

Excitability changes in human hand motor area induced by voluntary teeth clenching are dependent on muscle properties

by

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Research Note

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Abstract

To investigate whether the early effects of voluntary teeth clenching (VTC) among the first dorsal interosseous (FDI), abductor digiti minimi (ADM), and abductor pollicis brevis (APB) muscles are differently modulated depending on their different muscle properties, we examined the responses of motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation with selected current directions and by brainstem magnetic stimulation (BMS). Although MEP responses with anterior-medially (AM) current direction (preferentially elicited I1-waves) were facilitated in all three muscles, those responses with posterior-laterally (PL) current direction (preferentially elicited I3-waves) were different among FDI, ADM, and APB muscles. That is, MEP response in FDI and APB muscles were significantly reduced, whereas those responses in ADM muscle were not significantly reduced. Further, inhibitory effects of VTC in FDI muscle were more potent than those in ADM or APB muscles. On the other hand, the responses to BMS were unchanged by VTC in all three muscles, suggesting that the modulations of MEP were attributed to the cortical origin. Based on our previous findings that the inhibitory connections in FDI muscle are more potent than those in ADM muscle, the cortical effects of VTC among three hand muscles are differently modulated, depending on muscle properties, presumably the extents of inhibitory connections to corticospinal tract neurons. Further, considering that functional capacity in FDI muscle is higher than that in ADM or APB muscles, the cortical inhibitory effect of VTC might contribute to sophisticated regulation of the motor outputs even during VTC.

Keywords Voluntary teeth clenching (VTC) • Motor cortex • Transcranial magnetic stimulation (TMS) • Motor evoked potential (MEP) • I-waves

Introduction

We often clench our teeth during a great and/or forceful effort such as lifting a heavy weight. This voluntary teeth clenching (VTC), similar to the Jendrassik maneuver, is a common technique used to enhance the deep tendon- and H-reflexes in the lower limb muscles in clinical practice (Miyahara et al. 1996). In addition, several lines of evidence indicate that VTC can facilitate the responses in remote upper muscles through actions at both the spinal and cortical levels (Boroojerdi et al. 2000; Furubayashi et al. 2003; Sugawara and Kasai 2002). In particular, Furubayashi et al. (2003) has demonstrated that facilitation occurs in the hand motor area for the first dorsal interosseous (FDI) muscle just after the onset of teeth clenching and that spinal facilitation occurs at a later phase.

We have recently examined the early effects of VTC on motor evoked potentials (MEPs) from FDI muscle using transcranial magnetic stimulation (TMS) with different current directions, anterior-medially (AM) and posterior-laterally (PL) (Sugawara et al. 2005; Takahashi et al. 2004). VTC enhanced MEP responses with AM current direction (preferentially eliciting I1-waves), whereas reduced those responses with PL (preferentially eliciting I3-waves). Considering that I3-waves are more susceptible to the intracortical inhibition (ICI) than I1-waves (Di Lazzaro et al. 1998; Hanajima et al. 1998; Nakamura et al. 1997), cortical inhibitory effects could be preferentially detected by responses with PL current direction. However, the functional significance of this cortical inhibitory effect of VTC is still unclear.

The general consensus regarding the physiological function of VTC in the lower limb muscles would be to improve the stability to the stance (Miyahara et al. 1996; Takada et al. 2000; Takahashi et al. 2001). On the other hand, hand muscles are required the smoothness of movements rather than the posture stabilization (Furubayashi et al. 2003). In addition, cortical inhibitory control might contribute to finely controlled motor tasks (Abbruzzese et al. 1999). Thus, we hypothesized that cortical inhibitory effects of VTC may contribute to

sophisticated regulation of the motor outputs. In other words, cortical inhibitory effects of VTC may be variable depending on muscle properties.

