# Functional demanded excitability changes of human hand motor area

Zhen Ni・Makoto Takahashi・Takamasa Yamashita・Nan Liang・Yoshiyuki Tanaka・Toshio Tsuji・Susumu Yahagi・Tatsuya Kasai

Research Article

Z. Ni・M. Takahashi・T. Kasai

Division of Sports and Health Sciences, Graduate School for International Development and Cooperation, Hiroshima University, 1-5-1 Kagamiyama, Higashihiroshima, 739-8529 Japan

E-mail address: tkasai@hiroshima-u.ac.jp

Tel.: +81 82 424 6938 Fax: +81 82 424 6904

T. Yamashita・N. Liang

Graduate School of Health Sciences, Hiroshima University, 1-2-3 kasumi, Minami-ku, Hiroshima 734-8551 Japan

Y. Tanaka・T. Tsuji

Department of Biological System Engineering in the Graduate School of Engineering, Hiroshima University, 1-4-1 Kagamiyama, Higashihiroshima Japan

S. Yahagi

Department of Human Environment Sciences, Hiroshima Shudo University, 1-1-1, Ozukahigashi, Asaminami-ku, Hiroshima, 731-3195 Japan

**Abstract** The present study was performed to examine whether there are functional differences between the first dorsal interosseous (FDI) and abductor digit minimi （ADM）muscles depending on different muscle contractions, dynamic and static contraction of index and little finger abduction. We recorded motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) and simultaneously recorded force curves during the muscle contractions. We also defined rest motor threshold (RMT) and active motor threshold (AMT, during dynamic and static contraction) in two muscles. F-waves were recorded in same procedures as MEPs. In all trials of MEP and F-wave, background EMGs (B.EMGs) were kept at same level. Force matching errors of dynamic contraction were statistically smaller in FDI muscle than those in ADM. In the FDI muscle, AMT during dynamic contraction was significantly lower than that during static one. Additionally, we employed MEP/B.EMG ratio as an index to assess functional differences between two muscles. In the FDI muscle, the ratios were larger during dynamic contraction than those during static ones. But such results were not found in the ADM muscle. F-waves remained steady in either muscle. Thus, we conclude that there are functional demanded excitability changes between FDI and ADM muscles, although they share the same innervations of ulnar nerve.

**Keywords** Transcranial magnetic stimulation (TMS); Motor evoked potential (MEP); FDI and ADM muscle; Dynamic and static muscle contraction

## 1. Introduction

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

Concerning another question of dynamic and static muscle contraction (isometric), Arányi et al. (1998) demonstrated that MEP amplitudes in the deltoid muscle are larger during dynamic contraction than those during static contraction despite of equal background EMGs (B.EMGs) just prior to the stimulations applied. In abductor digit minimi (ADM) muscle, however, such differences were not found. With regard to these differences, the lack of task-dependent extra facilitation of MEP in the ADM is explained by the predominant recruitment principle for dynamic contractions in small hand muscles, which is in contract to the predominant frequency principle used in proximal muscles (Arányi et al. 1998).

It is natural to suspect whether the principle works similarly in all small hand muscles. In this regard, ADM and first dorsal interosseous (FDI) muscles are the same small hand muscles, which share same innervation of ulnar nerve, it seems that there are functional differences between them. Therefore, we postulate that a different task-demanded extra facilitation of MEP exists between the FDI and ADM muscle. To address this hypothesis, the present study was undertaken to examine differences of the sum of excitatory synaptic inputs to corticospinal tract neurons (CTNs) between different muscle contractions (dynamic and static) in these two muscles, using MEP

response to TMS.

## 2. Materials and methods

### Subjects

Ten right-handed subjects (2 female, 8 male; age range 19-37 years) volunteered for the present study. All of them participated in the experiment of MEP protocols. Five out of ten subjects participated in measuring matching errors to target force during dynamic contraction for estimating functional differences between FDI and ADM muscle. Three out of them also participated in recording F-waves. All subjects were informed of the purpose of the study and experimental procedures in advance. The ethical committee of Hiroshima University approved the experimental procedures described here.

