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Short Communication

INTERHEMISPHERIC MOTOR CORTEX INFLUENCE DURING BIMANUAL UNLOADING

VERA L. TALIS*, OLEG V. KAZENNIKOV and IRINA A. SOLOPOVA

Laboratory of Neurobiology of Motor Control
Institute for Information Transmission Problems
Russian Academy of Science, Moscow, Russian Federation
**talis@iitp.ru*

MARAT E. IOFFE

Institute of Higher Nervous Activity and Neurophysiology
Russian Academy of Science, Moscow, Russia
labdo@mail.ru

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Using the transcranial magnetic stimulation (TMS) of motor cortex we examined changes in the motor evoked potential (MEP) during natural bimanual unloading, during lifting of an equivalent weight by the contralateral arm while the ipsilateral forearm was held stationary (CONTRA) and during practice of unnatural unloading. During natural unloading, MEP amplitude decreased proportionally to the muscle activity. In CONTRA task MEP amplitude decreased, but the muscle activity was not changed. It suggests that the motor cortex activity related to the "postural" arm was inhibited by the contralateral motor cortex related to the "lifting" arm. This inhibition was diminished during the unloading task. When learning the unnatural unloading, the muscle activity decreased significantly with insignificant changes of MEP amplitude. Active role of the motor cortex during learning of the new task might be related to the reduction of the contralateral inhibition. This suggestion is supported by the observation that MEP amplitude decreased stronger than muscle activity in the first learning session similar to that in CONTRA task. MEP amplitude and background activity of the muscle proportionally decreased in the last learning trial. The results show that motor cortex activity in natural and unnatural unloading task might be related to the reduction of the interhemispheric inhibition.

Keywords: Bimanual unloading; anticipatory postural adjustment; transcranial magnetic stimulation.

1. Introduction

The role of the motor cortex in premovement adjustment is being intensively studied [1, 2]. It was found that the corticospinal influences were not important in well-known movements and were expressed only during the formation of such adjustment that followed the learning of a new motor task [3–5]. This suggestion was based on

analysis of the difference in the changes of muscle activity and the amplitude of muscle potential evoked by stimulation of the motor cortex [4].

Voluntary activation of a contralateral homologous muscle group changes motor responses to a TMS stimulus, probably via interhemispheric inhibitory pathways [6]. Reports on these changes, however, have been controversial, including the facilitation, inhibition, or both, depending on the level of voluntary muscle activation and the type of muscle contraction [6].

This study was focused on the possible effects of practice on interhemispheric effects during the anticipatory postural adjustments (APA). Based on results of previous studies [3, 4], we hypothesized that the active role of the motor cortex in APA might exert an influence on the contralateral inhibition. To evaluate the role of the motor cortex in APA in the preceding paper we investigated the motor potential (MEP) evoked by transcranial magnetic stimulation (TMS) in forearm flexor at the time of natural and artificial bimanual unloading. Therefore, the aim of this paper is to reanalyze the data with special focus on the changes of interhemispheric inhibition.

2. Methods

2.1. *Natural unloading*

A group of eight healthy right-handed volunteers (23–52 years old, 3 females and 5 males) participated in the study. The subject sat comfortably in an armchair with eyes closed. The instruction to the subject was to hold the right forearm and the wrist horizontally in a semi-prone position against a one kilogram weight suspended in a basket. The basket was fitted with a handle for lifting. In the case of "active unloading" (ACT), the subject placed the index finger and thumb of the left arm near the handle and closed his/her eyes. Upon hearing a signal ("beep"), the subject grasped the handle with left index finger and thumb and lifted the basket.

The handle on the basket was equipped with a force sensor to measure the grip force. Another sensor between the box and the forearm measured the force acting on the forearm. Surface EMG was recorded from *musculus biceps brachii* of the right forearm.

In the active unloading task, the TMS stimulus was triggered by the thumb and index finger touching the handle. The moment of the touch was obtained from the derivative of grip force signal after 4 Hz filtering. For active unloading, TMS was delivered at the moment of the touch (ACT-0), 20 ms (ACT-20), and 40 ms (ACT-40). The MEP amplitude was measured offline by calculating the EMG peak-to-peak amplitude in the interval from 15 ms to 40 ms after the stimulus.

During the active unloading task, the left hand grasped and lifted the weight. Such manipulation is associated with enhanced activity in the right motor cortex which could influence the excitability of the left motor cortex. Thus, interhemispheric motor cortex interaction was examined in the additional "contralateral" task in

which the subject constantly supported the weight with the right arm and lifted another equivalent weight with the left hand (CONTRA).

