filled bars) tasks were statistically significant at 0.8 ($p < .01$), 0.9 ($p < .01$), and 1.1 ($p < .05$) xMTs of TMS intensity, respectively.**

Middle: $t = 2.79$, $df = 5$, $p < .05$) in spite of identical background EMG activity. Then, we calculated correlations between MEP amplitudes and background EMG activities in the same way as the FDI muscle (Figure 5E). The results showed that there were definitely different regression lines for isometric and isotonic muscle contractions—that is, the regression line was steeper in the isotonic than in the isometric muscle contractions. These relationships between MEP amplitudes and background EMG activities were consistently observed across the subjects in spite of individual differences in their regression coefficients.

## Discussion

Under both muscle contraction modes, the background EMG (e.g., the background muscle electrical activity during the 100 ms just prior to the stimulation) reflects the number and firing frequency of supra-threshold activated motoneurons due to voluntary movements. Thus, the MEP amplitude could be regarded as a rough

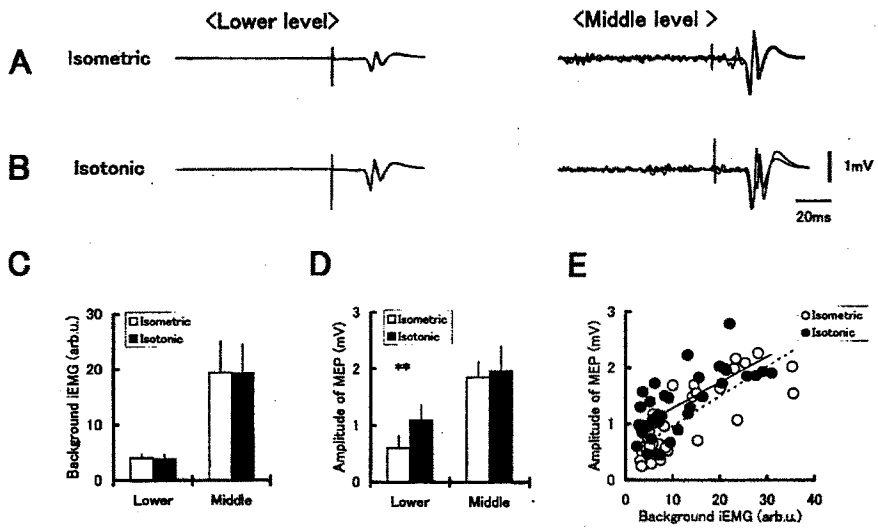


**Figure 4 — A and B: Specimen records of the background EMG activity and MEPs (superimposed three trials) at lower (5% MVC; left traces) and middle (15% MVC; right traces) FDI muscle contraction levels in isometric (A) and isotonic (B) muscle contractions. C: Means and standard deviations of background EMG activity levels obtained from a single subject in isometric (open bars) and in isotonic (filled bars) tasks at both muscle contraction levels. D: Means and standard deviations of MEP amplitudes from the same subject. Differences of MEP amplitude between isometric and isotonic tasks were statistically significant only under the lower muscle contraction level. E: Correlations between the MEP amplitude (ordinate: mV) and the background EMG activity (abscissa: arbitrary unit) in isometric (open circles) and in isotonic (filled circles) muscle contractions obtained from the same subject. The regression line for the isometric contraction was y = 0.0536x + 0.4186 (y: MEP amplitude, x: background EMG) and y = 0.0459x + 0.8201 for the isotonic contraction.**

estimate of not only the excitable portion of pyramidal cells and spinal motoneurons, but also the cells that have not yet reached their firing threshold during the voluntary movement (subliminal fringe). In other words, the cortical stimulation will lead to the discharge of a preselected set of pyramidal cells and motoneurons, depending on the task (Aranyi et al., 1998). Based on these theoretical points, we measured and calculated the dependence of the MEP amplitude on the background EMG activity to evaluate for task-dependent and muscle-dependent differences in MEP excitation. The first interesting finding in this study was that we could observe the different active MEP threshold intensities between isometric and isotonic muscle contractions in the FDI muscle but could not observe them in the MD muscle—that is, in the FDI muscle the active MEP threshold intensity was lower in the isotonic than in the isometric contraction. Second, MEP amplitudes induced by the same TMS intensity were larger in isotonic than in isometric muscle contractions in spite of identical background EMG activity levels. Third, the dependency of the MEP amplitude on the background EMG activity was different, not only between

