YNIMG-12853; No. of pages: 12; 4C: 2, 4, 6, 7, 8, 9

NeuroImage xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

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

Upregulation of cortico-cerebellar functional connectivity after motor learning

Saeid Mehrkanoon [a,*,1], Tjeerd W. Boonstra [b,c,*,1], Michael Breakspear [c,d], Mark Hinder [a], Jeffery J. Summers [a,e]

[a] School of Medicine Human Motor Control Laboratory, University of Tasmania, Private Bag 51, Hobart TAS 7001, Australia
[b] Black Dog Institute, University of New South Wales, Randwick, Sydney, NSW 2052, Australia
[c] QIMR Berghofer Medical Research Institute, Brisbane, QLD 4006, Australia
[d] Metro North Mental Health Service, Brisbane, QLD 4006, Australia
[e] Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool L3 5UA, UK

ARTICLE INFO

Article history:
Received 21 August 2015
Accepted 30 December 2015
Available online xxxx

Keywords:
Neural plasticity
Intrinsic connectivity
Motor learning
EEG source analysis
Cerebellum

ABSTRACT

Interactions between the cerebellum and primary motor cortex are crucial for the acquisition of new motor skills. Recent neuroimaging studies indicate that learning motor skills is associated with subsequent modulation of resting-state functional connectivity in the cerebellar and cerebral cortices. The neuronal processes underlying the motor-learning-induced plasticity are not well understood. Here, we investigate changes in functional connectivity in source-reconstructed electroencephalography (EEG) following the performance of a single session of a dynamic force task in twenty young adults. Source activity was reconstructed in 112 regions of interest (ROIs) and the functional connectivity between all ROIs was estimated using imaginary part of the coherence. Significant changes in resting-state connectivity were assessed using partial least squares (PLS). We found that subjects adapted their motor performance during the training session and showed improved accuracy but with slower movement times. A number of connections were significantly upregulated after motor training, principally involving connections within the cerebellum and between the cerebellum and motor cortex. Increased connectivity was confined to specific frequency ranges in the mu- and beta-bands. Post hoc analysis of the phase spectra of these cerebellar and cortico-cerebellar connections revealed an increased phase-lag between motor cortical and cerebellar activity following motor practice. These findings show a reorganization of intrinsic cortico-cerebellar connectivity related to motor adaptation and demonstrate the potential of EEG connectivity analysis in source space to reveal the neuronal processes that underpin neural plasticity.

Introduction

Neural plasticity is the ability of the brain to adapt its intrinsic functional organization to environmental changes and pressures, physiologic modifications and experiences (Pascual-Leone et al., 2005). Motor skill learning is a paradigmatic example of neural plasticity (Karni et al., 1995; Sanes and Donoghue, 2000; Hikosaka et al., 2002; Doyon and Benali, 2005; Halsband and Lange, 2006). Analogous to perceptual learning, the acquisition of new motor skills advances through two distinct stages: a single-session improvement that can be induced by a limited number of trials and subsequent slowly evolving post-training incremental performance gains (Karni et al., 1998; Pascual-Leone et al., 2005; Luft and Buitrago, 2005; Doyon and Benali, 2005). In many instances, most gains in performance that evolve in a latent manner not during training but rather after training have ceased. The latent phase in human skill learning is thought to reflect a process of consolidation of experience-dependent changes in the cortex that are triggered by training but continue to evolve thereafter (Karni and Sagi, 1993). Fast (single session) and slow (multi-session) learning processes are thought to involve distinct neural processes: disinhibition of existing connections within neural populations may induce changes on a short timescale, whereas structural modifications of connections and synapses may subserve slow learning and memory consolidation (Karni et al., 1998; Dudai, 2004; Dayan and Cohen, 2011).