### Experimental procedures

Before the experiments, we measured the force levels during maximum voluntary contraction (MVC) of right FDI (prime mover of index finger abduction) and ADM (prime mover of little finger abduction) muscle, when subject abducted right index and little finger in maximum effort. In the experiment of dynamic muscle contraction, 50% MVC according to each muscle was set as a target force level. Protocols of FDI and ADM muscle were separately undertaken. Subjects were instructed to abduct their fingers at a speed of generating the target force at one second. Concretely, an assumed force generation line was illustrated on a computer monitor, in advance. After the starting signal (“Ready ”) was given, a signal beam point ,which indicated real force

level of each subject, appeared at left side on the monitor. The point ran from left to right at the speed of four divisions every one second, and arrived at starting timing 0.5 second later. The subjects were requested to perform tracking this beam, following the assumed line illustrated (see Fig. 1A). In static muscle contraction, a horizontal line indicating 10% MVC of each subject was illustrated instead of the assumed line described above. Subject was instructed to abduct the finger and coincide the signal beam point with the line for several seconds. All subjects were required and trained to abduct their fingers only at the metacarphalongeal joint and follow the line as accurately as possible. Distal interphalongeal joint was immobilized by an adhesive tape to a bar that was connected to a strain gauge amplifier. A custom-built device was used to support and restrict movements of 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 (outside diameter of each loop 9.5 cm) were used to provide TMS. The slightly angulated coil was placed tangentially to the scalp with the junction region pointing backwards at appropriately 30 ° to the mid-sagittal line (Peinemann et al. 2004). Induced current in the brain was anterior-medially directed, which could activate the corticospinal system trans-synaptically (Mills et al. 1992; Di Lazzaro et al. 2001; Kaneko et al. 1996a). We determined the optimal position for the right FDI or ADM muscle by moving the coil in 0.5 cm steps around the presumed hand area of the

primary motor cortex (M1). The site named motor hot-spot, at which stimulation of slightly superthreshold intensity consistently produced the largest MEP was marked with a pen (swimming cap was placed on the scalp, paper tapes were adhered to the cap in 2 cm steps as a reference). We paid special attention to the position and orientation of the coil (the coil was maintained on the scalp by an experimenter). We defined the hot-spots of FDI and ADM separately, because they were not always at the same position.

At the beginning of each experiment, we determined the rest motor threshold (RMT) of FDI and ADM muscle, respectively. RMT was defined as the minimum output of the stimulator that induced a reliable MEP (above 50 μV in amplitude) in at least 5 out of 10 consecutive trials when each muscle was completely relaxed. We used the stimulation intensities referring to RMT through the protocols.

After several sessions of training trials of dynamic contraction in each muscle (the performances during training were showed in Fig. 1B as an insight of the present study), all subjects could do the performances accurately. During the data collections of dynamic (Fig. 1C, upper traces) and static contraction (Fig. 1C, lower traces), TMSs were automatically applied at 10% MVC level using the above-mentioned trigger circuit. These data collections were repeated at five TMS intensity steps according to RMT (0.7-1.1 times RMT), until twenty trials for every condition were recorded. To avoid fatigue effects, the order of trials was randomly arranged, and adequate rest was taken inter-trials. Additionally, we defined active motor threshold (AMT) of each muscle contraction by off-line analysis. AMT was defined as the minimum output of the stimulator that could induce MEP responses in at least 5 out of 10 consecutive trials. The amplitude qualification was set above 200 μV so that it could be distinguished reliably from the B.EMG.

F-wave recordings

To make sure whether excitability of the spinal motoneuron pool was affected by physiological changes of motor cortex, we employed F-wave studies. Excitability of spinal motoneuron pool can partly be assessed by testing the magnitude of F-wave, which is generated by a recurrent discharge of antidromically activated spinal motoneuron pool (Meyer and Feldman 1967). The supra-maximum electric stimulation on the ulna nerve was delivered to elicit F-waves in the right FDI and ADM muscle. For each condition (muscle crosses contraction), ten successful F-waves were recorded using the same procedures as MEP protocols.

EMG and force recordings

Surface EMGs were recorded from FDI and ADM muscles with 9 mm diameter Ag-AgCl surface cup electrodes. The active electrode was placed over the belly of the right FDI and ADM muscle, and the reference electrode over the ipsilateral metacarpophalangcal joint. 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. In particular, we paid specific attention to keep the same B.EMG between each muscle contractions (dynamic and static). Recordings with different proceeding B.EMG were excluded from the final data.

Data analysis

In each trial, there was a recording of MEP preferred by successive EMG activity. We integrated the EMG activity just 50 ms prior to the TMS as the value of B.EMG. Each value was normalized as a percentage of B.EMG under MVC contraction (B.EMGmax). MEP amplitude was measured as the peak-to-peak value. In addition, we also recorded maximum M wave (Mmax) before and after experiment for checking the amount of motoneuron pools. MEP amplitude was normalized as the value of Mmax.

