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Effects of remote muscle contraction on transcranial magnetic stimulation-induced motor evoked potentials and silent periods in humans

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Abstract

Objective: To determine to what extent tonic contraction of the testing muscle modulates the effect of remote muscle contraction on motor evoked potentials (MEPs) and cortical silent periods (CSPs) in resting and active proximal and distal muscles following transcranial magnetic stimulation (TMS). In addition, we tested whether the remote effect on MEP was observable when the test MEP was small.
Methods: While performing tonic abductions of the first dorsal interosseous (FDI), flexor carpi radialis, or anterior deltoid muscles, subjects made phasic dorsiflexions of the right ankle at various forces. MEPs and CSPs were induced by separately optimized TMS intensities and locations in the left motor cortex and recorded electromyographically.
Results: Phasic dorsiflexion increased MEP amplitude and shortened CSP duration in a dorsiflexion intensity-dependent manner in all muscles tested. At test MEPs <10% of Mmax, remote effects on MEP amplitude and CSP duration were significantly attenuated while the testing muscle was active.
Conclusions: Phasic contraction of remote muscles potentiates excitatory- and suppresses inhibitory intracortical neuronal pathways converging on corticospinal tract cells innervating the upper limb muscles even when they are active. However, the magnitude of the remote effect on MEP amplitude strongly depends on the test MEP amplitude.
Significance: Although remote effects on MEP amplitude and CSP duration are observed even when the test muscle is active, the magnitude of the remote effect strongly depends on TMS intensity.

Keywords: Motor evoked potential; Cortical silent period; Remote effect; Transcranial magnetic stimulation

1. Introduction

It is known that phasic and intensive contraction of a muscle produces potentiation of Hoffmann (H-) and stretch reflexes of muscles located in remote segments (remote effect, Jendrássik, 1883; Delwaide and Toulouse, 1981; Miyahara et al., 1996; Zehr and Stein, 1999; Tazoe et al., 2005). The remote effect on the excitability of the corticospinal tract was also demonstrated with motor evoked potentials (MEPs) following transcranial magnetic stimulation (TMS) (Kawakita et al., 1991; Péréon et al., 1995; Stedman et al., 1998; Boroojerdi et al., 2000; Muellbacher et al., 2000; Hortobágyi et al., 2003). In addition, intracortical inhibition and facilitation induced by paired pulse TMS were diminished and enlarged by voluntary teeth clenching, respectively (Boroojerdi et al., 2000). It was

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recently reported that the TMS-induced cortical silent period (CSP), while stimulating areas of the hand, was shortened during phasic contraction of ankle dorsiflexor muscle (Sohn et al., 2005; Tazoe et al., 2007).

TMS is known to produce both MEPs and subsequent CSPs, although there is ample evidence suggesting that the two are mediated by independent neural circuitries. There was only weak correlation between the magnitude of MEP amplitudes and CSP durations when TMS intensity was kept constant (Inghilleri et al., 1993; Wilson et al., 1993). The threshold for inducing CSP was reported to be lower than that for MEP (Davey et al., 1994) and the representation of CSP on the scalp was more extensive than that of MEP (Wassermann et al., 1993). Changes in MEP amplitude and CSP duration differed depending on the level of background electromyographic (EMG) activity, stimulus intensity (Inghilleri et al., 1993; Wu et al., 2002) and motor task (Tinazzi et al., 2003). Recent technical progress in repetitive TMS demonstrated an independent modulation of both MEP amplitude and CSP duration (Gilio et al., 2003). These studies strongly suggest that CSPs and MEPs are mediated by discrete neural pathways, and that the remote effects on both cortical responses probably also differ.

Many studies of the remote effect on MEP were conducted with the test muscle at rest, and facilitatory effects were reported (Kawakita et al., 1991; Péréon et al., 1995; Stedman et al., 1998; Boroojerdi et al., 2000; Muellbacher et al., 2000; Hortobágyi et al., 2003). However, it was also recently demonstrated that the remote effect on H-reflex amplitude was markedly attenuated when the testing muscle was tonically activated (Tazoe et al., 2005). Furthermore, Takahashi et al. (2006) demonstrated that MEPs in the intrinsic hand muscle were significantly suppressed by voluntary teeth clenching when the hand muscle was tonically contracted. It was also reported that phasic contraction of the remote muscle resulted in shortening of CSP duration though no significant increase in MEP amplitude was seen when the testing muscle was active (Sohn et al., 2005; Tazoe et al., 2007). Thus, it is still debatable whether the remote effect on MEP exists when the testing muscle is active. To address this issue, input–output relationships of the MEP should be taken into account (Capaday, 1997), because susceptibility of the MEP to excitatory and inhibitory inputs may strongly depend on the size of the test MEP (Capaday, 1997; Crone et al., 1990). In general, the magnitude of the MEP is sigmoidally related to increasing stimulus intensity (Capaday, 1997; Devanne et al., 1997). Hence, susceptibility of the MEP to excitatory and inhibitory inputs is expected to be high when its magnitude is located on the ascending limb of the input–output curve. However, the size of the test MEP was not necessarily controlled in other studies. In our previous study (Tazoe et al., 2007), the remote effect on MEP was less pronounced when the test MEP amplitude was ~20% of the maximal M-response (Mmax), which may account for absence of the remote effect in other conditions (Crone et al., 1990). Thus, optimal stimulus parameters to test the remote effect on the MEP should be determined.

The remote effect on the H-reflex was demonstrated to depend on proximity to the trunk (i.e., proximal vs. distal muscles, Toulouse and Delwaide, 1980). Also, short-term plastic changes in MEP were reported to differ from distal to proximal muscles (Brasil-Neto et al., 1992; Rossini et al., 1996). It remains, however, unclear how the remote effect on MEP and CSP is modulated from proximal to distal muscles.

Therefore, the first objective of the present study was to determine optimal stimulus parameters for detecting the remote effect when the testing muscle is active. The second objective was to determine to what extent the remote effects on MEP amplitude and CSP duration were modulated during tonic contraction of the testing muscle compared to when it was at rest (state dependency). The third objective was to test the state dependency of the remote effect on the MEP and CSP while stimulating three muscles with different anatomical locations and functions (the first dorsal interosseous; FDI, the flexor carpi radialis; FCR, and the anterior deltoid; AD).

2. Materials and methods

2.1. Subjects

Subjects were 11 neurologically intact healthy male volunteers between 22 and 33 years of age. All gave informed consent prior to participate in the experiments. The protocol was approved by the local Ethical Committee and was in accordance with the guidelines established in the Declaration of Helsinki.

2.2. Recordings

EMG signals were recorded from the FDI, FCR, AD and tibialis anterior (TA) muscles on the right side of the body. Active and reference surface electrodes (Ag–AgCl, 8 mm diameter) were positioned 20 mm apart over the muscle belly, except for the FDI in which the active electrode was on the muscle belly and the reference electrode was on the metacarpophalangeal joint of the index finger. EMG signals were amplified and filtered (bandwidth 16–3000 Hz) with a conventional bioamplifier. Isometric dorsiflexion force was measured using strain gauges (Kyowa Dengyo Co., Ltd., Tokyo, Japan) attached to the immovable footplate and used for visual feedback to the subjects. All signals were stored on a computer with a sampling rate of 6 kHz using a CED 1401 A/D converter (Cambridge Electronic Design, Cambridge, UK) for later off-line analysis.

2.3. Stimulation

TMS was delivered with a figure 8-shaped coil (each diameter 95 mm) connected to a Magstim 200 (Magstim,