Because EMG activity was significantly changed during active unloading, the background activity in this task was calculated as the mean value of rectified EMG activity in the interval 5–15 ms after the stimulus for each trial. The background activity in CONTRA task was measured in 50 ms interval before the stimulus for each trial. In summary, TMS was delivered in four different tasks: (1) active unloading (ACT-0, ACT-20, ACT-40), (2) the stationary loaded arm (LOAD), (3) the stationary unloaded arm (NO LOAD), and (4) the contralateral task (CONTRA). In order to pool data across subjects, the background activity in the LOAD trials, averaged across all trials, was considered to be 100%. The background activity in each of the other series was expressed as the percentage of this value. In order to compare the MEP response across subjects, the MEP amplitude averaged across all LOAD trials was considered to be 100% and the response in other tasks was normalized to this value.

2.2. *Unnatural unloading*

A group of eight healthy right-handed volunteers (33–55 years old, 8 males) participated in the study. The experimental set up was equal to "natural unloading", but the basket was loaded by one kilogram weight by means of electromagnet. Another one kilogram weight was firmly fixed to the left forearm, which was lying on the table. In the experimental condition (learning), the subject was instructed to lift the left forearm in reply to "beep" as fast as possible. Lifting triggered the release of electromagnet and the load release from the right forearm (To).

The learning process consisted of three tasks (LEARN1, LEARN2, LEARN3), with 20 trials each. Inter-trial interval was 5–7 s, intervals between sessions were 5–7 min. There were also two other tasks, where electromagnet was continuously "on": (1) subject held the forearm in horizontal position with one kilogram weight (Stationary loading, LOAD), (2) subject stationary held the postural forearm in horizontal position with one kilogram weight and contralateral forearm lifted one kilogram weight (CONTRA).

2.2.1. *Transcranial Magnetic Stimulation (TMS)*

TMS was delivered by a Mags1 (Schwarzer, Germany, maximum output: 2T) using a 9 cm round coil. The stimulation intensity was set at 40–50% of maximum stimulator output and this intensity was used throughout the whole experiment. During the LEARN sessions TMS was delivered at To. In LOAD session TMS was delivered at 500 ms after the start of recording. TMS was delivered during the first five trials of LEARN1 and last ten trials of LEARN3 sessions. CONTRA task before learning consisted of five trials with TMS. TMS was also applied during the first five and last five trials in LOAD sessions.

2.2.2. *Data analysis*

In order to calculate the degree of muscle activity depression before unloading, the activity of EMG in the interval of 5–20 ms before To (BG2) and in the interval of 200–450 ms before To (BG1) were compared. The effect of practice was assessed by analyses of two blocks of trials, trials 1–20 (LEARN1) and trials 41–60 (LEARN3). Changes in biceps muscle TMS-response in LEARN1, LEARN3, LOAD and CONTRA sessions were quantified by means of two indexes: MEP amplitude and background activity of biceps muscle (BG2). The MEP amplitude was measured by calculating the peak-to-peak amplitude of EMG signal in the interval from 15 ms to 50 ms after the stimulus. In order to pool data across subjects for statistical analysis, the background activity in the LOAD trials, averaged across all trials of each subject, was taken to be 100%. The background activity in each of the other series was expressed as the percentage of this value. In order to compare the MEP response across subjects, the MEP amplitude averaged across all LOAD trials was considered to be 100% and the response in other tasks was expressed as the percentage to this value.

2.2.3. *Statistical analysis*

Activity of biceps muscle during learning were analyzed using one-way ANOVA (factors: number of learning sessions (LEARN1, LEARN2, LEARN3)). MEP amplitudes at the beginning (LEARN1) and at the end of learning (LEARN3) were analyzed using *t*-task. The level of statistical significance was set at 0.05.

3. Results

The amplitude of MEP changed drastically during the active unloading. The averaged data across all subjects is shown in Fig. 1(a). The MEP amplitude had already decreased by the time of handle grasp (ACT-0) to $57 \pm 27\%$ of that in the LOAD condition and remained decreased in ACT-20 and ACT-40 at $50 \pm 32\%$ and $63 \pm 33\%$, correspondingly. Background EMG activity at these times also decreased. The average background activity at ACT-0 was $64 \pm 34\%$ of the background EMG during the LOAD condition, $55 \pm 31\%$ at ACT-20 and $55 \pm 33\%$ at ACT-40. ANOVA shows that both MEP amplitude and background activity changed during active unloading ($p < 0.05$, $\mathrm{F}(4,28) = 14.48$). Post-hoc testing revealed that MEP amplitude and background activity were smaller in ACT-0, ACT-20, and ACT-40 (Tukey test, $P < 0.05$) than in LOAD. Statistical analysis of the ratio of MEP/background also did not reveal any difference between ACT-0, ACT-20, ACT-40 responses ($p > 0.31$). However, although the background EMG activity in CONTRA and LOAD tasks were equal, the amplitude of MEP in CONTRA was $30 \pm 13\%$ smaller than in LOAD task ($p < 0.05$, *t*-test). Statistical analysis of the changes in MEP amplitude and background activity of muscle between ACT-0, ACT-20, ACT-40 and CONTRA did reveal significant differences (ANOVA, $F(3, 24) = 6.76$, $p < 0.002$). Post-hoc test