Neuroimaging studies have investigated the neural substrates of these two phases of motor learning (Ungerleider et al., 2002; Kelly and Garavan, 2005; Tomassini et al., 2011; Krakauer and Mazzoni, 2011). Fast learning of sequential motor tasks modulates regional brain activity in the dorsolateral prefrontal cortex (DLPFC), primary motor cortex (M1), and pre-supplementary motor area (preSMA) (Sakai et al., 1999; Floyer-Lea and Matthews, 2005) – which show decreased activation as learning progresses – and in the premotor cortex, supplementary motor area (SMA), parietal regions, striatum, and cerebellum – which show increased activation with learning (Honda et al., 1998; Grafton et al., 2002; Floyer-Lea and Matthews, 2005). M1 is one of the key brain regions

* Corresponding authors.
E-mail addresses: smehrkanoon@gmail.com (S. Mehrkanoon), t.boonstra@unsw.edu.au (T.W. Boonstra).
[1] The authors contributed equally to this work.

http://dx.doi.org/10.1016/j.neuroimage.2015.12.052
1053-8119/© 2016 Published by Elsevier Inc.

involved in fast motor learning. Likewise, slow learning – reflected by improved motor performance over multiple training sessions – is associated with increased activation in neuronal populations in M1 (Floyer-Lea and Matthews, 2005), primary somatosensory cortex (Floyer-Lea and Matthews, 2005), SMA (Lehéricy et al., 2005), putamen (Lehéricy et al., 2005; Floyer-Lea and Matthews, 2005), premotor cortex, supplementary motor area, parietal regions, and the cerebellum (Grafton et al., 2002; Floyer-Lea and Matthews, 2005), as well as an increase of gray matter in the supplementary motor area (Hamzei et al., 2012).

It is hence apparent that different parts of the distributed motor system, including subcortical structures such as the cerebellum and basal ganglia, are associated with motor skill learning (Karni et al., 1998; Galea et al., 2011). Therefore, understanding the functional role of multiple brain regions in motor learning requires investigation of distributed brain networks and connectivity patterns. Task-driven functional connectivity (Coynel et al., 2010) and effective connectivity (Ma et al., 2011; Tzvi et al., 2014) have indicated changes in the connections between M1 and the cerebellum during motor learning (Raymond et al., 1996; Inoue et al., 2000; Della-Maggiore et al., 2009). Alternatively, cortico-cerebellar connectivity has been indirectly assessed by evaluating changes in somatosensory-evoked potentials (SEP) or motor-evoked potentials (MEP) (Haavik and Murphy, 2013; Andrew et al., 2015; Baarbé et al., 2014). Recent resting-state fMRI studies revealed increased functional connectivity in cortical and subcortical regions after a short course of motor learning (Vahdat et al., 2011; Ma et al., 2011; Taubert et al., 2011; Tung et al., 2013; Sami et al., 2014). These findings further emphasize the involvement of the cerebellum in motor control and the consolidation of motor memory (Raymond et al., 1996; Inoue et al., 2000; Della-Maggiore et al., 2009).

Because of their superior temporal resolution, the connectivity analysis of MEG and EEG data may provide additional information about the neuronal processes underpinning the changes in intrinsic connectivity following motor skill learning. Several MEG studies have shown changes in beta-band synchronization in the motor cortex during motor learning, reflecting a modulation in cortical excitability (Boonstra et al., 2007; Houweling et al., 2008; Pollok et al., 2014). However, few studies have investigated connectivity changes in the distributed motor system using EEG or MEG. Motor-related changes in beta-band coherence have been observed in surface EEG (Deeny et al., 2009; Tropini et al., 2011). Coherence within the primary motor area in resting-state EEG has been used to predict subsequent motor acquisition in single-session motor skill learning (Wu et al., 2014). Recent studies have shown that the connectivity analysis of source-reconstructed MEG and EEG permits a better comparison to functional connectivity in fMRI data than sensor-based analyses (Mantini et al., 2007; Brookes et al., 2011; Mehrkanoon et al., 2014c). The ability to detect robust resting-state networks in source-reconstructed MEG and EEG suggests that this approach may also be sensitive to changes in intrinsic connectivity induced by motor learning. We hence performed source connectivity analysis in resting-state EEG recorded directly before and after a single session of motor skill learning. Given the prior results in fMRI connectivity analysis, we hypothesized that motor training would change the functional connectivity in the distributed motor system, in particular between the cerebellum and motor cortex. To examine this hypothesis, we compared whole-brain resting-state connectivity in source-reconstructed EEG before and after motor training and studied changes in intrinsic connectivity. By examining the frequency, phase, and temporal information of resting-state coherence, we sought to further elucidate the neuronal processes involved in neural plasticity during motor learning.