In particular, we employed MEP/B.EMG ratio as an index in the data analysis. Relationship between MEP and increasing intensity is demonstrated in a sigmoid function. B.EMG can shift the slope steeply (Capaday 1997; Carroll et al. 2001). Namely, using the paradigm of TMS intensity change, B.EMG is a crucial factor. On the other hand, MEP amplitude of small hand muscle linearly develops with the increment of B.EMG within 30%MVC, although excitatory effects of TMS on MEP differ for muscles (Kischka et al. 1993; Taylor et al. 1997). Therefore, when we fixed the B.EMG in the present study, MEP/B.EMG ratio could be recognized as the slope of MEP-B.EMG generation curve. Since we only desired to compare the relative steepness between dynamic and static contraction in each muscle, the intercept could be ignored.

Statistic analysis used a two-way ANOVA (muscle contractions cross TMS intensities). Paired *t*-test with Bonferroni correction for multiple comparisons was used to determine differences as a post-hoc test. Common paired *t*-test was used for comparing MEP thresholds (RMT and AMT). All of the significant levels were set at a criterion of $P<0.05$.

## 3. Results

Target matching errors during dynamic muscle contraction

Fig. 1B showed superimposed ten force curves of dynamic contraction by FDI and ADM muscle obtained from the training sessions. There were definitely discrepant force curves between two muscles. Then we measured the errors to the target force as a simple index to indicate it. We calculated the absolute difference of generated force to the target at the timing when the dynamic contraction was end (one second after starting). The value named target matching error was normalized as a percentage of the force value during MVC. The results were shown in Table 1. Errors produced by FDI muscles were statistically smaller than that by ADM ($t=3.75$, $df=4$, $p<0.05$).

MEP threshold

Table 2 showed the MEP thresholds in the different muscles and contractions. Related to RMT, there was no difference between FDI and ADM muscle. In FDI muscle, AMT was significantly lower in dynamic contraction than in static one ($t=3.61$, $df=9$, $p<0.01$). However, similar evidence was not observed in ADM muscle. In dynamic contraction, AMT was significantly lower in FDI muscle than in ADM ($t=2.41$, $df=9$, $p<0.05$). But AMT was same in static contraction.

MEP amplitude and B.EMG

Fig.1C showed the example recordings of MEP, B.EMG and force curve obtained from one subject. In the FDI muscle, MEP amplitude during dynamic contraction was definitely larger than that during static one despite of the same force level and B.EMG,

but such difference was not observed in the ADM muscle. In Fig. 2A, we showed the MEP specimen recordings of the FDI and ADM muscle, which were elicited by three steps of TMS intensity during dynamic and static muscle contractions (superimposed three trials), obtained from the same subject. The results of all subjects were summarized in Fig. 2B, using the above-mentioned index of MEP/B.EMG ratio. That is, in the FDI muscle, there were statistically significant differences of the ratio between dynamic and static contractions ($F_{1,40}$=52.42, $p<0.01$) and across the intensity steps ($F_{4,40}$=183.97, $p<0.001$). Post-hoc test indicated that the ratios during dynamic muscle contractions were larger than that during static muscle contractions at four lower TMS intensities (0.7, 0.8, 0.9 and 1.0 times RMT, $p<0.01$). However, in the ADM muscle, there was no significant difference at any steps of TMS intensity.

F-waves

Fig. 3A showed the typical recordings of F-waves in dynamic and static muscle contractions in the FDI and ADM muscle. Fig. 3B showed the means and standard deviations of F-waves and B.EMGs, which were obtained from all three subjects we tested. Extra facilitation between two contractions in either small hand muscle, was not found, when B.EMGs were achieved equivalently.

## 4. Discussion

Although task-dependent MEPs in the proximal and distal muscles were noted (Arányi et al. 1998; Kasai and Yahagi 1999; Lemon et al. 1995; Rossi et al. 1999; Schieppati et al. 1996; Yahagi et al. 2003), study of functional demanded excitability changes

occurred in distal muscles was rare (Ziemann et al. 2004). Regarding to the daily life, it is easily expected that index finger can do a motor task more perfectly than little finger. Thus, we gave an insight of task performance during dynamic contractions of two muscles which related to the different fingers in the present study. It was no wonder to the result, that force matching errors were smaller in FDI muscle during the training sessions. What is the neurophysiological mechanism? In the present study, therefore, we addressed this problem. Namely, although the FDI and ADM muscle are the same small hand muscles, there are functional demanded excitability changes between them. In detail, our major findings can be recapitulated as following: 1) In relaxed FDI and ADM muscle, there was no clear difference of RMT between them. During dynamic contraction, however, the AMT was lower in FDI muscle than that in ADM. In addition, when FDI muscle generated a force dynamically (dynamic contraction), the AMT became lower than the time when it maintained a force (static contraction). In ADM muscle, no such difference was found. 2) MEP/B.EMG ratios were larger during dynamic contraction than that during static one in FDI muscle, but not in ADM. 3) F-wave maintained stably in each muscle, not being relevant to the kind of contraction. In the documents below, we will interpret these findings.