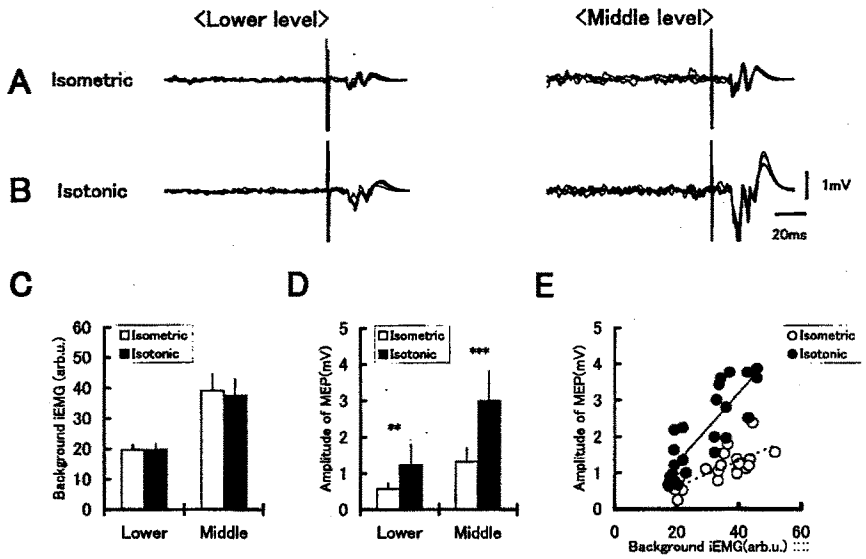


**Figure 5 — A and B: Specimen records of the background EMG activity and MEPs (superimposed three trials) at lower (5% MVC: left traces) and middle (15% MVC: right traces) MD muscle contraction levels in isometric (A) and isotonic (B) tasks. C: Means and standard deviations of background EMG activity levels obtained from a single subject in isometric (open bars) and isotonic (filled bars) at both muscle contraction levels. D: Means and standard deviations of MEP amplitudes obtained from the same subject. Significant differences in the MEP amplitudes between isometric and isotonic tasks were observed at both muscle contraction levels. E: Correlations between the MEP amplitude (ordinate: mV) and the background EMG activity (abscissa: arbitrary unit) in both tasks are visible. The regression line for the isometric contraction was y = 0.0366x – 0.1254 (y: MEP amplitude, x: background EMG), and y = 0.0961x – 0.6487 at the isotonic contraction. The difference between the regression coefficients of the tasks was statistically significant ($p < .001$).**

isometric and isotonic muscle contraction modes, but also between distal (FDI) and proximal (MD) muscles. In particular, differences among these two muscle contraction modes were observed only at a low background EMG activity level in the FDI muscle but, in the MD muscle, these differences were observed at all background EMG activity levels. Thus, these present results will be discussed as follows: (a) task-dependent differences of the active MEP threshold intensity, (b) task-dependent differences of the MEP amplitude, (c) muscle-dependent differences of the MEP recruitment, and (d) functional and clinical implications.

## *Task-Dependent Differences of the Active MEP Threshold Intensity*

The threshold must give information about a central core region of neurons. Changes in the threshold reflect the excitability of this region, which comes from the excitability of individual neurons and their local density. The threshold level to assess the output neurons is affected by drugs (Ziemann et al., 1996), and thus the active threshold intensity of MEP recruitment reflects the excitability of the most excitable parts of the motor cortex; therefore, the difference of the active MEP threshold is more closely linked to the central motor output than to the peripheral input generated by muscle force and/or limb displacement. We investigated whether

