BRAIN RESEARCH 1576 (2014) 52–62

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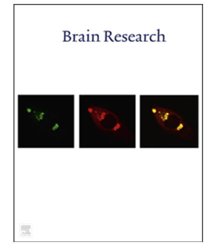

Research Report

Transcranial direct current stimulation of the premotor cortex: Effects on hand dexterity

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ARTICLE INFO

Article history:
Accepted 19 June 2014
Available online 27 June 2014

Keywords:
Transcranial direct current stimulation
tDCS
Dorsal premotor cortex
PMd
Dexterity
Strength–Dexterity test

ABSTRACT

Premotor cortex activity is associated with complex motor performance and motor learning and offers a potential target to improve dexterity by transcranial direct current stimulation (tDCS). We explored the effects of tDCS of premotor cortex on performance of a Strength–Dexterity test in healthy subjects. *Methods*: During the test a slender spring held between thumb and index finger should be compressed as much as possible without buckling. Finger forces assessed in the test provided a measure of dexterity. First, task performance was tested in 12 persons during anodal tDCS to the primary motor cortex (M1) contralateral to the performing hand, and sham stimulation. Another 12 persons participated in five sessions of anodal and cathodal tDCS over the left and the right premotor cortex and sham stimulation. *Results*: tDCS over M1 as well as over the left, but not the right premotor cortex resulted in significant improvement of performance. Performance alterations correlated positively between left anodal and right cathodal tDCS and negatively between anodal tDCS of the two sides. Effective polarity for premotor stimulation to improve task performance differed between participants. Individuals who improved with anodal stimulation used lower finger force and experienced the test as more difficult compared to those who improved with cathodal stimulation. *Conclusions*: This study demonstrates that tDCS over the left premotor cortex can improve performance of a dexterity demanding task. The effective polarity of stimulation depends on the task performance strategies. The study moreover shows a functional relevance of interactions between the left and right premotor cortex.

1. Introduction

Manipulation of objects with the fingertips, referred to as dexterity, plays an important role in daily activities (Carroll, 1993). Precise dynamic control of fingertip force magnitude and direction is crucial for performance of dexterous tasks (Birznieks et al., 2001; Johansson and Flanagan, 2009; Valero-Cuevas et al., 2003).

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http://dx.doi.org/10.1016/j.brainres.2014.06.023
0006-8993/

As shown in imaging studies, dexterity tasks require contribution of the intraparietal cortex, ventral and dorsal premotor cortex, supplementary motor area (SMA), cingulate motor areas (CMA), insula, basal ganglia and cerebellum, depending on the particular task conditions (Binkofski et al., 1999a, 1999b; Ehrsson et al., 2000, 2001; Holmström et al., 2011; Kawashima et al., 1998; Kuhtz-Buschbeck et al., 2001, 2008; Mosier et al., 2011). The dorsal premotor cortex (PMd) seems primarily engaged when motor performance is challenged either by a demanding task or by impaired motor function: activation of PMd is associated with task complexity in healthy subjects (Catalan et al., 1998; Haaland et al., 2004; Sadato et al., 1996; Winstein et al., 1997), and PMd is thought to play a compensatory role for motor task performance in neurological disorders (Bestmann et al., 2010; Konrad et al., 2002; van Nuenen et al., 2009; Samuel et al., 1997; Ward and Frackowiak, 2003). It is involved in many aspects of fine motor control including integration of multisensory movement-relevant information from the intraparietal cortex, and its translation into motor behavior (Gentile et al., 2011; Johnson et al., 1996; Wise et al., 1996; Marconi et al., 2001), motor preparation and movement selection (Kurata, 1993; Riehle and Requin, 1989), online control of movements (Gomez et al., 2000; Lee and van Donkelaar, 2006), conditional motor behavior (Kurata and Hoffman, 1994), and storage of motor sequences in spatial working memory (Catalan et al., 1998).