MEP threshold

The finger function related to the distal muscles is deeply affected by the degree of cortical control required by the task (Lemon et al. 1998). Powerful facilitatory effect of weak voluntary contraction is most pronounced in the small hand muscles. Small hand muscles are mainly involved in finely controlled motor tasks, where a sharp, sudden modulation of the force is often required (Lemon et al. 1995; Schieppati et al. 1996).

Concerning the findings related to M1 in primate species (Lemon et al. 1998; Maier et al. 1997), the large pyramidal cell bodies and high proportion of mono-synaptic connections to spinal motoneurons are correlated with the control of the musculature of the fingers, hand and wrist (Bortoff and Strick, 1993). If that is the case in human M1, these specializations can be interpreted as evidence of functional differences among human digital muscles. Recently, Wu et al. (2002) demonstrated that differences of finger dexterity are probably resulted from the different degrees of direct corticomotoneuronal inputs to each muscle and the inherent properties of the spinal motoneruons. These interpretations are likely to explain the present MEP threshold differences between the FDI and ADM muscles. Namely, MEP threshold can be affected by the large pyramidal cells, cortical excitatory and inhibitory interneurons, and spinal motoneurons. In a word, the global excitability and sum of the motor pathway determine MEP threshold in small hand muscles. There was no different MEP threshold between FDI and ADM muscle in the relax condition and during the static contractions. But when the muscles generated a force dynamically, AMT became lower in FDI muscle than that in ADM. It may be explained that the extra part of motor pathways, which elicits lower MEP threshold in FDI muscle than in ADM, has a relatively small proportion in M1 or in motoneuron pool since two muscles share same nerve innervations. During dynamic contractions, following increasing B.EMG, the relatively small part ones may be magnified by the branched-axon input from CTNs to motoneuron pools and the synchronizations in the pools, which can produce larger groups of subliminal fringe in the pools.

MEP/B.EMG ratio

We employed the MEP/B.EMG ratio as a function of facilitatory index to investigate neural mechanisms of functional significances of different muscles and contractions. As described in the part of method, the ratio can indicate the different steepness of MEP-B.EMG curve, resembling the slope when equivalent B.EMGs are achieved between dynamic and static contraction. Moreover, the most important reason why we employed this index instead of the custom parameter of MEP can be explained that, B.EMG is a good estimate of activity level of motoneuron pools (Capaday 1997), and MEP can assess this level together with the activity level of subliminal fringe in the motoneuron pools and CTNs. Therefore, when MEP/B.EMG ratio increases, it can be explained that there is a more active or larger subliminal fringe existing in the pool and CTNs. As present result showed that there was different MEP/B.EMG ratio between dynamic and static contraction in FDI muscle, but not in ADM. Ashe (1997) reported, that functional differences of finger muscles are likely to reflect selective changes in the excitability of CTNs, and that the dynamic contraction is an important determinant of CTN activity. Thus, one possible explanation of functional differences between the FDI and ADM muscle is that they distribute different organizations in CTNs. That is to say, CTNs may act as a network of highly diverse elements and territory dependent on individuated finger movements. Selective activation of a hand muscle is accompanied by selective effect in the CTN networks. This assisted the pyramidal tract systems in producing fractionated activity of intrinsic hand muscles (Zoghi et al. 2003).

In addition, we should explain that at higher TMS intensity (1.1 times RMT), MEP became saturated, which was similar to our previous report (Kasai and Yahagi, 1999). This was not caused by the functional mechanisms of muscle contractions.

F-wave

According to the explanations above, the excitability of motoneuron pool is also an important factor to the present data. Because F-wave can partly indicate the excitability of the pool, it was employed. Since the result showed that F-wave remained stable, we prefer that the functional demanded excitability changes are contributed by the discrepant distribution in CTN networks rather than motoneuron pools.