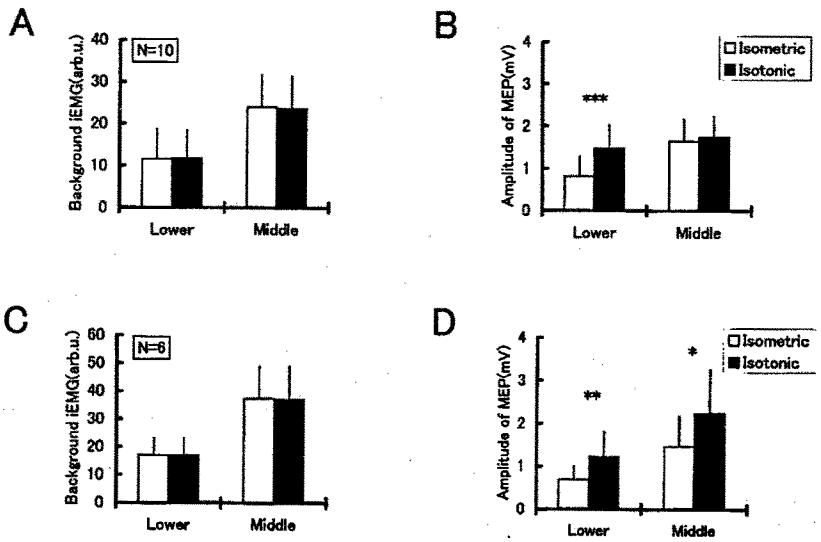


**Figure 6—A: Grand averages of the FDI background EMG activity in all subjects tested ($n$ = 10) in isometric (open bars) and isotonic (filled bars) at both muscle contraction levels. B: Grand averages of the MEP amplitudes of the FDI muscle. Representations are the same as shown in A. A statistically significant difference between isometric and isotonic tasks was observed only under the lower muscle contraction level. C: Grand average of the MD background EMG activity in all subjects tested ($n$ = 6) in isometric (open bars) and isotonic (filled bars) at both contraction levels. D: Grand averages of the MEP amplitudes of the MD muscle. Representations are the same as shown in A. Statistically significant differences between isometric and isotonic tasks were observed under both muscle contraction levels. *$p$ < .05, **$p$ < .01, ***$p$ < .001.**

there were different threshold intensities in the two muscle contraction modes. The present results indicated that there were different active MEP threshold intensities between isometric and isotonic muscle contractions in the FDI muscle, but we could not observe any in the MD muscle as described above.

With regard to the functional representation of the primary motor cortex (M1), Keller (1993) suggests that low-threshold zones in cats contain neurons that converge on individual motoneuron pools, whereas high-threshold zones contain cells that diverge in the spinal cord to contact several motoneuron pools. If that is the case in humans, the present results in which the active MEP threshold intensity was lower in isotonic than in isometric muscle contractions in the distal (FDI) muscle could be explained in line with the above-mentioned representations of the M1. That is, the isotonic muscle contraction is elicited from low-threshold zones' neurons that converge on individual motoneuron pools, whereas the isometric muscle contraction is elicited from high-threshold zones' neurons that diverge in the spinal cord to contact several motoneuron pools. These different threshold zones' neurons related to isometric and isotonic muscle contractions, even though they are in the same muscle, might produce different MEP threshold intensities.

On the other hand, there is accumulating evidence that the central nervous system (CNS) uses a different control strategy for isometric and isotonic muscle contractions. That is, the recruitment thresholds were lower and the initial firing rates were higher in isotonic than in isometric muscle contractions (Tax et al., 1989, 1990). If the CNS employs different MU discharge frequencies for isometric and isotonic muscle contractions (Kukulka & Clamann, 1981), it would be reasonable to suggest that under identical EMG activity, the active MEP threshold intensity in an isotonic muscle contraction would be lower than in an isometric muscle contraction as appears in the results obtained from the present study. These explanations, different MU recruitment threshold and firing rate, could also be applied to MEP amplitude differences—that is, the MEP amplitudes induced by the same TMS intensity were larger in the isotonic than in the isometric muscle contractions in spite of identical background EMG activity levels (see below).