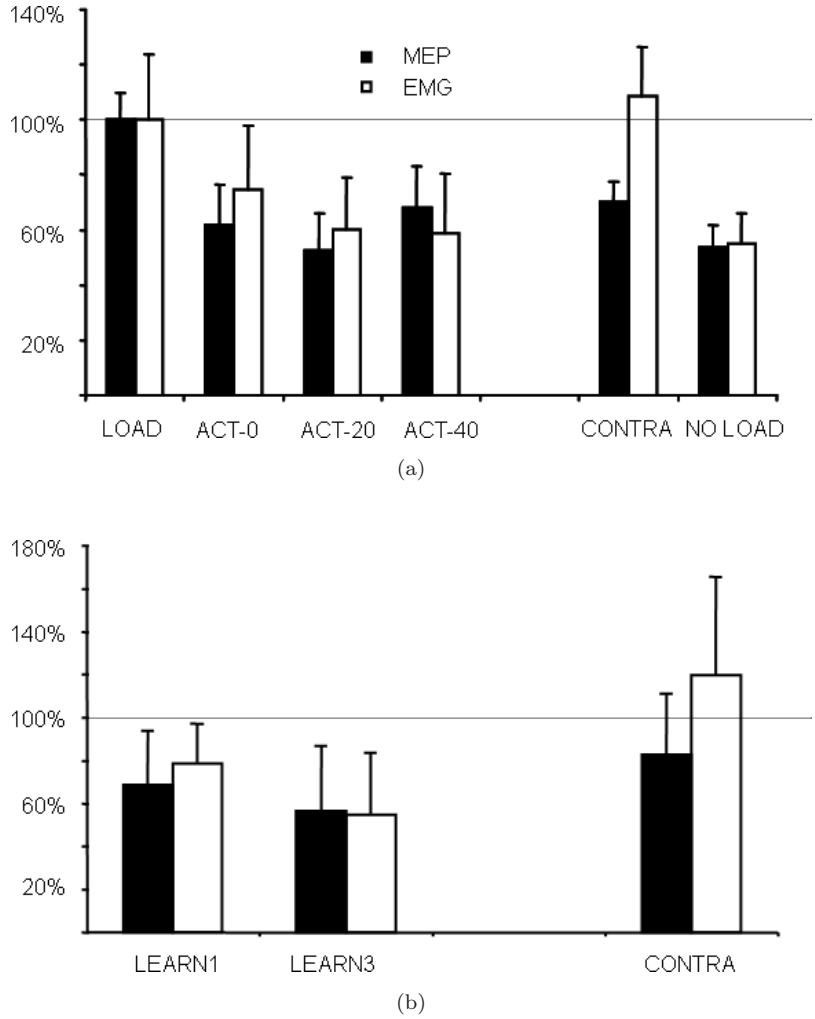

Fig. 1. MEP response and background *m. biceps* activity (EMG) during natural bimanual unloading (a) and learned bimanual unloading (b). (a) MEP and background EMG in stationary tasks (LOAD, CONTRA, NO LOAD) and at different times after natural bimanual unloading start (0 ms, 20 ms, 40 ms). (b) MEP and background EMG in stationary task (CONTRA) and at different series of learning the artificial bimanual unloading task (LEARN1, LEARN3). MEP amplitude and background muscle activity were measured relative to the LOAD task considered as 100%.

showed insignificant difference between MEP amplitude in CONTRA and unloading tasks ($p > 0.05$) despite the larger level of background EMG in CONTRA task ($p < 0.05$, Tukey test). Therefore, in CONTRA task the relation between MEP amplitude and background muscle activity differed from that in ACT-0, ACT-20, ACT-40 and LOAD.

