Neuroscience Letters 647 (2017) 117–121

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Changes in motor cortex excitability for the trained and non-trained hand after long-term unilateral motor training

Matthias Grothe[b], Karla Doppl[a], Charlotte Roth[a], Sybille Roschka[c], Thomas Platz[c], Martin Lotze[a,*]

[a] Functional Imaging Unit, Center for Diagnostic Radiology, University of Greifswald, Germany
[b] Department for Neurology, University of Greifswald, Germany
[c] BDH-Klinik Greifswald, Neurorehabilitation Centre and Spinal Cord Injury Unit, University of Greifswald, Germany

HIGHLIGHTS

- We investigated intracortical facilitation (ICF) in M1 after unilateral long term hand training.
- Motor performance improved for both hands but ICF was only altered for the untrained hand.
- The ICF-decrease is associated with a transfer of training-induced improvement of performance.

ARTICLE INFO

Article history:
Received 22 December 2016
Received in revised form 15 February 2017
Accepted 11 March 2017
Available online 19 March 2017

Keywords:
Long-term training
Excitability
TMS
ICI
Primary motor cortex

ABSTRACT

Repetitive unilateral upper limb motor training does not only affect behavior but also increases excitability of the contralateral primary motor cortex (M1). The behavioral gain is partially transferred to the non-trained side. Changes in M1 intracortical facilitation (ICF) might as well be observed for both hand sides. We measured ICF of both left and right abductor pollicis brevis muscles (APB) before and after a two-week period of arm ability training (AAT) of the left hand in 13 strongly right handed healthy volunteers. Performance with AAT-tasks improved for both the left trained and right untrained hand. ICF for the untrained hand decreased over training while it remained unchanged for the left trained hand. Decrease of ICF for the right hand was moderately associated with an increase of AAT-performance for the untrained right hand. We conclude that ICF-imbalance between dominant and non-dominant hand is sensitive to long-term motor training: training of the non-dominant hand results in a decrease of ICF of the dominant hand. The ICF-decrease is associated with a transfer of training-induced improvement of performance from the non-dominant to the dominant hand.

1. Introduction

Strong lateralization in handedness results in unbalanced representation size between the muscle representations in the primary motor cortex (M1)of either hemisphere [38,40]. This functional difference is associated with differences in M1 grey matter volume [1] and cortico-spinal tract volume favoring the dominant hemisphere [36].

Double pulse transcranial magnetic stimulation (TMS) is capable to measure intracortical facilitation (ICF) non-invasively [24]. ICF can be seen as a net facilitation consisting of a glutamatergic facilitation effect and a weaker, GABA-ergic inhibitory effect, proven by pharmacological modulation of the ICF with both glutamatergic [42] and GABA-ergic [41] drugs. Both glutamatergic and GABA-ergic properties are essential for training-induced motor plasticity, as pharmacological modulation and its influence on motor learning has been shown [5].

Inhibitory processes seem to be reduced for the dominant hand side: Ilic and colleagues [20] but also Civardi et al. [9] and Ridding and Flavel [33] reported a decreased short intracortical inhibition (SICI) in the dominant compared to the non-dominant hemisphere. Additionally, Priori et al. [32] reported a reduced duration of the silent period (M. abductor digiti minimi (ADM) and first dorsal interosseus muscle (FDI)). In contrast to inhibitory processes, intracortical facilitation (ICF) is increased on the dominant side [9,19].

---

* Corresponding author at: Functional Imaging Unit, Center for Diagnostic Radiology and Neuroradiology, University of Greifswald, Walther-Rathenau-Straße 46, D–17475 Greifswald, Germany.
E-mail address: martin.lotze@uni-greifswald.de (M. Lotze).

http://dx.doi.org/10.1016/j.neulet.2017.03.016
0304-3940/

Overall, anatomical and electrophysiological differences may contribute to asymmetries in hand performance [37] and differences in use-dependent plasticity may be the basis of some of these performance differences [20].

Repetitive motor training alters the balance of agonist and antagonist in unilateral finger movements [11,17] and an increased M1 representation of movement patterns in the hemisphere contralateral to the trained hand side [26,21]. On the other side, immobilization results in an increase of intracortical inhibition in M1 [10], shrinkage of M1-representation areas [25], and decrease of cortical grey matter [18]. Repetitive motor training results in an increase of ICF [26] and performance changes after training are positively associated with ICF increase [4,34].

In addition, intracortical facilitatory and inhibitory processes are also relevant on the level of interhemispheric interactions: The dominant left hemisphere exerts greater inhibition on the non-dominant hemisphere in both right and left handed people [3,14].

Training is capable to modulate both intra- and interhemispheric excitability. For moderate motor training, only a few studies on ICF changes have been published: a 30 min' serial reaction time training with the right hand had no effect on ICF in a previous trial [6] but showed a performance transfer to the non-trained hand. Knowledge about intracortical facilitation changes after longer training periods (i.e. multiple days to weeks) would be advantageous for motor rehabilitation. However, such studies have not been reported.