### *Task-Dependent Differences of the MEP Amplitude*

Previous studies have revealed that the degree of modulation of the MEP amplitude is dependent upon TMS intensity—that is, the degree of modulation is strongest at stimulus strengths just below threshold (Hess et al., 1987; Lemon et al., 1995; Shubert et al., 1997). It is very important to decide on an appropriate MEP size of the control response because the amount of excitation is dependent upon the control MEP size (Terao et al., 1995). In the present experiment, therefore, we have selected an appropriate test stimulus intensity to evaluate MEP excitation induced by voluntary muscle contraction. However, in the present results, we obtained different dependencies of the MEP amplitude on the background EMG activity between isometric and isotonic muscle contractions in spite of identical background EMG activity levels. How can we explain these present results?

As described above, there were different results from active thresholds and firing rates between isotonic and isometric muscle contractions. Thus, one possible explanation is that a significant extra excitation during the isotonic muscle contraction as opposed to the isometric muscle contraction might occur in spite of identical background EMG activity levels. Rossini et al. (1987), with electrical brain stimulation and Abbruzzese et al. (1994) with magnetic brain stimulation,

reported similar experimental results. In particular, Abbruzzese et al. (1994) suggested a selective recruitment of large units during lengthening contractions and orderly recruitment during shortening contractions. Taking these recruitment behaviors together, the larger size of the subliminal fringe during the isotonic muscle contraction could result from a larger number of projections to the motoneuron pool activated or from changes in the motoneuron membrane excitability (see also, Sergio et al., 1998).

It is well known that magnetic stimulation of the M1 produces rate coding and recruitment of forearm and hand muscle motoneurons similar to voluntary contractions. That is, rate coding, or an increase in firing probability with increasing intensity of TMS, has been shown previously for FCR (Calancie & Bawa, 1990), deltoid (Colebatch et al., 1990), and FDI (Boniface et al., 1991) MUs. Furthermore, Bawa and Lemon (1993) have clearly demonstrated that the order of recruitment for magnetic stimulation is the same as for voluntary contractions by separating these two inputs. Thus, in the present study, different MEP excitations obtained from different muscle contraction modes could indicate quite different susceptibilities of motor neurons to TMS in spite of identical background EMG activity levels. This suggests that the complex and non-specific corticospinal volley generated by TMS can recruit motor neurons in an orderly fashion as described above, and consequently CNS must play a major role in determining the order of recruitment dependent upon the different muscle contraction modes. As further evidence of this, Stedman et al. (1998) recently suggested that contributions of the M1 and spinal level are different in proportion to the muscle contraction level. This indicates that isotonic muscle contractions seem to require more cortical control than isometric ones and show larger increases in cortical excitability (Di Lazzaro et al., 1998; Kaneko et al., 1996; Mazzocchio et al., 1994; Thompson et al., 1991; Ugawa et al., 1995). Thus, the present results in the FDI muscle, in which task-dependent differences in the excitation of MEPs were observed at low voluntary contraction levels and those differences disappeared at relatively higher contraction levels, could be explained in line with this evidence—that is, in voluntary isotonic contraction of the distal muscle, cortical control might play a dominant role and saturation of cortical excitability occurs at relatively lower contraction levels in comparison with the proximal muscle contraction (see below).

### *Muscle-Dependent Differences of the MEP Amplitudes*

Several recent studies have employed TMS to study corticospinal projections in humans (Colebatch et al., 1990; Lemon et al., 1995; Palmer & Ashby, 1992) and suggested projections from the M1 to motoneurons of both proximal and distal muscles. These findings indicate that the strength of the CM projection to proximal muscles is as strong as that to distal muscles, although Palmer and Ashby (1992) found that TMS produced strong net facilitation of motoneurons of the FDI muscle. Additionally, the relationship between the degree of MEP excitation and the amount of voluntary contraction is quite specific and varied from muscle to muscle. For intrinsic hand muscles, up to 90% of facilitation has been observed during very weak voluntary effort (within 10% MVC; see also, Lim & Yiannikas, 1992). That is, voluntary drive to the distal muscle is dependent on fast corticospinal output elements to a much greater extent than to the proximal muscle (Turton & Lemon, 1999). In contrast, the pattern of excitation with increasing effort was seen to be