To test this hypothesis, we compared the cortical and subcortical effects of VTC among three intrinsic hand muscles: FDI, abductor digiti minimi (ADM), and abductor pollicis brevis (APB) muscles. These three muscles are engaged in various extents of functionally important finger movements. In fact, Ziemann et al. (2004a, b) have recently reported that the monosynaptic corticomotoneuronal projections, which provide the capacity for independent control of the digits and skilled use of the hand, are more powerful to the alpha-motoneurons of FDI muscle than those of ADM or APB muscles. The purpose of the present study was, therefore, to address whether the cortical effects of VTC among three hand muscles are different depending on their functional demands. These results would also reveal the functional significance of the cortical effect of VTC on hand motor area.

Materials and methods

Subjects

Ten healthy right-handed volunteers (nine males and one female, age range: 23-38 yrs) participated in the present experiments after giving their informed consent. The experiments were performed in accordance with the Declaration of Helsinki and with the approval of the Local Ethics Committee of Hiroshima University.

Electromyographic (EMG) recording and cortical stimulation

The surface EMGs were recorded from right FDI, ADM, APB, and masseter muscles with pairs of surface Ag/AgCl cup electrodes (outer diameter 1.0 cm) in a belly-tendon montage. The EMG signals were amplified at a bandwidth of 5 Hz to 5 kHz, sampled at 5 kHz, and fed to a computer for off-line analysis.

TMS was given through a figure-of-eight-shaped coil, external diameter of wings 9 cm

(The Magstim Company, Whitland, UK). At the beginning of each experiment, the position of the coil was systematically adjusted on the scalp over the left motor cortex to find the optimal location for the activation of each target muscle. As shown by previous investigations (Day et al. 1989; Di Lazzaro et al. 2001; Hanajima et al. 1998; Sakai et al. 1997; Trompetto et al. 1999; Zoghi et al. 2003), it is possible to preferentially elicit different I-waves by different current directions in the brain. Thus, we chose two current directions induced in the brain, AM; preferentially evoke I1-waves and PL; preferentially evoke I3-waves (Sugawara et al. 2005; Takahashi et al. 2004, 2005). We confirmed that the onset latencies of the MEPs with PL current direction were about 3 ms later than those with AM current direction, corresponding to the difference between I1- and I3- waves in human corticospinal volleys. After adjustment of the coil position and orientation, the active motor threshold (AMT) of each muscle was determined. AMT was defined as the lowest stimulus intensity evoking MEP with amplitudes of about 200 μ V in at least four out of eight successive trials in slightly isometric contracting muscles (5-10% maximal voluntary contraction as assessed visually on an oscilloscope screen). The test stimulus was adjusted to evoke a control response with a peak-to-peak MEP amplitude of approximately 0.5 mV in each active muscle. We chose this MEP size as control responses, so as to evoke almost purely one group of descending volleys by the selected current direction (Hanajima et al. 1998).

Subcortical stimulation

To make sure whether the modulation of MEP was affected by subcortical activation, we employed brainstem magnetic stimulation (BMS) (Taylor and Gandevia 2004; Ni et al. 2005; Ugawa et al. 1994). BMS was given by a Magstim 200 stimulator 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 theinion. The current flowed downward at the junction region of

the coil, so that the maximum current induced in the head flowed upward. The intensity was set at 75-85% of the maximum output of the stimulator to evoke a control response with a peak-to-peak amplitude of approximately 0.5 mV in each active muscle. Stimulation of the motor roots is a major problem with magnetic stimulation as the wings of the double-cone coil lie over the upper neck, although we obtained appropriate latencies in each muscle (range: 16.0-17.5 ms, mean: 16.9 ± 0.5 ms). Four subjects were tested in this experiment.

Experimental procedures

All experiments were conducted under the active muscle condition (5-10% maximal voluntary contraction), since it was already shown that the early effects of VTC were clear under active muscle condition rather than relaxed condition (Sugawara et al. 2005). The subjects were asked to perform VTC as rapidly and forcefully as possible at any time when he/she was ready, after the go signal (experimenter's voice "Ready"). Every subject practiced at the beginning of test, and all of them were able to clench sufficiently during the data collection. Control (without VTC) and conditioned (with VTC) trials were randomly intermixed in the same session, and at least 10 responses were collected in each condition. The test orders of muscles and current directions were randomized and balanced across subjects. Data of FDI, ADM and APB were separately collected in the same session using the TMS intensities and stimulation sites appropriate for each muscle. Regarding the time course of the effect of VTC, Furubayashi et al. (2003) have already shown that hand motor area is facilitated without any spinal cord facilitation at the early phase (shorter than 50 ms after the onset of masseter). Thus, in the conditioned trials, the onset of VTC was detected by the computer (Signal Processor 7T23S; Nihondenkisanei, Tokyo, Japan) when rectified EMG of the masseter muscle exceeded the pre-set level, and magnetic stimulation was given at a certain interval after the EMG onset of the masseter muscle. Further, the actual interval between the onset of EMG of the masseter muscle and the stimulus was measured in off-line

