LONG-LATENCY INTRACORTICAL INHIBITION DURING UNILATERAL MUSCLE ACTIVITY

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Abstract. The aim of the present study was to investigate the effect of co-activation of antagonist muscles on long-latency intracortical inhibition (LICI) in comparison to isometric index finger abduction. EMG signals were recorded from the first dorsal interosseous muscle (FDI) in response to single-pulse and paired-pulse transcranial magnetic stimulation (TMS).

In 10 healthy right-handed volunteers, TMS was used to estimate LICI at 3 different interstimulus intervals (ISIs) - 50, 100 and 150 ms. The intensity of the conditioning and test stimuli was 130 % of the motor threshold in relax. The stimulation procedure was repeated at rest and during tonic isometric index finger abduction and co-activation of antagonist muscles.

At rest, LICI was significant at ISIs of 100 and 150 ms and not evident at ISI of 50 ms. During isometric index finger abduction and co-activation of antagonist muscles, LICI was evident at all used ISIs and was even better pronounced at 50 ms. At ISIs of 50 and 100 ms during abduction, LICI was significantly stronger in comparison to co-activation.

During abduction and paired-pulse TMS, the mean values of cSP at all used ISIs were significantly shorter compared to single-pulse TMS. The shortening of cSP recorded in response to paired-pulse TMS was gradual, with increasing of ISI from 50 to 150 ms. In contrast, during co-activation, the duration of cSP was almost independent of the value of ISI and similar to the duration of cSP in response to single-pulse TMS.

Key words: transcranial magnetic stimulation (TMS), long-latency intracortical inhibition (LICI), co-activation of antagonist muscles, isometric index finger abduction.

Introduction

The main result of muscle activity is a movement of the whole body or a movement of some parts of the body. The other important function of muscle activity is to keep body position by adaptation of mechanical impedance of joints to external perturbations by co-activation of antagonist muscles [1] The co-activation increases joint stiffness and provides mechanical stability in holding posture [2] and during limb movement [1]. Antagonistic co-activation occurs in anticipation of predictable movements and in motor learning [3, 4]. Also, increased co-activation of antagonist muscles is counted among the requirements for higher accuracy of multi-joint movements [5].

Although co-activation of antagonistic muscles occurs during a number of motor tasks, the underlying neurophysiological mechanisms are unknown. Evidences from behavioral studies suggest that the antagonistic co-activation may be controlled, separately from the reciprocal activation of joint muscles during usual movement. It seems that the co-activation can varies over a wide range of values while maintaining zero net torque at a joint [6]. Further, several

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studies provide evidences that maximal muscle activity during co-activation with zero net torque at the ankle, is lower than the maximal muscle activity during reciprocal activation of muscles [7]. The physiological mechanism responsible for a limited muscle activity during co-activation may involve a postsynaptic inhibition at spinal level or may originate from central voluntary commands. The "common drive" of some motor units of agonist and antagonist muscles during voluntary co-activation is consistent with the idea of centrally originated co-activity. The findings that some neurons in motor cortex and cerebellar cortex are active during co-activation of antagonists but are inactivated during reciprocal activation also support central mechanisms involvement in the co-activation control [8].

Cortical inhibition of pyramidal neurons is mediated by gama-amino butyric acid (GABA) receptors [9]. Brain studies in animals and humans have revealed two main phases of inhibition following stimulation: a "fast" phase mediated by ionotropic GABAA receptors and a "slow" phase mediated by metabotropic GABAB receptors [10]. In conscious humans, cortical inhibition can be measured using paired-pulse transcranial magnetic stimulation (TMS) [11]. When preceded by a suprathreshold TMS pulses at ISIs of 50-200 ms, MEP amplitude is significantly reduced and it is referred as long-latency intracortical inhibition (LICI) [11]. LICI is thought to reflect GABAB-mediated cortical inhibition. The goal of the present study is to investigate the effect of co-activation of antagonist muscles on LICI in comparison to reciprocal activation of target muscle.

Methods

Ten healthy right-handed volunteers (Edinburgh Handedness Inventory [12]), aged 27-60 years, gave their informed consent and participated in the study approved by the local ethics committee. Subjects were seated with right arm gently fixed in slight abduction from the trunk (20^o) and flexion in the elbow (110^o). The hand and forearm were pronated and fixed on horizontal supports. The index finger was placed on manipulandum and securely clamped by two pads. The axis of manipulandum was positioned to align the axis of rotation of index finger. The torques in abduction - adduction as well as in direction of index finger flexion during isometric contractions were measured using appropriately placed transducers.

