

Transcranial Alternating Current Stimulation to the Inferior Parietal Lobe Decreases Mu Suppression to Egocentric, but not Allocentric Hand Movements

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ABSTRACT

Egocentric vs. allocentric perspective during observation of hand movements has been related to self-other differentiation such that movements observed from an egocentric viewpoint have been considered as self-related while movements observed from an allocentric viewpoint have been considered as belonging to someone else. Correlational studies have generally found that egocentric perspective induces greater neurophysiological responses and larger behavioural effects compared to an allocentric perspective. However, recent studies question previous findings by reporting greater (μ) suppression and greater transcranial magnetic stimulation (TMS) induced motor-evoked potentials (MEPs) during observation of allocentric compared to egocentric movements. Furthermore, self-other differentiation has been generally related to activity within the inferior parietal lobe (IPL), but direct evidence for a causal and functional role of IPL in self-other differentiation is lacking. The current study was therefore designed to investigate the influence that IPL exerts on self-other differentiation. To this aim, we measured the impact of individually adjusted alpha-tuned transcranial alternating current stimulation (tACS) applied over IPL on μ -suppression during hands movement observation from an egocentric and allocentric perspective. Electroencephalography (EEG) was recorded during movement observation before and immediately after tACS. Results demonstrated that tACS decreased μ -reactivity over sensorimotor (but not visual) regions for egocentric (but not allocentric) movement observation providing direct evidence for a causal involvement of IPL in the observation of self-but not other-related hands movement.

Key words: EEG; tACS; self-other differentiation; perspectives; IPL

Word count: 4538

INTRODUCTION

Neuroimaging studies investigating the neural basis of self-recognition and self-other differentiation have consistently pointed to the involvement of the inferior parietal lobule (IPL) and the inferior frontal gyrus (IFG) (Chaminade & Decety, 2002; Decety et al., 2002; Farrer & Frith, 2002; Farrer et al., 2003; Kaplan et al., 2008; Ruby & Decety, 2001; Uddin et al., 2006). However, neuropsychological literature suggests that the pivotal role is rather played by the IPL. For example, individuals with schizophrenia experiencing the passivity phenomenon (the belief that one's thoughts or actions are being controlled by someone else) demonstrate IPL hyperactivity (Spence et al., 1997), while lesions to the IPL have been associated with impaired ability to imitate (Goldenberg, 1995; Goldenberg & Karnath, 2006) and with disruption of body schema and corporeal awareness (Berlucchi & Aglioti, 1997). Additionally, disruptive brain stimulation to areas within the IPL (right angular gyrus and temporo-parietal junction) results in the out-of-body phenomenon (Blanke et al., 2002; Blanke et al., 2005) and impaired performance on a self-other discrimination task (Uddin et al., 2006).

Self-other relations have frequently been studied by means of perspectives or viewpoints (e.g. David et al., 2006; Frenkel-Toledo et al., 2013; Jackson et al., 2006; Vogt et al., 2003). Typically, these studies reason that the observation of a movement presented as if the observer is conducting the movement (egocentric) is more self-related than the observation of the movement observed as if facing another agent conducting the movement (allocentric). Hence the neurophysiological response during the observation of egocentric movements is a correlate of self-related actions, while the response to an allocentric movement is related to actions conducted by others (e.g. Decety & Chaminade, 2003; Gallagher & Meltzoff, 1996; Meltzoff & Decety, 2003). Typically, correlational studies investigating perspectives as an indication of self-other differentiation have shown that egocentric stimuli induce greater neurophysiological and behavioural responses compared to allocentric stimuli. For example, it has been observed: greater cortical activity in the sensory-motor cortex (Jackson et al., 2006), greater visuomotor interference (Bortoletto et al., 2013; Vogt et al., 2003) and larger motor-evoked potentials (MEPs) as induced by transcranial magnetic stimulation (TMS) during the observation of egocentric movements (Maeda et al., 2002). However, these correlational reports have not

always been consistent; Alaerts and colleagues (2009) reported that MEPs are not necessarily larger for egocentric movements per se; rather, MEP's are larger for an egocentric right hand and for an allocentric left hand. No difference in MEPs between perspectives has also been reported by Burgess and colleagues (2013).

Furthermore, greater suppression in the EEG μ -rhythm (Frenkel-Toledo et al., 2013) and larger TMS induced MEPs (Fitzgibbon et al., 2014) have been reported during observation of allocentric hands movements compared to egocentric. In addition to these inconsistencies, causal assessment of the neurophysiological underpinning of self-other differentiation for egocentric vs. allocentric perspective is currently lacking.