analysis for each trial. We discarded a few trials that stimuli were given over 50 ms after the onset of VTC, and analyzed the trials within 50 ms (range: 22.8-49.6 ms, mean: 40.8±5.8 ms).

Data and statistical analyses

The differences in active motor thresholds and test TMS intensities of each muscle between AM and PL current directions were compared by a paired *t*-test with Holm's sequential Bonferroni correction (Holm 1979). To investigate the effects of VTC, MEP amplitudes between control (without VTC) and conditioned (with VTC) trials in each muscle and with each current direction were independently compared using a paired *t*-test with Holm's sequential Bonferroni correction. Furthermore, in order to investigate the differences of VTC effect between muscles and current directions, the mean peak-to-peak MEP amplitudes during VTC were expressed as a ratio of the control MEP amplitudes for each subject, and then calculated group mean ratio with standard deviation from pooled data. These data were analyzed using two-way ANOVA with repeated measures (factors; muscle and current direction). If a significant interaction was obtained, post hoc analyses were done using a paired *t*-test with Holm's sequential Bonferroni correction. The MEP onset latencies and background EMG activities (rectified and averaged for a 100 ms window just prior to TMS) in each muscle were compared among current direction and condition (with and without VTC) using a paired *t*-test with Holm's sequential Bonferroni correction. The level of statistical significance was defined as $P < 0.05$. The data are expressed as means ± SD.

Results

Thresholds and test TMS intensities

The AMT and test TMS intensities of three muscles with different current directions in slightly isometric contracting muscles are summarized in Table 1. The AMT of all three muscles with AM current direction were significantly lower than those with PL ($P < 0.01$). To

obtain the same size of the control MEP amplitudes between AM and PL current directions, test TMS intensities of all three muscles with AM were also significantly lower than those with PL ($P<0.01$).

The effects of VTC on MEP responses

Fig. 1a shows representative examples of the effects of VTC on MEP responses in FDI, ADM, and APB muscles with different current directions obtained from a single subject. As shown in Fig. 1b, MEP onset latencies with PL current direction were 2.8 ± 0.1 ms (range: 2.6-3.0 ms) longer than those with AM current direction. These values correspond to the ~3 ms difference between I1- and I3- waves in human corticospinal volleys. Mean size ratios of all subjects tested ($n=10$) were calculated and are shown in Fig. 1c. VTC significantly enhanced MEP responses with AM current direction in all three muscles ($P<0.01$). On the other hand, VTC significantly reduced MEP responses with PL current direction in FDI and APB muscles ($P<0.01$), whereas it tended to be slightly suppressed the responses in ADM muscle, but this was not statistically significant ($P=0.09$). Further, a significant interaction between muscles and current directions was found ($F=4.44$, $P<0.05$). Post hoc analyses showed that the control/conditioned ratios of all three muscles were significantly different between AM and PL current directions ($P<0.01$). The ratio of FDI muscle with PL current direction was significantly different from that of ADM or APB muscles ($P<0.01$). That is, inhibitory effects of VTC in FDI muscle with PL current direction were more potent than those in APB or ADM muscles.

On the other hand, amounts of background EMG activities in each muscle were not significantly different in all conditions, suggesting that the modulations of MEP amplitudes could not be secondary effects due to the changes of background EMG activity levels during VTC (Fig. 1d).