Motor evoked potentials (MEPs) were recorded from the first dorsal interosseous muscle (FDI) of the right hand using conventional surface Ag/AgCl disc electrode (8 mm diameter) and differential techniques. The active pole of the electrode was fixed on the muscle belly and the reference pole - on distal tendon at the index finger base. Myoelectrical signal was amplified (band pass 10 Hz--1 kHz) and digitized (sampling rate 2 kHz). Epochs of 1 s duration (starting 0.5 s prior to the test stimulus) were stored on a disk. The EMG activity as well as the force signals were continuously monitored to control the level of tonic activity in the right hand.

Two MagStim 200 stimulators connected to the eight-shaped stimulating coil (mean diameter 7 cm) through a BiStim module were used. The BiStim module was used to combine the single-pulse from the two stimulators to a paired-pulse configuration delivered through the coil, with a possibility to control the interstimulus interval between both pulses. The coil was adjusted over the left hemisphere to evoke optimal responses from the right FDI. Motor threshold (MT) was determined at relax condition as the lowest stimulus intensity which elicited three MEP responses of at least 0.05 mV peak to peak amplitude in five consecutive TMS applications.

Five single-pulse stimuli with an intensity of 130 % of the MT were applied to obtain control MEPs in the relaxed muscle. Then, 15 paired-pulse stimuli (five with ISI of 50 ms, five with ISI of 100 ms and five with ISI of 150 ms) were applied. The different ISIs were applied in random order. The intensity of the conditioning and test stimuli was 130% of the MT. The same stimulation procedure was repeated during tonic isometric index finger abduction and co-activation of antagonist muscles without external force production (controlled by visual force feedback). During antagonistic co-activation the mean value of rectified EMG was the same as the corresponding value during isometric abduction (20% of maximal voluntary contraction).

Data analysis was performed offline. Only trials showing similar levels of tonic EMG (mean rectified EMG) activity during the 400 ms prestimulus period in both co-activation and isometric abduction were considered. The measured parameters were peak-to-peak amplitude of MEPs and duration of cortical silent period (cSP) (Fig.1). The differences between control and test values were assessed using a Wilcoxon matched-pair signed-rank test. Probability values (p) less than 0.05 were considered as significant. The effects of tonic muscle activity (relax, co-activation and abduction) on the duration of ISI were assessed by two-way repeated measures ANOVA and in case of significance its locus was identified by Wilcoxon matched- pair signed-rank test.

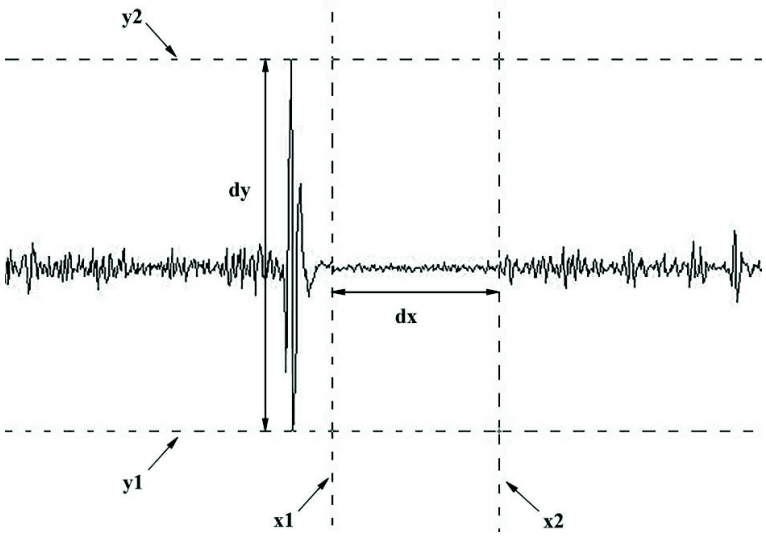

Fig. 1. Responses recorded to single-pulse TMS during isometric index finger abduction. The peak-to-peak MEP amplitude (dy) and the duration of cortical silent period (dx) were measured with two horizontal and two vertical cursers, respectively.