Other factor

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

More recently, using a penta-stimulation technique, Ziemann et al. (2004) demonstrated that CTN excitation differs between intrinsic muscles and it is stronger in the FDI muscle than in the ADM. This paper can strongly support our data.

To our knowledge, the present study provides the first systematic investigation of different properties of the FDI and ADM muscle associated with monosynaptic connections of CTNs to spinal motoneurons. In conclusion, we prefer that organizations in corticospinal tract neurons accompanying with functional demanded excitability changes are different in FDI and ADM muscle.

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## Legends of figures

Fig. 1.

(A) Illustration of the experimental setup of dynamic muscle contractions. Bottom dashed line is baseline and top dashed line is target (50% MVC). The middle leaning one shows the assumed force generation. TMS was applied at 10% MVC, automatically.

(B) Typical force curves (superimposed ten trials) of FDI (left traces) and ADM muscle

(right traces) during dynamic muscle contraction for tracking the assumed force generation line. Dash lines show the target force levels. Arrows are the best timing for matching the target (one second after starting).

(C) Typical recordings of MEP, B.EMG and force curve during dynamic (upper traces) and static (lower traces) muscle contraction in the FDI (left traces) and the ADM (right traces) muscle obtained from one subject. B.EMG was calculated as integrated value of EMG activities 50ms prior to TMS artifact.

Fig. 2.

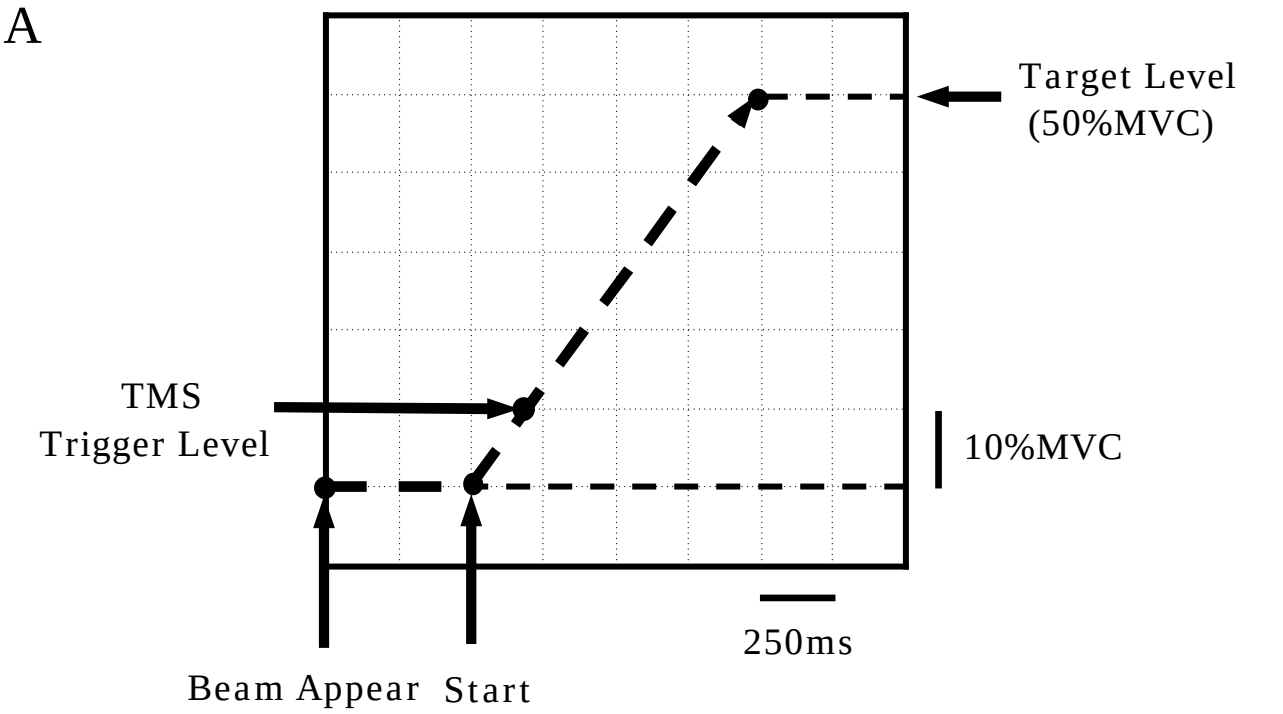
(A) Typical MEP recordings (superimposed three trials) during dynamic (left traces) and static (right traces) contraction in FDI (left panel) and ADM (right panel) muscle elicited by three TMS intensities. Vertical lines show the timings of TMS applied.