Responses to brainstem magnetic stimulation

Representative examples of the effects of VTC on the responses to BMS in three muscles are shown in Fig. 2a and mean size ratios of all subjects tested (n=4) in Fig. 2b. VTC neither reduced nor enhanced the responses to BMS in all three muscles at early phase of VTC. Meanwhile, amounts of background EMG activities in each muscle were not different between with and without VTC (Fig. 2c).

Discussion

The major new finding is that MEP responses by VTC with PL current direction were different among FDI, ADM, and APB muscles. MEP responses in FDI and APM muscles were significantly reduced by VTC, whereas those responses in ADM muscle were not significantly reduced. Furthermore, inhibitory effects of VTC in FDI muscle were more potent than those in APB or ADM muscles. On the other hand, the responses to BMS were unchanged by VTC in all three muscles, suggesting that the modulations of MEP were attributed to the cortical origin without any changes of spinal cord. With these findings taken together, the cortical effects of VTC among FDI, ADM, and APB muscles are differently modulated, which presumably reflect their different functional demands. Further, the cortical inhibitory effect of VTC on FDI muscle would provide the capacity for fine and purposeful hand movements even during VTC.

Muscle dependent excitability changes in hand motor areas during VTC

MEP responses with AM current direction were facilitated in all three hand muscles at the early phase of VTC, whereas those responses with PL current direction at least were not facilitated. Considering that the responses to BMS were unchanged in all three muscles at the early phase of VTC, which is consistent with the previous report by Furubayashi et al. (2003), these differences between AM and PL current directions should be attributed to the

cortical origin without any changes of spinal cord. In the present study, TMS with AM current direction preferentially elicits I1-waves, whereas that with PL current direction preferentially elicits I3-waves (Fig. 1a and b). The exact nature of the generation of I-waves is still unclear, but there may be two different and independent cortical mechanisms responsible for the generation of I1- and I3-waves (Di Lazzaro et al. 2004; Ziemann and Rothwell 2000). I1-waves are usually taken to indicate that it is produced by a monosynaptic input to corticospinal neurons. Therefore, it could be assumed VTC increases the excitability of corticospinal neurons directly or affect the synapse between the I1 inputs and the corticospinal neurons. On the other hand, I3-wave generation involves more synapses in the motor cortex than I1-wave generation, and hence I3-waves are more susceptible to ICI than I1-waves (Di Lazzaro et al. 1998; Hanajima et al. 1998; Nakamura et al. 1997). Thus, one possible explanation for the present results is that VTC also increases the excitability of ICI circuits, and consequently corticospinal neurons are indirectly inhibited, acting upstream to the corticospinal neurons on the mechanism generating I3-waves. At the present time, we can only speculate on what the differences of cortical effect of VTC between I1- and I3-waves could be. To gain insight into the precise mechanisms, especially the excitability changes of intracortical neural circuits, we need additional experiments using such a paired-pulse TMS paradigm in future study.

On the other hand, MEP responses in FDI and APB muscles with PL current direction were significantly reduced during VTC, whereas those responses in ADM muscle were not significantly suppressed. Thus, inhibitory effects of VTC in FDI muscle were more potent than those in APB or ADM muscles, even though we cannot rule out the possibility that the inhibition in ADM muscle may become significant when more subjects are studied. One possible explanation for these difference is that the cortical effects of VTC are related to muscle properties, since the monosynaptic corticomotoneuronal projections are more powerful to the alpha-motoneurons of FDI muscle than those of ADM or APB muscles

(Ziemann et al. 2004a, b). Furthermore, using paired-pulse TMS with PL current direction, we have recently demonstrated that the inhibitory connections operating for the corticospinal tract neurons in FDI muscle are more potent, and, conversely, that those in ADM muscle are weaker (Takahashi et al. 2005). Taken together these findings with the present results, although the information of ICI circuits in APB muscles is unclear, the cortical effects of VTC among three intrinsic hand muscles are differentially modulated, depending on muscle properties, presumably the extents of inhibitory connections to corticospinal tract neurons.