One of the suggested explanations of the stronger engagement of PMd in difficult tasks is the requirement for more complex planning during the preparation phase, demand for selection of several effectors and abstract organization of the movement (Haaland et al., 2004; Stinear et al., 2009). PMd is also engaged in motor learning (Doyon et al., 2003, 2009, Nitsche et al., 2010). A recent meta-analysis of fMRI studies identified the left dorsal premotor cortex as one core element of motor learning, independent of motor task type (sensory-motor or serial reaction time task) (Hardwick et al., 2013). Thus, premotor cortex, in particular PMd, is an attractive target for modulation of neural activity to improve fine motor skills. This can be accomplished by transcranial direct current stimulation (tDCS), a non-invasive method for modulation of brain activity and excitability.

tDCS induces polarity-dependent changes of cortical excitability. Anodal stimulation enhances, and cathodal stimulation diminishes cortical excitability (Nitsche and Paulus, 2001; Nitsche et al., 2003a). The suggested primary mechanism is a corresponding modulation of resting membrane potentials, as demonstrated in animal experiments (Bindman et al., 1964; Purpura and McMurtry, 1965). NMDA receptors are critical for excitability changes lasting after the stimulation, which indicates similarities with neurophysiological correlates of learning – long-term potentiation and long-term depression (Liebetanz et al., 2002, Nitsche et al., 2003a, 2003b). In addition to the local effects at the stimulation sites, modulation of functional motor networks can be induced (Polanía et al., 2012).

So far, most studies explored the effect of tDCS of M1 on motor performance. These studies demonstrate that tDCS can modulate motor performance and motor learning in healthy subjects (Nitsche et al., 2003c; Reis et al., 2008; Reis and Fritsch, 2011), and in patients suffering from neurological diseases (Nowak et al., 2009; Williams et al., 2009; Wu et al., 2008;). Data on the effect of tDCS on premotor cortex are fewer and less consistent. Anodal stimulation of premotor tDCS improved performance in a serial reaction time task, when stimulation was performed during re-consolidation in REM sleep, but not when applied during learning (Kantak et al., 2012; Nitsche et al., 2003c, 2010). Other studies indicate that different types of non-invasive brain stimulation prior to or during task performance may have an impact and suggest that modulation of PMd with excitatory stimulation improves (Stinear et al., 2009) and inhibitory stimulation impairs motor performance (Mochizuki et al., 2005; Schlaghecken et al., 2003; Schluter et al., 1998). However, more studies are needed to understand the effect of tDCS of the premotor cortex on tasks that require fine motor control.

Here we explored the effects of tDCS on dexterity in healthy subjects in a challenging task, which requires fine-tuned dynamic regulation of fingertip forces – the Strength–Dexterity test (Dayanidhi et al., 2013; Valero-Cuevas et al., 2003). This test evaluates dynamic control of fingertip forces during compression of slender springs, where the spring becomes increasingly unstable and requires better dynamic force regulation as it is compressed (Dayanidhi et al., 2013; Mosier et al., 2011; Valero-Cuevas et al., 2003; Venkadesan et al., 2007). Ability for dynamic force regulation and dexterity can therefore be expressed in fingertip forces which can be sustained during compressions (Dayanidhi et al., 2013; Venkadesan et al., 2007). Two force sensors are attached to the spring end-caps and records fingertip forces during spring compressions. These forces serve as a measure of dexterity. Higher forces in fingertips which can be sustained during compressions reflect better dynamic force regulation and correspond to higher dexterity (Dayanidhi et al., 2013).

An initial experiment tested the sensitivity of the Strength–Dexterity test to modulation by tDCS by use of anodal and sham tDCS applied to M1 contralaterally to the dominant task-performing hand. In the main experiment we investigated the effect of anodal or cathodal tDCS applied over the right and left premotor cortex on Strength–Dexterity test performance. Since bilateral activation of the premotor cortex is often observed during performance of dexterous tasks (Holmström et al., 2011; Kawashima et al., 1998; Mosier et al., 2011), we hypothesized that anodal stimulation of both, right and left premotor cortex, improves performance of fine motor skills, whereas cathodal tDCS was expected to have none or a negative effect.

2. Results

2.1. *Experiment 1*

No adverse effects of tDCS were reported by the subjects. Participants could not distinguish between real and sham stimulation (according to the results of the questionnaire) (Sign Test, $Z=-0.5$, $p=0.6$). However, they experienced the task as easier when anodal tDCS of the primary motor cortex contralateral to the performing hand was applied compared to sham stimulation (Sign Test, $Z=2.27$, $p=0.023$). No significant differences were revealed for the amount of sleep during the night before the respective sessions, the ability to concentrate, the amount and the last time of coffee