Neuropsychologia 71 (2015) 46–51

Contents lists available at ScienceDirect

Neuropsychologia

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

Enhancing the mirror illusion with transcranial direct current stimulation

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ARTICLE INFO

Article history:
Received 25 November 2014
Received in revised form
3 February 2015
Accepted 17 March 2015
Available online 19 March 2015

Keywords:
Mirror therapy
Mirror feedback
Reaching
Transcranial direct current stimulation

ABSTRACT

Visual feedback has a strong impact on upper-extremity movement production. One compelling example of this phenomena is the mirror illusion (MI), which has been used as a treatment for post-stroke movement deficits (mirror therapy). Previous research indicates that the MI increases primary motor cortex excitability, and this change in excitability is strongly correlated with the mirror's effects on behavioral performance of neurologically-intact controls. Based on evidence that primary motor cortex excitability can also be increased using transcranial direct current stimulation (tDCS), we tested whether bilateral tDCS to the primary motor cortices (anode right-cathode left and anode left-cathode right) would modify the MI. We measured the MI using a previously-developed task in which participants make reaching movements with the unseen arm behind a mirror while viewing the reflection of the other arm. When an offset in the positions of the two limbs relative to the mirror is introduced, reaching errors of the unseen arm are biased by the reflected arm's position. We found that active tDCS in the anode right-cathode left montage increased the magnitude of the MI relative to sham tDCS and anode left-cathode right tDCS. We take these data as a promising indication that tDCS could improve the effect of mirror therapy in patients with hemiparesis.

1. Introduction

The influence of visual feedback on upper extremity movement production is well documented (Desmurget et al., 1998). One compelling application of this finding comes from mirror therapy (MT) as it is used to treat post-stroke hemiparesis. Originally developed as a treatment for phantom limb pain (Ramachandran and Altschuler, 2009), MT involves the patient being seated in front of a vertically-oriented mirror (Fig. 1). The patient places her unimpaired arm on the reflective side of the mirror and her impaired arm behind the mirror so that it is hidden. When the mirror is placed midway between the two limbs, movements of the unimpaired limb (viewed in the mirror) appear in the same location as the impaired limb. Thus, the MT setup creates a compelling illusion in which movements of the impaired arm behind the mirror appear to be made as effectively as the unimpaired arm.

Although previous clinical research indicates that MT is efficacious (Thieme et al., 2013) the underlying neural changes associated with MT are poorly understood. Because MT-like effects can also be observed in neurologically-intact controls (which we will term the "mirror illusion," or MI, to differentiate it from the therapeutic use of the mirror setup), several studies have examined the possible neural mechanisms of the MI. Many of these studies, as well as studies of stroke survivors, suggest that mirror feedback modifies functioning within the primary motor cortex of the hemisphere that controls the arm *behind* the mirror (the lesioned hemisphere in stroke survivors). In controls, the MI increases primary motor cortex excitability (Garry, et al., 2005) and this change in excitability is strongly correlated with the mirror's influence on movements of the arm behind the mirror (Nojima et al., 2012). These changes in excitability may come about via intra- or inter-hemispheric neuroplasticity (Hamzei et al., 2012; Nojima et al., 2012). In stroke survivors, effective connectivity between the primary motor cortex and the somatosensory cortex in the lesioned hemisphere is increased under single-session MT conditions (Saleh et al., 2013) and completing 6 weeks of MT increases BOLD activation of the lesioned hemisphere's primary motor cortex relative to the intact hemisphere's primary motor cortex (Michielsen et al., 2011).

While many studies indicate that the mirror feedback in the MI and during MT primarily changes neural functioning within the hemisphere controlling the hand behind the mirror, conflicting findings have been reported. For example, increased reliance on regions within the hemisphere controlling the *visible* hand have

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http://dx.doi.org/10.1016/j.neuropsychologia.2015.03.017
0028-3932/

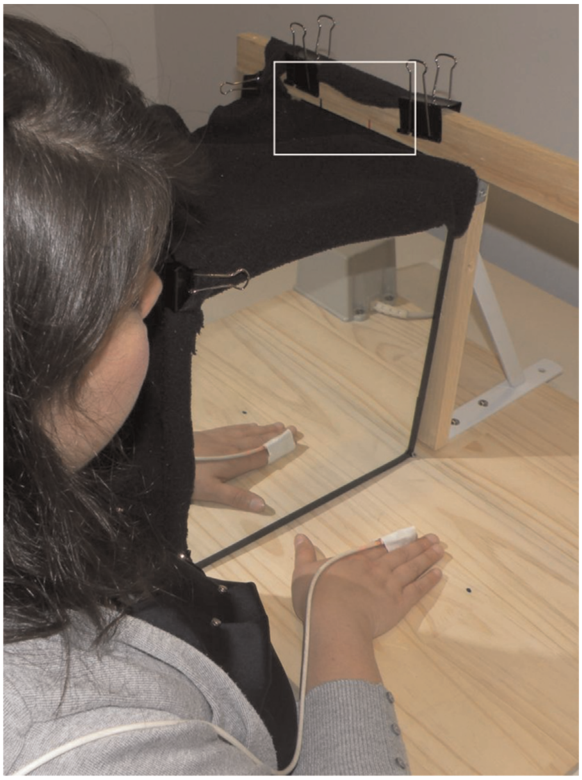

Fig. 1. Reaching task setup. The participant's right hand covers the near (R1) start location, while the dot indicating the R2 start location is visible to the right of the hand. The white box above and to the left of the mirror highlights the two dots that indicated the position of the imagined target locations along the platform, which the participant reached for with the unseen left hand.