(B) Means and standard deviations (N=10) of MEP/B.EMG ratios. 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. ** $p<0.01$

Fig. 3.

(A) Typical F-wave recordings from one subject. Upper traces are during dynamic contractions and lower ones are during static contractions. Recordings in FDI muscle are at the left side, ADM are at right side. Each trace is superimposed three trials.

(B) Means and standard deviations of F-wave amplitudes (percentage value of Mmax) and B.EMGs was calculated in subject S1, S2 and S3. Columns indicate the B.EMGs, circles above the columns indicate F-wave amplitudes.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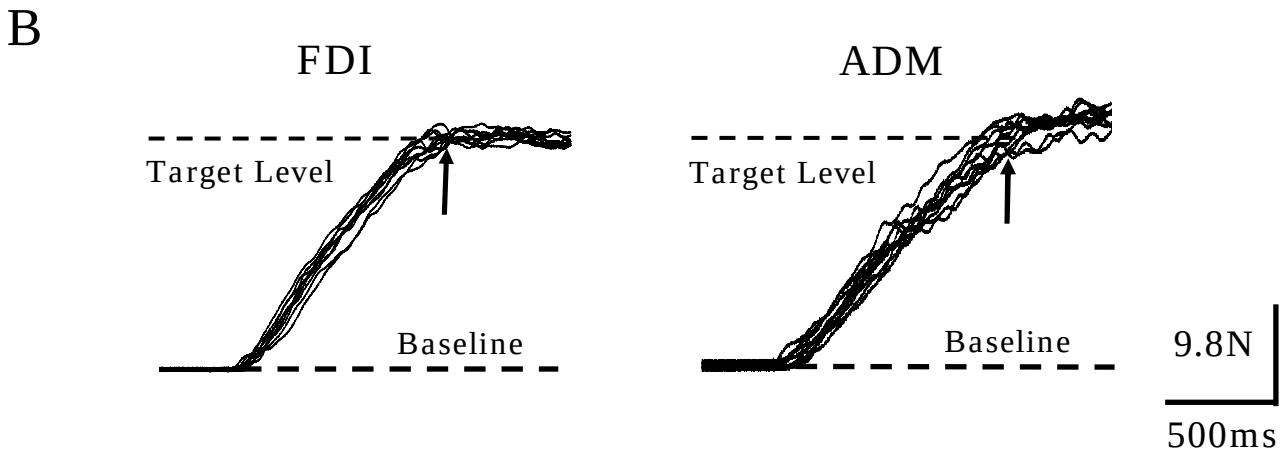
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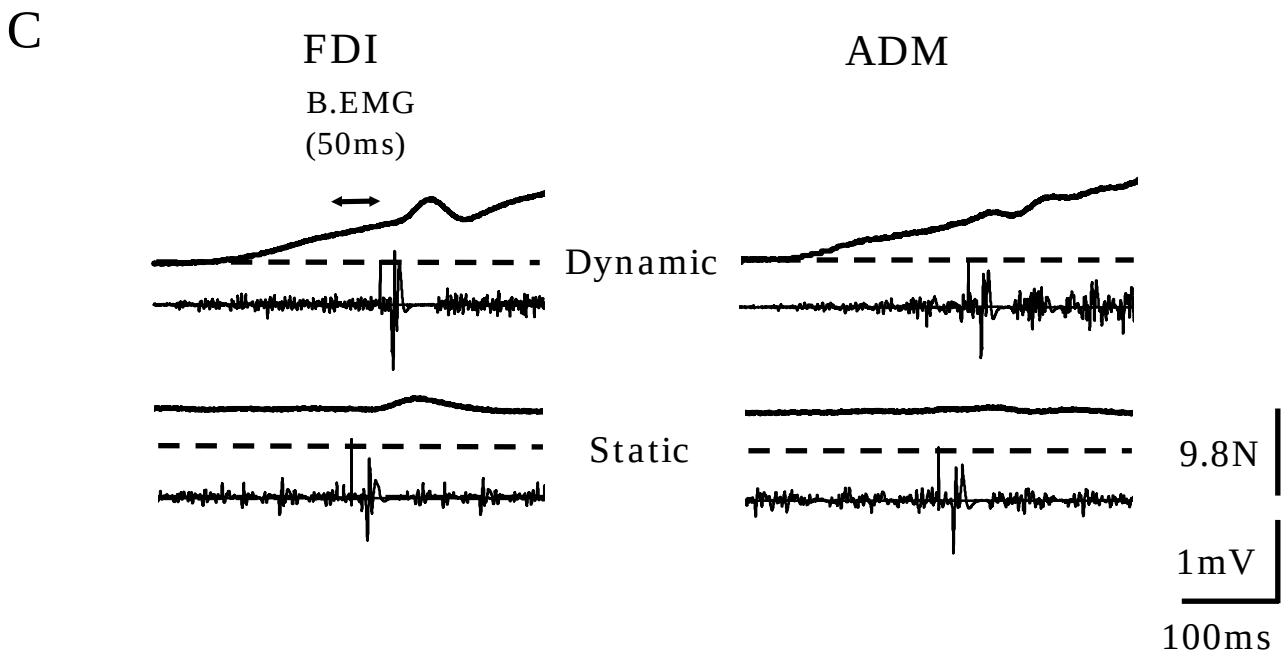
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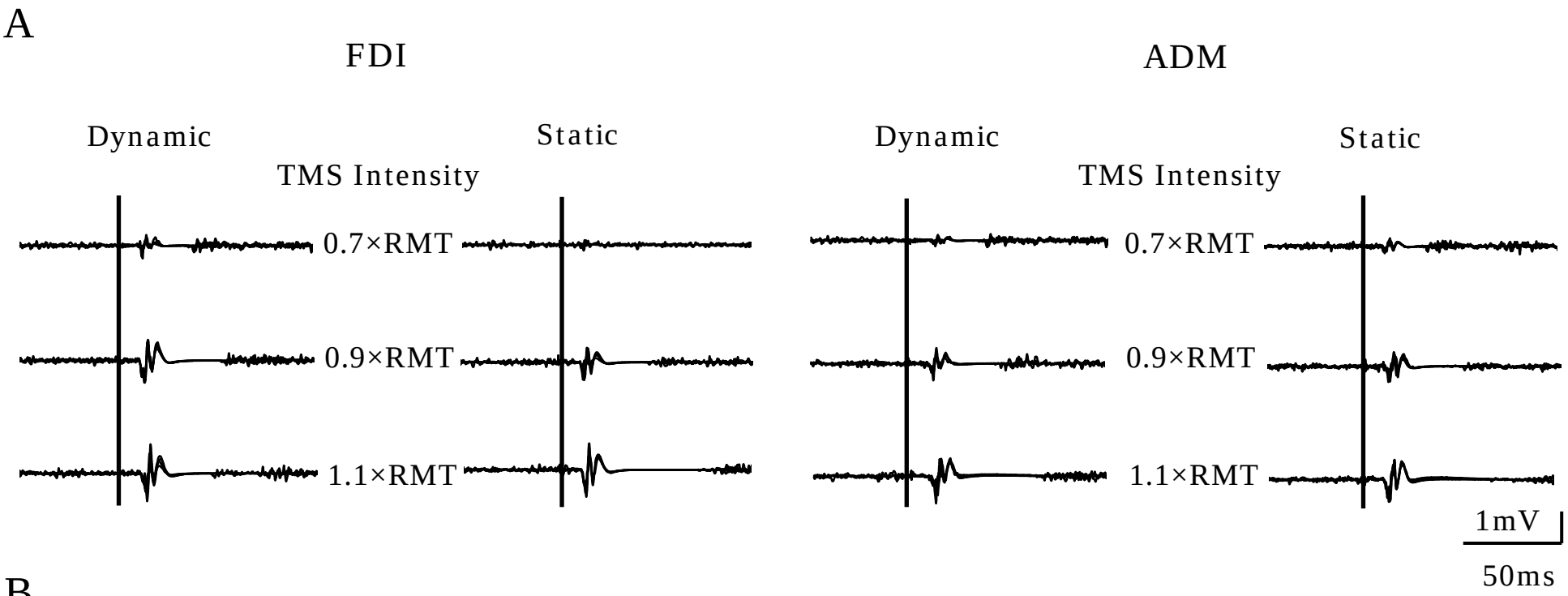
Fig. 1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TMS Intensity [×RMT]