Functional significance

Furubayashi et al. (2003) previously demonstrated that at the early phase of VTC hand muscles are controlled by the motor cortex without any restriction of the spinal cord, so as to support fine finger movements. The present study provides further evidences that at this early phase of VTC the inhibition of MEP response with PL current direction was more prone in FDI muscle than that in ADM or APB muscles. Functional capacity defined by maximal finger movement rate is higher in FDI muscle than that in ADM or APB muscles (Ziemann et al. 2004a). On the other hand, cortical inhibitory control might contribute to finely controlled motor tasks (Abbruzzese et al. 1999). Thus, we propose that the cortical inhibitory effect at early phase of VTC may contribute to the capacity for fine finger movements even during VTC. This conclusion is partially supported by the recent findings that static shoulder position affects ADM but not FDI cortico-motoneuronal output (Dominici et al. 2005). These finding indicate that FDI muscle is controlled independently without any restriction of the proximal-distal synergies. Similarly, FDI muscle may be finely controlled with less restriction of VTC, and the cortical inhibitory effect may contribute to sophisticated regulation of the motor outputs.

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Legends for figures

Fig.1. a: Representative examples of the effects of VTC on MEP responses in FDI, ADM, and APB muscles with different current directions (AM: upper two traces and PL: lower two traces) obtained from a single subject. Five responses were averaged in each trace. Vertical dot lines on each MEP recording indicate the onsets of each MEP. **b:** MEP onset latencies in each ten subjects at each condition with AM and PL current directions. **c:** Means and standard deviations of MEP size ratio obtained from ten subjects at each condition with AM and PL current directions. **d:** Means and standard deviations of the amount of background EMG activities obtained from ten subjects at each condition with AM and PL current directions. *Significant difference between AM and PL current direction. †Significant difference between muscles.

Fig.2. a: Representative examples of the effects of VTC on MEP responses in FDI, ADM, and APB muscles with brainstem magnetic stimulation obtained from a single subject. Five responses were averaged in each trace. **b:** Means and standard deviations of MEP size ratio obtained from four subjects. **c:** Means and standard deviations of the amount of background EMG activities obtained from four subjects at each condition.