Materials and methods

Participants

Twenty healthy right-handed adults (age: 21.3 ± 1.8 years; 10 males) participated as volunteers in this study. The Human Research Ethics Committee of the University of Tasmania approved the protocol. All participants gave their informed consent according to National Health and Medical Research Council guidelines.

Experimental design

We compared intrinsic connectivity in source-reconstructed EEG before and after motor learning. For motor skill acquisition, we used a simple motor task in which participants were required to make a transition between two force levels as fast and accurately as possible. In a previous study, we have shown a reorganization in corticomuscular coherence when participants make an overshoot when reaching the second target (Mehrkanoon et al., 2014b). Here we investigated how movement accuracy changes during a single session of motor training and compared cortico-cortical and cortico-cerebellar coherence during resting-state pre- and post-motor training. The task design involved three consecutive sessions: (1) an initial 10-min resting-state session, (2) 20 motor skill training trials, and (3) a further 10 min of resting state.

Participants were seated in a light- and sound-attenuated room with their right hand on a flat panel and their forearm supported. In the resting-state conditions, participants were instructed to relax with eyes closed and refrain from falling asleep. During the motor training session, participants were required to generate force by using their index finger and thumb (i.e., a pincer grip) against a force sensor (Fig. 1C). Participants received visual feedback of the exerted force and were instructed to keep their force within pre-defined force intervals (target 1: 0.7–1.1 N, target 2: 1.9–2.3 N) displayed on a computer screen (Fig. 1A). At the start of each trial, participants had to move the cursor into target 1 and keep it in the middle of the target until they perceived an auditory stimulus (a 1-s tone at 500 Hz). Once the stimulus was finished, participants had to move the cursor into target 2 as quickly as possible by increasing the exerted force and keep it in the middle of target 2 until the end of the trial. The auditory stimulus was presented after a variable time interval (9–11 s) from the onset of the trial. The movement trajectory from target 1 to target 2 was used to quantify motor performance.

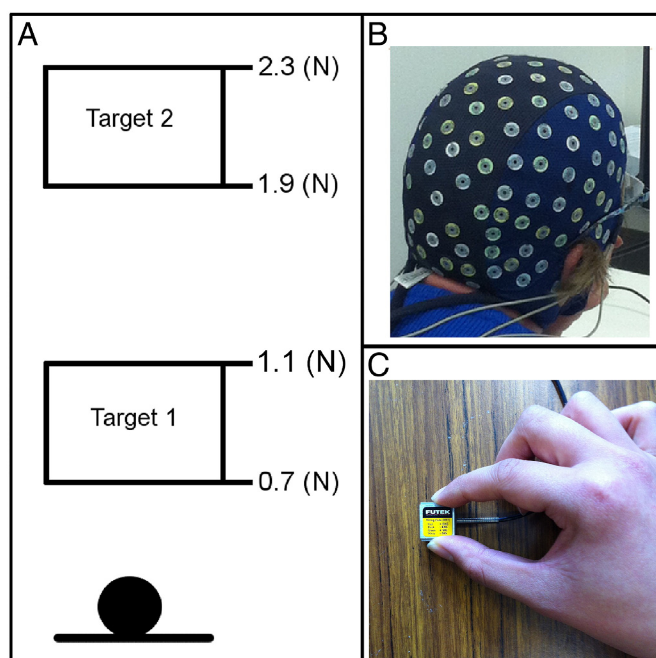

Fig. 1. Task design. (A) Diagram of the two force targets. (B) Participant with an EEG cap. (C) The force transducer. Subjects exerted force by using the index finger and thumb against the force sensor.