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Transcranial direct current stimulation (tDCS) of the inferior frontal gyrus disrupts interpersonal motor resonance

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ABSTRACT

Interpersonal motor resonance (IMR) is presumed to result from activity within the human mirror neuron system, which itself is thought to comprise the inferior parietal lobule (IPL) and inferior frontal gyrus (IFG). Twenty healthy adults underwent anodal, cathodal, and sham transcranial direct current stimulation (tDCS) to either IPL or IFG immediately before the assessment of IMR (using transcranial magnetic stimulation). IMR (i.e., motor-evoked potential amplitude during transitive action observation relative to static observation) was significantly reduced following both anodal and cathodal stimulation of IFG (relative to sham), but there was no effect of stimulation for IPL. These data support the role of IFG, a presumed mirror neuron region, in IMR.

1. Introduction

Interpersonal motor resonance (IMR) describes the activation of an individual's motor system during the observation of another's behaviour (Uithol, van Rooij, Bekkering, & Haselager, 2011), that is, during the observation of an action by another the visual representation of action is presumed to be 'mapped' onto the motor representation of that particular action (Rizzolatti & Craighero, 2004). IMR has been assessed using a variety of methods. When using transcranial magnetic stimulation (TMS), IMR is reflected in enhanced motor corticospinal excitability (CSE) during the observation of behaviour involving the stimulated muscle (Fadiga, Craighero, & Olivier, 2005). IMR is also measured behaviourally (e.g., spontaneous mimicry when observing another's facial expression) (Oberman, Winkielman, & Ramachandran, 2007; Sato & Yoshikawa, 2007).

IMR is thought to be underpinned by the mirror neuron system (MNS). Initially discovered in macaque monkeys (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992), mirror neurons are cortical brain cells that fire during the performance and observation of behaviour. An analogous system has since been established in humans (Rizzolatti & Craighero, 2004). While the human MNS involves a broad neural network comprising temporal, parietal, and frontal cortices, mirror neurons themselves are thought to reside in two cortical regions: inferior parietal lobule (IPL) and inferior frontal gyrus (IFG) (Iacoboni & Dapretto, 2006) (although other regions have also been implicated; Molenberghs, Cunnington, & Mattingley, 2012; Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried, 2010). With respect to TMS, action observation is thought to promote mirror neuron activity in IPL and IFG, which then inputs to M1 and increases motor CSE (Fadiga et al., 2005). Thus, any subsequent increase in CSE during action observation (relative to the observation of an appropriate static or control display) is typically interpreted as reflecting mirror neuron activity (Enticott, Kennedy, Bradshaw, Rinehart, & Fitzgerald, 2010; Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995; Gangitano, Mottaghy, & Pascual-Leone, 2001; Gangitano, Mottaghy, & Pascual-Leone, 2004; Maeda, Kleiner-Fisman, & Pascual-Leone, 2002; Theoret et al., 2005).

The extent to which IFG and IPL are involved in IMR, however, is not established, and any causal link might be best explored via brain stimulation. This includes transcranial direct current stimulation (tDCS), which is a non-invasive brain stimulation technique that involves the application of mild electrical stimulation to the scalp in order to modulate cortical excitability. Typically, anodal stimulation is associated with an increase in cortical excitability, while cathodal stimulation yields a decrease in excitability (Stagg & Nitsche, 2011). Brain stimulation support for MNS regions in measures linked to IMR comes from TMS studies. Using bilateral paired-pulse TMS, Catmur, Mars, Rushworth, & Heyes (2011) found that a conditioning pulse delivered to either dorsal or ventral premotor cortex (often included with IFG as a broader MNS region) enhanced a TMS measure of IMR. Although not directly

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assessing motor resonance, repetitive TMS to IFG in both hemispheres has also been found to disrupt motor imitation (Heiser, Iacoboni, Maeda, Marcus, & Mazziotta, 2003), while theta burst TMS to IFG (but not posterior parietal cortex) appears to disrupt automatic motor imitation (Catmur, Walsh, & Heyes, 2009). TMS to IFG has also been shown to disrupt weight-judgments of items lifted by a human hand, which was interpreted as reflecting action understanding (Pobric & Hamilton, 2006). Thus, while there has been some research looking at the effect of brain stimulation on abilities thought to arise from the MNS, there has been very little research looking at the effect of these regions on measures of putative mirror neuron activity, and none looking at the influence of IPL or tDCS.