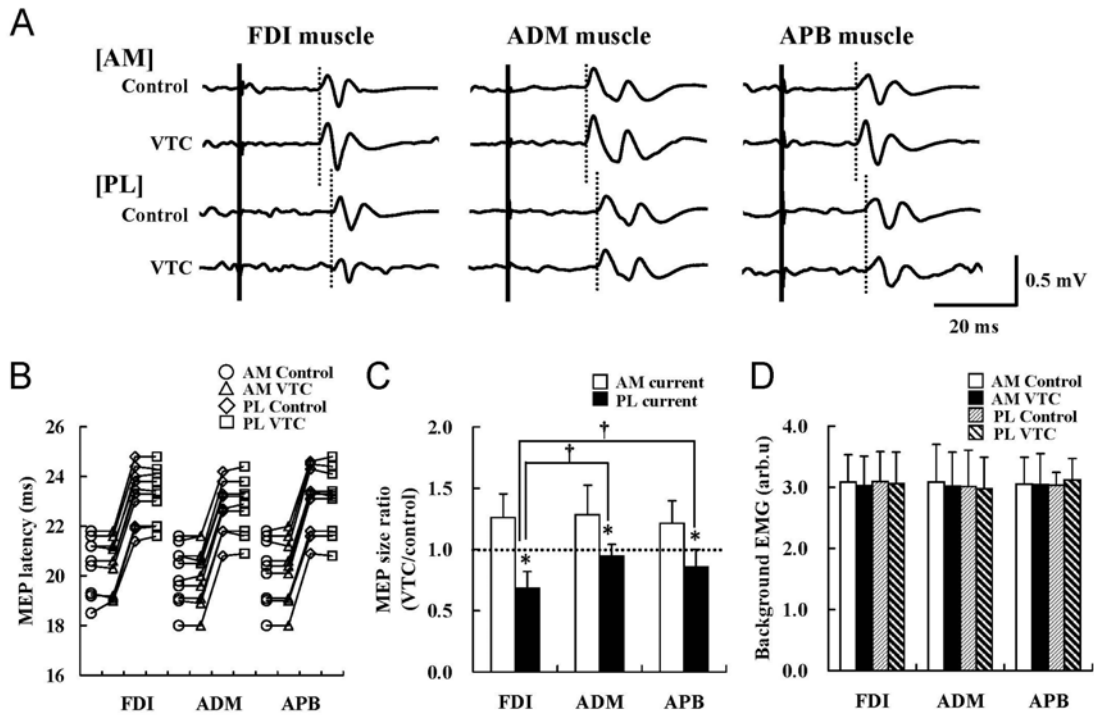


Figure 1

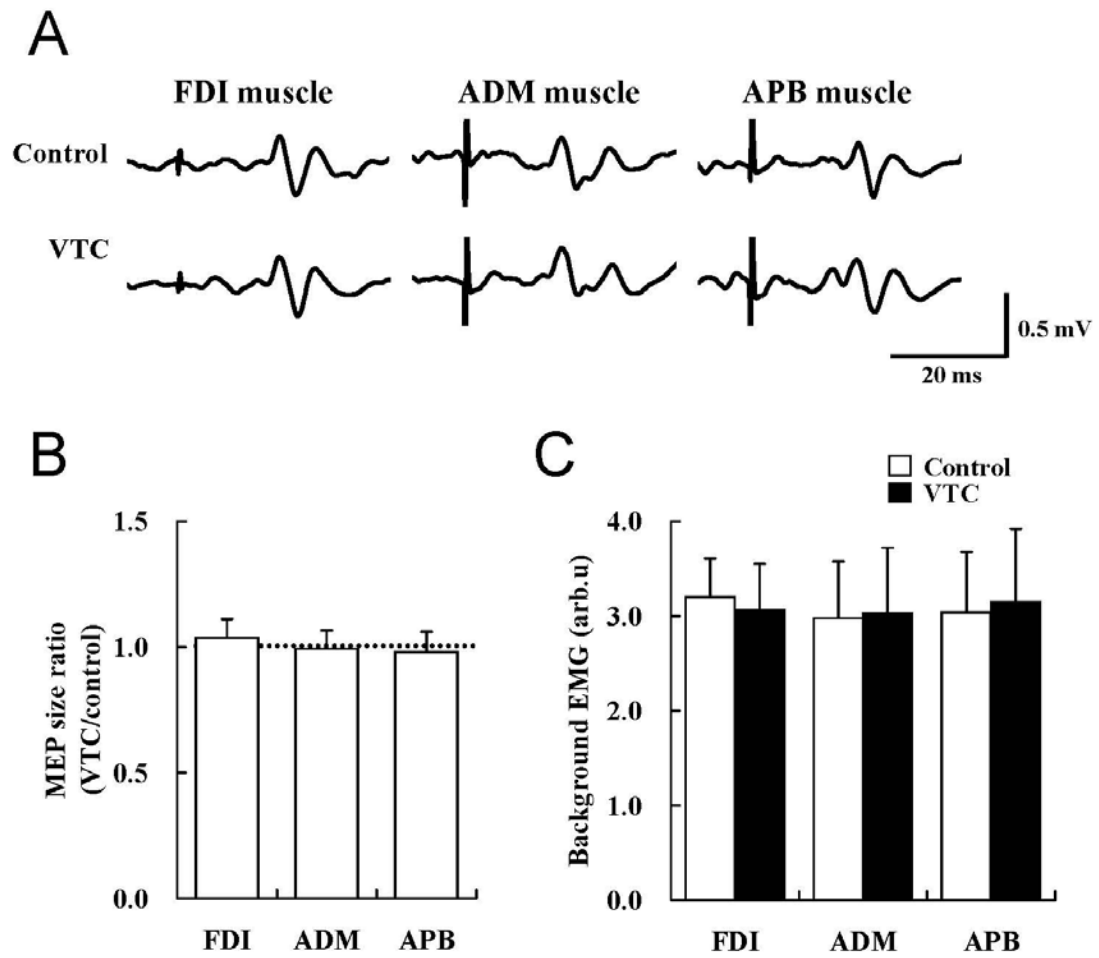


Figure 2