more gradual in the arm muscle (Taylor et al., 1997), in the leg muscle (Devanne et al., 1997), and in the external oblique muscles of the abdomen (Plassman & Gandevia, 1989). The present results showed that most motoneurons of the FDI muscle were recruited at a low level of voluntary contraction and, consequently, at strong muscle contractions, its dependency disappeared. In contrast, in the MD muscle, additional motoneurons were recruited to up to 20% MVC (see Figures 4E & 5E), and the dependence of the MEP excitation on background EMG activity was clearly observed. Taken together, the present results and above-mentioned previous findings, the pattern of excitation may be related to the absolute extent of corticospinal inputs to particular muscles and intrinsic properties of the motoneuron pool, which may reflect the muscle's function (Davey et al., 1999)—that is, the hand muscles would be expected to receive larger compound EPSPs from the CM cells than those in proximal muscles (Clough et al., 1968; Lemon, 1990).

Another possible explanation is the different diameters of cortical projection fibers for distal and proximal muscles. A stronger CM influence (probably large diameter CM fibers) on motoneurons innervating the distal muscles has been found in humans (Palmer & Ashby, 1992). Furthermore, it has been shown that the different sizes of pyramidal fibers are differently susceptible to finely graded forces (Evarts et al., 1983; Fromm & Evarts, 1981; see also, Ashe, 1997). In the present study, active threshold differences were observed in the distal muscle dependent on different muscle contraction modes but not in the proximal muscle. Since active threshold differences reflect on different sizes of CM cells in the M1, the existence of large or small neurons in the cortical representation areas between proximal and distal muscles may partly explain the MEP amplitude differences and different MEP dependence on background EMG activity obtained in both muscles. That is, the present study confirmed that the relationship between the degree of MEP excitation and the amount of voluntary contraction is quite specific and varied from muscle to muscle. In particular, our present results strongly confirm Palmer and Ashby's speculation that TMS produces strong net facilitation of motoneurons of the distal (FDI) muscle.

### *Functional and Clinical Implications*

With regard to functional differences between distal and proximal muscles, two systems for motor control appear to coexist in the M1: one for execution of small precise movements, particularly by distal musculature, and another for postural stabilization, particularly by proximal musculature (McKiernan et al., 1998). Based on the present results, intrinsic hand muscles are mainly involved in finely controlled motor tasks, where a sharp, sudden modulation of the produced force can often be required. A strong inhibitory control, therefore, might be necessary in the case of distal muscles. In contrast, proximal arm muscles are frequently engaged in postural motor tasks, where force modulation can be less substantial and more progressive (see also, Abbruzzese et al., 1999). The present results of task-dependent differences of the MEP amplitude and recruitment in distal and proximal muscles reflect on the above-mentioned functional significance.

Our present findings also have potential clinical significance. The neurological syndromes that result from discharging or destructive lesions of the brain have unequal effects on different muscle groups (Colebatch & Gandevia, 1989). These clinical observations are commonly believed to be due to the characteristics of the

corticospinal projection to different muscles. Present findings in which there were different MEP dependencies on the background EMG activity between proximal and distal muscles have confirmed these characteristics of the corticospinal projection to different muscles—that is, the pattern represents the net effect of stimulation of many corticospinal neurons non-specifically, and revealed that there were more corticospinal neurons projecting to motoneurons of distal hand muscles than to motoneurons of proximal arm muscles (Colebatch et al., 1990). These different distributions of short latency corticospinal projections might play an important role in performing different tasks. This could be related to functional differences between distal and proximal muscles required by the particular task.

In physiotherapeutic practice, the facilitatory effect was observed following repetitive isotonic muscle contractions (wrist extension-relaxation task) at a low frequency (Butefisch et al., 1995; Hauptmann et al., 1997). In general, the particular kind of use-dependent effects in the central motor structures differs in relation to the respective motor condition. Thus, the present study contributes to a better understanding of the effects in central structures induced by different contraction modes (isometric or isotonic) and different muscles (proximal or distal). Further studies of patients with various disorders are necessary to develop applicable methods for motor rehabilitation.

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