The current study investigated the effect of tDCS to IFG and IPL on subsequent IMR (measured via TMS, with enhanced IMR indicated by greater cortical excitability during the observation of a transitive hand action relative to the observation of a static hand). It was hypothesised that anodal stimulation would enhance IMR during action observation, and that cathodal stimulation would decrease this response, thus supporting the roles of both IFG and IPL in IMR.

2. Methods

2.1. Participants

Participants were 24 healthy adults (15 females, 23 right-handed; mean age: 22.58 [SD = 5.87] [IFG group], 28.58 [SD = 8.71] [IPL group]) recruited from advertisements placed within Monash University and The Alfred hospital. Participants were screened to ensure that they met the safety requirements of TMS. All participants provided signed informed consent and were reimbursed AU$30 for each of the three sessions attended. This project was approved by the human research ethics committees of Monash University and The Alfred.

2.2. Procedure

Each participant attended three separate sessions, during which they received anodal, cathodal, or sham tDCS prior to an assessment of IMR using TMS. There were at least seven days between each session for each participant. For 10 participants, the site of stimulation was the left IPL, while for the other 10 participants the site of stimulation was the left IFG. The order of sessions was randomised, and both participants and experimenters were blind to tDCS condition (i.e., active or sham), but experimenters were not blind to polarity. This was achieved by experimenters being provided with a code to input to the stimulator (yielding either active or sham stimulation) and an instruction for either anodal or cathodal stimulation. Off-line processing of EMG signals was also blinded. tDCS and TMS procedures are described below.

2.2.1. Transcranial direct current stimulation

Twenty minutes of 2 mA tDCS was provided using a pair of saline-soaked surface sponge electrodes (35 cm^2) and a battery-driven, constant current DC-Stimulator (neuroConn). The two active conditions (anodal and cathodal) involved a fade-in over 120 s, 20 min of 2 mA stimulation, and a fade-out over 15 s. The sham condition involved a fade-in over 120 s, 30 s of 2 mA stimulation, and then a fade-out of 15 s (followed by 19 min 30 s of no stimulation).

Stimulation sites were determined according to the international 10–20 system for electrode placement sites that are presumed to lie above the relevant cortical regions. For left IPL this corresponded to position P3, and for left IFG this corresponded to one-third of the distance from F7 to C5 (Kim et al., 2007; Loui, Hohmann, & Schlaug, 2010). Anodal stimulation involved placing the anodal electrode over the IPL/IFG, while cathodal stimulation involved placing the cathodal electrode over the IPL/IFG. For each site, the second electrode was placed over the contralateral (right) supraorbital region, which is a very common reference site for stimulation of frontal and parietal cortex (Nitsche et al., 2008).

2.2.2. Transcranial magnetic stimulation

IMR was assessed via TMS of the left primary motor cortex, and the EMG recording of subsequent activity in the right first dorsal interosseous (FDI), during video presentation of static and active hands. Stimulation was achieved using a Magstim-200 stimulator (Magstim Company Ltd., UK) and a handheld figure-of-eight coil that was positioned against the scalp. EMG was recorded using self-adhesive electrodes, amplified and filtered (low pass: 500 Hz; high pass: 10 Hz) using PowerLab/4SP (AD Instruments, Colorado Springs, CO), and sampled via a CED Micro 1401 mk II analogue-to-digital converting unit (Cambridge Electronic Design, Cambridge, UK).