Fig. 2

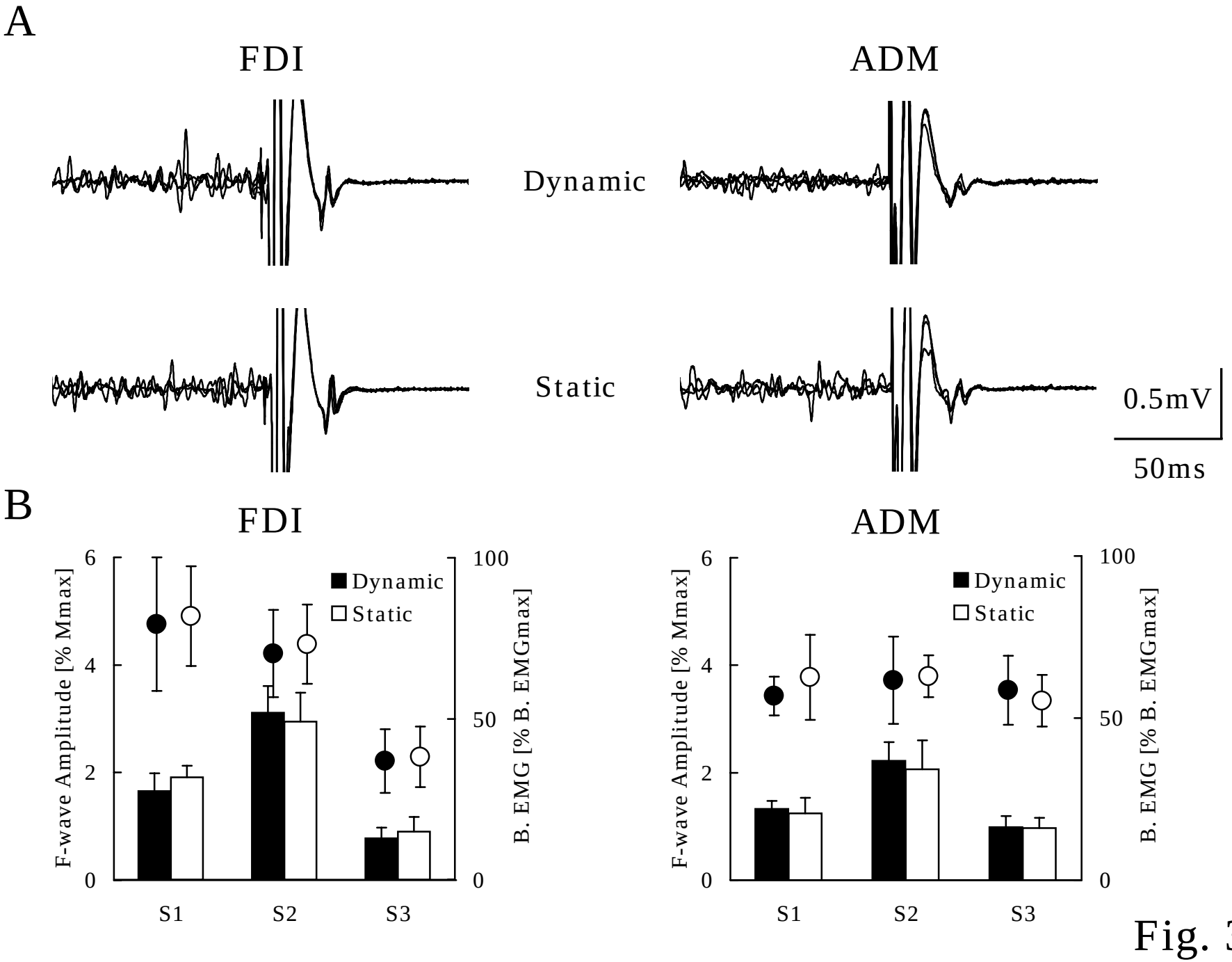
A
FDI
ADM
Dynamic
Static
0.5mV
50ms
B
FDI
ADM
F-wave Amplitude [% Mmax]
B. EMG [% B. EMGmax]
Dynamic
Static
0
2
4
6
0
50
100
S1
S2
S3

Fig. 3

Table 1: Force matching errors (% MVC) at the assumed timing after dynamic contractions by FDI and ADM

| Subject | FDI | | ADM |
|---|---|---|---|
| S1 | 1.48±0.87 | | 2.08±1.33 |
| S2 | 1.60±0.98 | | 1.63±1.44 |
| S3 | 1.81±1.37 | | 2.31±1.97 |
| S4 | 1.73±1.02 | | 2.30±1.59 |
| S5 | 1.72±1.18 | | 2.69±1.67 |
| Mean±SD | 1.72±0.19 | (*) | 2.20±0.39 |

* $p<0.05$

Table 2: MEP threshold (% of stimulator output) in the FDI and ADM muscle during relax and contractions

| | FDI | | ADM |
|---|---|---|---|
| RMT (Relax) | 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 |

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