In the present study, we compared EEG μ -suppression during observation of moving hands from both an egocentric and allocentric perspective subsequent to transcranial alternating current stimulation (tACS) to the IPL in order to investigate the functional relationship between μ -suppression and self-other differentiation. The rationale for this approach is that tACS interferes with ongoing oscillations non-invasively (Antal & Paulus, 2013) and has been shown to affect behavioural performance corresponding to the neuronal network or specific oscillation targeted (e.g. Miniussi et al., 2012; Cecere et al., 2015). The μ -rhythm is generated in the sensorimotor cortex and it is known that suppression in μ reflects activation of motor-related processes (Cheyne et al., 2003; Hari et al., 1998; Rossi et al., 2002). μ -suppression during observation of movement correlates with cortical activity in the IPL and IFG (e.g. Arnstein et al., 2011; Babiloni et al., 2016; Braadbaart et al., 2013), and therefore, tACS to the IPL enables a causal investigation of μ -rhythms during observation of egocentric and allocentric perspectives. Given that previous work has demonstrated reduced μ -suppression subsequent to stimulation to the IPL and IFG (Keuken et al., 2011; Puzzo et al., 2013), we predicted offline tACS over IPL to have a comparable impact. Two alternative hypotheses were made: 1) if IPL is specifically attuned to self-related stimuli (e.g. Kaplan et al., 2008; Uddin et al., 2006) then we expect tACS to selectively reduce μ -suppression during observation of egocentric (but not allocentric) movements; 2) if IPL is reactive to both self- and other-related stimuli alike (e.g. Spence et al., 1997; Goldenberg & Karnath, 2006) then we predict reduced μ -suppression following IPL stimulation regardless of perspective.

EXPERIMENTAL PROCEDURE

Participant selection

In total, 21 participants (10 females) were screened in relation to their suitability for tACS using the TMS safety screening questionnaire (TASS: Keel et al., 2001) and reported not suffering any known mental or neuropsychiatric conditions. Participants' age ranged between 18 and 35 (mean age = 23.71 SD = 4.69) and were randomly allocated to either active tACS or sham stimulation. All participants were right handed, signed the informed consent form, and were paid GB £10 for their time. The local ethics committee (Department of Psychology, University of Essex) granted ethical approval.

Stimuli

Participants observed video presentations of a female actor opening and closing her left or right hand (one at the time) at a rate of 1 Hz. These videos were based on stimuli used by several others (e.g. Bernier et al., 2007; Oberman et al., 2005; Puzzo et al., 2011; Raymaekers et al., 2009), but adapted to include both left and right hand. Two hands were included rather than one in light of Alaerts and colleagues (2009) finding that the effect of perspective may depend on the observed hand (left vs. right). The hands were visibly Caucasian skin coloured, presented against a black background, and shown from the egocentric and allocentric perspective. Images of these perspectives are presented in Figure 1 below.



Fig. 1. Graphical representation of hands from egocentric (a) and allocentric (b) perspective.

Hand movement sequences were constructed using Motion 5 (Apple Inc. version 5.1.2) video editing program. Videos included 5 sequences of various combinations of the left and right hand opening and closing. Each movement lasted 1 second x 5 movements = 5 seconds.

A schematic example of a hands movements sequence is presented in Figure 2 below.

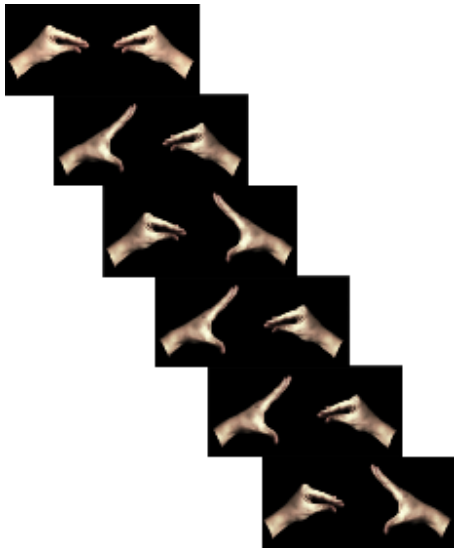


Fig. 2. Example of a hands movements sequence. Ten different egocentric and ten different allocentric sequences were presented twice in a randomised order before stimulation. A new set of ten sequences was presented twice for both the egocentric and allocentric perspective after stimulation: pre-stimulation period = 40 trials (20 x egocentric, 20 x allocentric); post-stimulation = 40 trials (20 x egocentric, 20 x allocentric).

Procedure

Participants completed an informed consent form and were fitted with electrodes to record eye movements and reference signal. Skin surface underlying electrodes for recording eye movements and reference signal were lightly abraded to reduce impedance of electrode-to-skin contact. Next, a 64-channel quick-cap (Compumedics, Neuroscan) was fitted for the EEG. Resting EEG was recorded for two minutes with eyes-open, before completing Croft & Barry's (2000) eye-movement calibration protocol. Subsequently, individual alpha frequency (IAF) was defined based on individual peaks in alpha. In order to establish IAF, the resting period was epoched to 1024 data points and subsequently the time domain data were transferred into power values in the frequency domain using fast Fourier transformation (FFT). IAF was defined based on each individual's most commonly occurring peak frequency between 8 and 12Hz over parietal and occipital electrodes (P3, P1, Pz, P2, P4, O1, Oz, O2). The occipital and parietal sites were chosen based on the rationale that alpha oscillations are strongest over these areas, and due to

numerous previous studies also using these electrodes to define IAF (e.g. Klimesch, 1999; Puzzo et al., 2013; Grandy et al., 2013; Gutman et al., 2015; Haegens et al., 2014; Cecere et al., 2015). Graphical representation and details of procedure are provided in Figure 3 below.