At the beginning of each session, TMS was used to determine both M1 and the minimum intensity required to produce a motor-evoked potential (MEP) of approximately 1 mV (mean TMS intensity: 47.71 [SD = 8.19]). This site and intensity was used to index IMR. We employed the same stimulus set as that described in Enticott et al. (2010), which involves the presentation of a static hand (with or without a mug present), a hand performing an intransitive action (i.e., pantomimed grasp) (with or without a mug present), and a hand performing a transitive action (i.e., grasping a mug). Each of the videos was presented 10 times in a quasi-random order. A single TMS pulse was administered 1000–1500 ms into each clip; for the motion conditions, this was immediately prior to contact between the thumb and index finger in the grasping motion. While we have previously found motor resonance for only the transitive action (Enticott et al., 2010, 2012), we employed the entire video sequence to offer increased variation in the stimulus presentation and thereby lessen potential habituation. The entire video sequence lasted 4 min and 39 s, which ensured that our index of motor resonance was completed within 6 min of the completion of tDCS. This was critical given the relatively short lasting effects of tDCS (Stagg & Nitsche, 2011).

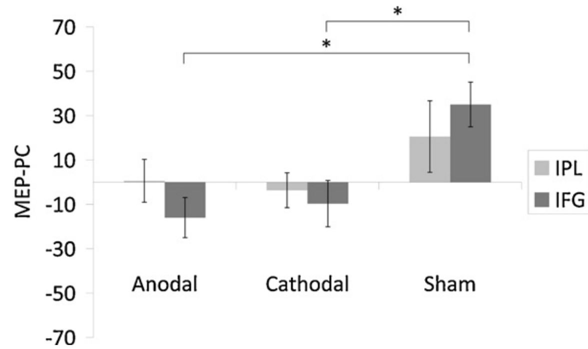

Fig. 1. MEP-PC (±SE) for the tDCS conditions. While there was the expected increase in MEP-PC following sham stimulation, this was significantly reduced (and suggestive of absent interpersonal motor resonance) following anodal and cathodal stimulation of IFG.

2.3. Data analysis

Consistent with our previous studies (Enticott et al., 2010, 2012), IMR was indexed by first extracting the median MEP amplitude for the “static hand” and “transitive hand action” conditions, and then calculating the MEP percentage change (MEP-PC):

$$\mathrm{MEP} - \mathrm{PC} = \frac{\text{transitive MEP} - \text{static MEP}}{\text{static MEP}} \times 100$$

A higher MEP-PC is indicative of greater IMR. We then conducted one-way repeated measures ANOVAs for each of the stimulation sites (IPL, IFG) examining the influence of tDCS (anodal, cathodal, sham), with MEP-PC serving as the dependent measure. Extraction of MEP amplitudes and the calculation of MEP-PC were blinded, but data analysis was not.

3. Results

There was no effect of tDCS for those undergoing IPL stimulation, $F(2, 22) = 1.49$, $p = 0.246$. There was, however, an effect of tDCS for those undergoing IFG stimulation, $F(2, 22) = 7.91$, $p = 0.003$. Paired samples t-tests (two-tailed; $\alpha = 0.017$ [simple Bonferroni]) revealed a greater MEP-PC for the sham condition relative to both anodal, $t(11) = -3.19$, $p = 0.009$, and cathodal stimulation, $t(11) = -3.15$, $p = 0.009$, but no difference between anodal and cathodal conditions, $t(11) = -0.55$, $p = 0.591$ (see Fig. 1). Inspection of mean values for those undergoing IFG stimulation reveals the expected increase above 0 in MEP-PC following sham stimulation (as there was for those undergoing IPL stimulation), which reflects IMR, but a negative value following anodal and cathodal stimulation, which reflects an absence of motor resonance.

To test whether there was a general effect of tDCS on CSE (i.e., whether IFG stimulation might directly affect motor cortical activity due to its proximity to M1, which could then affect our measure of IMR), we completed the same analysis for the IFG group with MEP amplitude (mV) during the observation of the static hand (i.e., raw baseline data) as the dependent measure. There was no effect of tDCS, $F(2, 18) = 0.43$, $p = 0.656$.