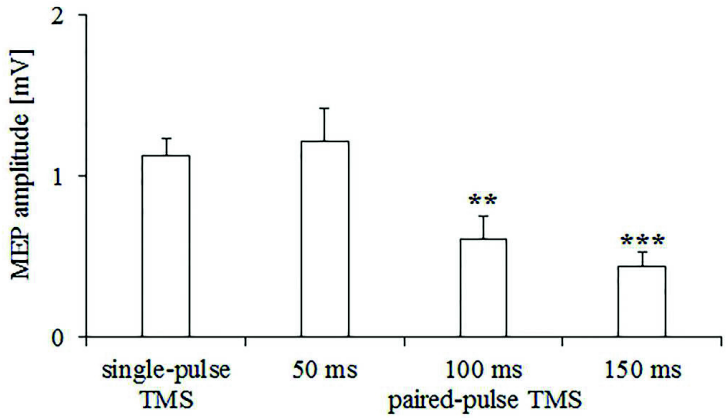

Fig. 2. MEP amplitudes (mean ± SE) recorded from the relax FDI in response to single-pulse and paired-pulse TMS with ISIs of 50, 100 and 150 ms. Asterisks indicate significant effect of LICI (** - $p<0.01$, *** - $p<0.001$).

Results

When the investigated muscle was relaxed LICI was evident at paired-pulse TMS with ISIs of 100 and 150 ms, and insignificant at ISI of 50 ms (Fig.2).

In order to avoid the interindividual differences we normalized the values of MEP amplitudes in response to the second TMS pulse at every ISI to the mean value of MEP amplitude in response to the first TMS pulse. In contrast to the relax muscle, during isometric tonic muscle activation (isometric index finger abduction or co-activation of antagonist muscles), LICI was evident at all used ISIs and was even better pronounced at 50 ms (Fig.3). At ISIs of 50 and 100 ms, LICI was significantly stronger during isometric index finger abduction compared to antagonistic co-activation (Wilcoxon matched-pair signed-rank test).

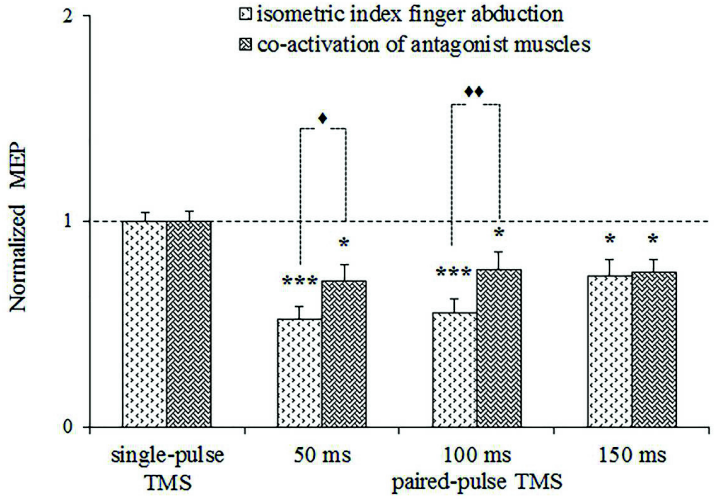

Fig. 3. Normalized MEP amplitudes (mean ± SE) recorded during isometric index finger abduction and co-activation of antagonist muscles in response to single-pulse and paired-pulse TMS with ISIs of 50, 100 and 150 ms. Asterisks indicate significant effect of muscle activity on LICI (* - $p<0.05$ and *** - $p<0.001$). Diamonds indicate significant differences of LICI during abduction and co-activation at one and the same ISI (♦ - $p<0.05$ and ♦♦ - $p<0.01$).