been reported using TMS (Läppchen et al., 2012) and neuroimaging (Hamzei et al., 2012) methodologies. In addition, all of the studies cited in the previous paragraph except one (Michielsen et al., 2011) involved *no* movement of the hand behind the mirror. These conditions differ from those typically used during MT, in which patients attempt to move both limbs simultaneously (Dohle et al., 2009; Michielsen et al., 2011). It is unknown whether the neural changes associated with uni- and bi-manual MT/MI are different, but one study in patients suggests that these conditions can lead to different behavioral outcomes (Selles et al., 2014).

Thus, to date there is conflicting evidence about the neural mechanisms of MT. Resolving this conflict may have significant therapeutic significance, as understanding these mechanisms could be used to augment MT's endogenous neural changes with exogenous non-invasive brain stimulation such as transcranial direct current stimulation (tDCS). The present study was designed to provide an initial step towards this goal by testing whether applying tDCS to the two primary motor cortices would affect the MI in neurologically-intact controls. Given our goal of applying the results of this study to post-stroke rehabilitation, we wanted to examine the effects of tDCS on motor performance when bimanual movements were sometimes required. To do so, we utilized a task developed by Holmes and Spence (2005) to elicit the MI. Participants began by making symmetric bilateral movements within the mirror setup. Then, participants made a reaching movement with the unseen left arm (behind the mirror) while viewing the reflection of the stationary right arm. When an offset in the positions of the two limbs relative to the mirror was introduced, the unseen hand's trajectory was biased as if it were starting nearer the position of the mirror-reflected right hand, an effect not observed when the mirror was covered. A more detailed description of how the task allowed quantification of the MI will be provided in the "Predictions" section below.

We used this task as an index of the effect that applying bilateral primary motor cortex tDCS had on the MI. Previous research indicates that anodal tDCS increases primary motor cortex excitability whereas cathodal tDCS decreases excitability (Nitsche and Paulus, 2000). If tDCS' effects on primary motor cortex excitability are similar to those reported from the MI (Garry et al., 2005; Nojima et al., 2012) then applying tDCS during the task should affect the MI. Predictions about the effect of tDCS depend on the presumed site of the MI effect and the tDCS montage. If one assumes that the MI results in increased excitability within the hemisphere primarily controlling the hand *behind* the mirror (the right hemisphere in the present study), then applying anodal stimulation to the right hemisphere and cathodal stimulation to the left hemisphere should increase the MI. Similarly, reversing the polarity of stimulation (right cathode-left anode) should reduce the MI. In contrast, if one assumes that the MI results in increased excitability within the hemisphere controlling the hand *in front of* the mirror (the left hemisphere in the present study), then the MI should be increased in the right cathode-left anode montage and decreased in the right anode-left cathode montage. The present study tested these contrasting predictions.

2. Methods

2.1. Participants

Twelve college-aged young adults [mean (s.d.) age 21.3 (2.4) years old; 5 females] completed the study. All participants were recruited through the University of Pennsylvania and received monetary compensation for their participation.

2.2. tDCS stimulation

Each participant completed three separate single-day testing sessions, each of which employed a different tDCS montage. In all sessions, two 5×7 cm^2 saline soaked electrodes were positioned over C3 and C4 of the International 10–20 EEG placement system. Within each session, a Magstim tDCS stimulator provided 1.5 mA of current in one of three montages: (1) right cathode-left anode, (2) left cathode-right anode or (3) sham. In the sham montage the same electrode locations were used (half of participants had right cathode-left anode, half had left cathode-right anode) but with a 30 s ramp up then 30 s ramp down of 1.5 mA simulation to provide tactile sensations similar to the other montages. Stimulation began at the start of each reaching task and continued until the task was complete (approximately 20 min). Each session was separated by at least two weeks to minimize any carry-over effects of both tDCS and the reaching task.

2.3. Reaching task

Within each session, participants completed the same reaching task. Participants sat slightly to the right of the vertically-oriented mirror (30 cm × 30 cm) so they could see the reflection of their right arm in the mirror (Fig. 1). Vision of the left arm was occluded by the mirror as well as by black fabric draped between the front of the apparatus and the participant's left shoulder. Each trial began when the experimenter instructed the participant to place his or her right index finger on one of two starting positions indicated by a red and blue dot on the platform (9 and 16 cm to the right of the mirror; approximately 19 cm in front of the participant's body). Next, the experimenter moved the participant's left arm to one of the four left hand start positions (9, 16, 23 and 30 cm to the left of the mirror; approximately 19 cm in front of the