Aim of our study was to investigate the modulation of the ICF in either hemisphere after unilateral, repetitive, long-term motor learning. We therefore asked healthy strongly right-handed participants to train their left non-dominant hand with a comprehensive hand motor training (arm ability training; [28]) for two weeks one hour a day. We used a comprehensive motor training that had clinically been validated for stroke patients with mild paresis [29,30], since observed changes in ICF with such a training could well be relevant for our understanding of complex, prolonged and clinically relevant motor training conditions. We hypothesized to find changes in the interhemispheric balance in the ICF of both the trained and the untrained hand. In addition, we tested whether ICF-changes are associated with changes in AAT-performance after training.

2. Material and methods

2.1. Participants

Thirteen participants (23 ± 3.5 years; 6 women) underwent a two-week arm ability training (AAT) for their left, non-dominant hand for one hour per day [28]. They were all strongly right-handed [average score of the Edinburgh Handedness Test [27]: mean laterality quotient (LQ) ± standard deviation (SD): 93.53 ± 5.5; range: 88–100]. All participants were healthy, without any neurological or cardio-vascular disease and were not taking any regular medication (except contraception). Participants were recruited by an announcement posted at the University. Full written consent was obtained from all participants in accordance to the Declaration of Helsinki. The study was approved by the ethics committee of the Medical Faculty of the University of Greifswald.

2.2. Training

All participants undertook an arm ability training (AAT) for their left, non-dominant hand for two weeks (training over 6 days a week and one day break). The training consisted of eight different motor tasks (aiming, steadiness (nuts and bolts), finger tapping (thumb, index and middle finger), finger dexterity (manipulate small wooden objects and turn metal coins), manual dexterity (manipulate large objects with hands and arms), and visuomotor tracking (crossing circles and following a labyrinth precisely under continuous visual control)). Improved performance was indicated by a reduced performance time, because the accuracy demands of the tasks were kept constant. Time needed to complete a motor task was recorded and fed back graphically via a computer by means of a specific software (Arm Ability software). The training has been performed by all participants in the same standardized manner with two runs of repetitive task training in a fixed sequence twice a day.

2.3. TMS

TMS was measured on the day before training started and on the day after training finished. Participants were seated comfortably on a reclining chair. Focal TMS was delivered to the optimal scalp position for activation of the musculus abductor pollicis brevis (APB) of each hand using a figure-of-eight coil connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK). The coil was placed tangentially to the scalp with the handle pointing backward and rotated away from the midline by approximately 45°. The current induced in the brain was posterior-anterior approximately perpendicular to the line of the central sulcus. The position was marked on the scalp to ensure identical coil placement throughout the experiment. Resting motor threshold (rMT) and intracortical facilitation (ICF) were used as measures of corticomotor excitability. Motor evoked potentials (MEP) were recorded from silver chloride surface electrodes overlying the APB of each hand. Relaxation was monitored by continuous visual feedback of the EMG signal amplified to 500 times. After amplification and band-pass filtering (20–500 Hz; CED 1902 Signal Conditioner, Cambridge Electronic Design, Cambridge, UK) the EMG-signal was digitized at 1 kHz (CED micro 1401 mkII, CED) and stored on a laboratory computer for off-line analysis (Signal, CED). The rMT for each hand was defined as the minimum stimulus intensity that produced MEPs $>50\,\mu V$ in at least five of ten consecutive trials [34]. A paired conditioning-test stimulus technique [24] was used to study ICF in the APB. The test stimulus intensity was adjusted to 120% rMT of the APB. The conditioning stimulus was set to 80% rMT of the APB. This low intensity stimulus does not produce changes in the excitability of spinal motorneurons [24], so that any changes in the size of the control MEP elicited by the conditioning stimuli are attributable to intracortical mechanisms [15]. An interstimulus interval (ISI) of 10 ms and a test stimulus alone were presented intermixed in a pseudorandomized order and were applied 10 times each according to techniques previously described to measure corticomotor excitability. MEP amplitudes were subsequently measured off-line peak-to-peak from single trials. MEP amplitudes obtained by combining the test stimulus with the conditioning stimulus were expressed relative to the MEP amplitudes elicited by the test stimulus alone [16].

2.4. Statistical analyses

Motor performance increase was expressed as changes in task completion time in seconds averaged over all 8 AAT-tasks. Normal distribution of data was tested using Shapiro-Wilk test. Since performance increase was violating normal distribution (performance changes left: $p < 0.04$), non-parametric tests were used. Wilcoxon tests were calculated for comparisons between pre and post measures of AAT-tasks and ICF measures. Spearman correlations were calculated for changes in ICF and overall averaged AAT-performance. Effect size was given as eta squared (η^2). Statistical comparisons were done with SPSS (Vs. 21.0.0; IBM).