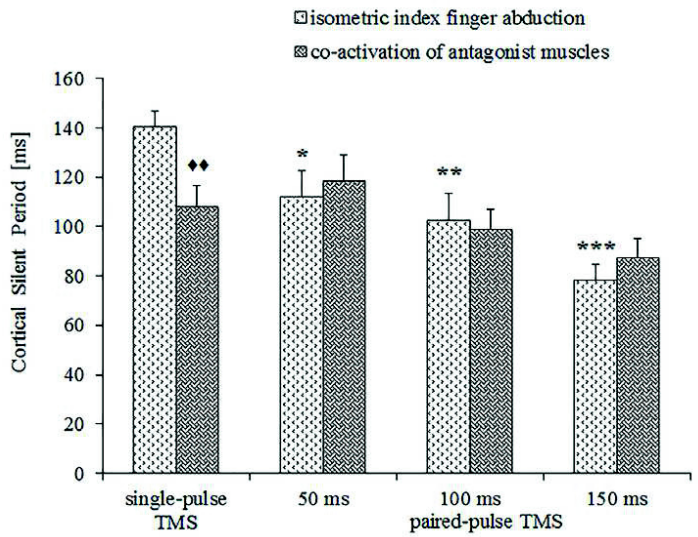

Fig. 4. Duration of cSP during isometric index finger abduction and co-activation of antagonist muscles in response to single-pulse and paired-pulse TMS with ISIs of 50, 100 and 150 ms. Asterisks indicate significant effect of paired-pulse TMS (* - $p<0.05$, ** - $p<0.01$ and *** - $p<0.001$). Diamonds indicate significant differences of cSP during abduction and coactivation in response to single-pulse TMS (♦♦ - $p<0.01$).

Two-way repeated measures ANOVA with parameters type of tonic muscle activity (three levels: relax muscle, isometric index finger abduction, co-activation of antagonist muscles) and type of TMS (four levels: single-pulse TMS, paired-pulse TMS with ISI of 50, 100 and 150 ms) demonstrated that both factors have significant effect on LICI ($F_{2.87}=29.03$, $p=0.00001$ and $F_{3.261}=3.103$, $p=0.027$, respectively).

The effect of the conditioning pulse on cortical silent period (cSP) in response to the test pulse is shown in Figure 4. The duration of cSP in response to the paired-pulse TMS at one and the same ISI was independent on the level of co-activation. During isometric index finger abduction and paired-pulse TMS, the mean values of cSP at all used ISIs were significantly shorter compared to single-pulse TMS. The shortening of cSP recorded in response to paired-pulse TMS was gradual with increasing of ISI from 50 to 150 ms. In contrast, during coactivation, the duration of cSP was almost independent of the value of ISI and similar to the duration of cSP in response to single-pulse TMS (Fig.4).

Discussion

The effect of tonic muscle activity on long-latency intracortical inhibition

In the present study, at relaxed muscle LICI was not evident at ISI 50 ms. Further with increasing of ISI, LICI became significant and was stronger at ISI 150 ms. In contrast, during tonic muscle contraction, LICI was significantly stronger at shorter ISIs (50 and 100 ms).

In our pervious study, using paired-pulse TMS with short ISIs (3 and 13 ms), we had found that the effect of tonic muscle activity on intracortical facilitation and short-latency intracortical inhibition was independent on the level of co-activation of antagonist muscles [13]. In the present study, at shorter ISI, LICI was significantly stronger during isometric index finger abduction compare to antagonistic co-activation. The level of LICI during coactivation practically was independent of ISI between the conditioning and the test stimulation. Thus, the antagonistic co-activation is accompanied by reduction of LICI. Up to our knowledge this is the first finding for significant effect of co-activation of known intracortical mechanisms.

The long-latency intracortical inhibition and cortical silent period

The question of connection between LICI and cSP is still open. Chen [14] proposed a hypothesis that LICI and cSP reflect respectively the intensity and the duration of one and the same inhibitory process. Wassermann et al. [15] also found that the offset of LICI coincide with the end of cSP. Furthermore pharmacological studies demonstrated that both processes reflect post-synaptic GAB AB inhibition [16]. Some other authors founded different modulation of LICI and cSP during application of some pharmacological substrates [17] in patient investigations [18] and during muscle fatigue [19]. The author's interpretation is in favor of different mechanisms for both inhibitory processes.

Using paired-pulse stimulation with short ISIs which induce short-latency intracortical inhibition recently have been published results that demonstrate the effect of cSP [20]. In the present study using single-pulse TMS we found shorter duration of cSP during co-activation of antagonists muscles compared to isometric index finger abduction. This result is in line with the other finding that LICI is also reduced during antagonistic co-activation. At paired- pulse TMS the duration of cSP depends on ISI during abduction. At paired-pulse TMS the duration of cSP is independent of ISI during co-activation. Our results are in support of the hypothesis that both inhibitory mechanisms are identical.

Conclusions

The main finding of our study is that during co-activation of antagonist muscles LICI as well as the duration of cSP are significantly reduced compared to isometric index finger abduction.

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