During learning the amount of EMG inhibition increased and this depression became better synchronized with the time of unloading. In the first trial of the first learning session the amplitude of biceps activity before unloading (BG2) did

not differ significantly from the amplitude of biceps activity long before unloading (BG1) ($p = 0.87$), but in the process of learning BG2 decreased significantly up to 76 ± 25, 72 ± 25 and $55 \pm 19\%$ of BG1 in LEARN1, LEARN2 and LEARN3, correspondingly (ANOVA, $F(2, 18) = 7.00$, $p < 0.05$). The activity of biceps muscles 200–450 ms before the unloading (BG1) was not changed across all three learning sessions (ANOVA, $F(2, 18) = 1.77$, $p = 0.2$). Already in the first trial of the first learning session MEP amplitude decreased up to 73% of the MEP in LOAD condition ($p < 0.05$). In the process of learning, MEP amplitude decreased in LEARN1 and LEARN3 sessions up to $69 \pm 30\%$ and $57 \pm 30\%$ of that in the LOAD condition, correspondingly; but the difference between MEP amplitudes in LEARN3 and LEARN1 sessions did not achieve the level of significance ($p = 0.28$). However, the ratio of MEP/BG2 in LEARN3 session was significantly higher than that in LEARN1 session and in CONTRA ($p < 0.05$, paired t-test). In LEARN3 session, the ratio of MEP/BG2 was approximately equal to that ratio in natural APA. Figure 1(b) shows MEP amplitude and the corresponding background EMG activity in CONTRA task and in learning sessions. The relationship between MEP and ongoing muscle activity in CONTRA task after learning corresponds to those in "natural" APA. In some subjects left arm lifting of one kilogram weight without right arm unloading resulted in an increase of right biceps muscle activity up to 40–50% of background muscle activity (BG1). Averaged across all subjects, this increase of muscle activity consisted of 19% and was not significant ($p = 0.13$). The averaged MEP amplitude in CONTRA task decreased up to 83% of the MEP amplitude in LOAD, but the difference between MEP amplitude in CONTRA and in LOAD tasks did not achieve the level of significance ($p = 0.27$). Statistical analysis of the changes of the ratio of MEP/BG2 between LEARN1, LEARN3 and CONTRA tasks did reveal significant differences (ANOVA, $F(2, 18) = 4.67$, $p < 0.02$). Post-hoc test showed that in CONTRA task the MEP/BG2 ratio was smaller than that in LEARN3 task ($p < 0.05$, Tukey test) but the difference between CONTRA and LEARN1 tasks was not significant ($p > 0.6$, Tukey test). Therefore, in CONTRA the relation between MEP and background did not differ from that in LEARN1 but did differ from LEARN3.

4. Discussion

It is known that MEP amplitude is related to both the excitability of motoneurones and activity of motor cortex. One could suggest that an anticipatory supraspinal command causes the decrease of flexor activity preceding the unloading (postural adjustment) through inhibitory interneurones. If this command is initiated from the motor cortex, one should expect an increase of the cortical excitability and, as a result, MEP increase. However, the present study revealed the opposite effect, namely, decrease of MEP amplitude. On the other hand, the decrease of MEP amplitude during lifting of a load by the contralateral arm (CONTRA task) occurred without a change in the background muscle activity in the ipsilateral forearm flexor.

This indicates, apparently, that corticospinal neurones of the motor cortex related to the "postural" arm are inhibited by the contralateral motor cortex, corresponding to the arm that lifted the load. Interhemispheric inhibition has been revealed by a number of experiments [7, 8]. This inhibition can be mediated by transcallosal connections or through subcortical structures [9].

The results of the present study show that during learning procedure MEP amplitude starts to decrease already at the beginning, in the first trial, i.e. before real learning start and before any decrease of EMG activity. Possibly, this initial suppression of the motor cortex excitability is a result of interhemispheric influence from contralateral motor cortex accompanying the command to lift the left forearm. This assumption is confirmed by a similar decrease of MEP amplitude in CONTRA task. MEP amplitude continues to decrease in the process of learning. MEP amplitude decrease during learning was not proportional to EMG activity, which is contrasted with that during natural synergy. Particularly, biceps muscle activity decreased significantly greater than MEP amplitude. As a result, the ratio of MEP/background EMG increased in the process of learning. This suggests an active involvement of the motor cortex in organization of a new EMG pattern of APA during learning forearm stabilization.

The role of the motor cortex might be related to the change of the interhemispheric inhibition in bimanual unloading. Indeed, the weight lifting by the contralateral arm in CONTRA task was accompanied by the decrease of MEP amplitude without change of the background EMG. It is likely that the decrease of MEP amplitude is a result of interhemispheric inhibition of the motor cortex. During natural bimanual unloading the change of the MEP and background muscle activity was proportional. This means that the interhemispheric inhibition was suppressed during unloading. Similar attenuation of interhemispheric inhibition was observed during learning process. In the first session (especially in the first trial), the decrease of the MEP amplitude was accompanied by a small change of the EMG, as it was observed in CONTRA task. After learning (LEARN3 task), EMG and MEP amplitude were changed proportionally in comparison to that in LOAD (Fig. 1(b)). This result shows that during learning the interhemispheric inhibition from contralateral motor cortex was diminished. It might be that the active process in the motor cortex could be related to the modulation of the interhemispheric motor cortex influences, particularly to the reduction of the inhibition from the contralateral motor cortex.

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