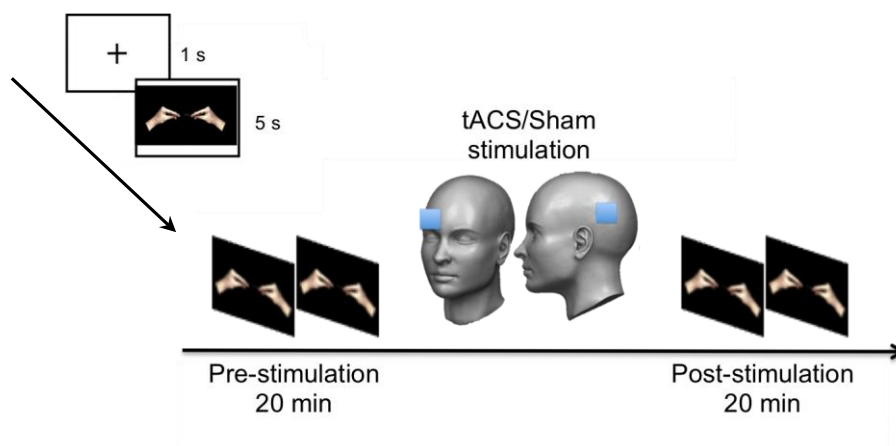


Fig. 3. Procedure. Each trial started with a 1000ms fixation cross, followed by a 5000ms video clip. Participants were assigned either to a tACS or sham stimulation condition and attended one block of 20 egocentric and 20 allocentric trials before stimulation, and another block of 20 new egocentric and 20 new allocentric trials after the stimulation period.

tACS procedure

Participants were randomly allocated to either active tACS or sham stimulation. Nine participants received sham stimulation while 11 received active tACS. Active tACS was delivered via two surface conductive-rubber electrodes (3 x 3 cm) enclosed in saline-soaked sponges sown to the inside of the EEG cap. The small size tACS electrodes were chosen to avoid overlap with more than one EEG electrode per tACS electrode. One stimulation electrode was positioned over the IPL (P3 on the 10/20 system) and the other was positioned over the contralateral frontal polar (FP2 on the 10/20 system) in line with the electrode montage used in several previous studies targeting this area (e.g. Wach et al., 2013; Moliadze et al., 2010; Nitsche & Paulus, 2000; Moliadze et al., 2012).

An alternating sinusoidal current individually adjusted (IAF) was delivered by a battery-operated stimulator system (DC-Stimulator Plus, NeuroConn GmbH,

Ilmenau, Germany). Current intensity was set to 1mA (peak-to-peak) in accordance with numerous previous studies (e.g. Wach et al., 2013; Moliadze et al., 2012) and safety protocols regarding DC and AC stimulation (Iyer et al., 2005; Nitsche et al., 2003). Impedance was kept below 10 k Ω . Active tACS was applied for 20 minutes based on work by Neuling and colleagues (2013) that indicated sustained after-effects lasting at least 30 minutes when applying 1 mA tACS for 20 minutes at IAF. The current intensity was faded-in and faded-out for 10 seconds to avoid perception of retinal phosphenes. The sham group received active stimulation for the first and last 10 seconds in order to elicit the typical tingling sensation under the electrode at the beginning of stimulation. The sham stimulation was delivered under the same parameters as the tACS group.

EEG data acquisition and preparation

EEG data were recorded using Synamps II amplifiers and SCAN 4.5 acquisition software (Compumedics, Melbourne, Australia) using 64 electrodes mounted on a quick-cap with electrodes arranged according to the extended 10-20 system. Electrodes were referenced online to an electrode on the left mastoid and grounded on AFz. Eye movements were recorded using four electrodes; above and below the left eye and on the outer canthi of each eye. Impedances for all of the electrodes were lowered to at least 10 k Ω in all electrodes before data acquisition. EEG data were sampled continuously at 1000Hz with a band-pass filter of .05 - 200Hz and a 50Hz notch filter.

Once acquired, data were visually inspected and bad electrodes were rejected on a participant-by-participant basis. Eye-movement artefacts were rejected according to methods described by Croft & Barry (2000). All data were re-referenced to a common average reference, before undergoing demodulation and concurrent filtering (zero phase-shift, 24 dB roll-off, envelope computed). The data were then epoched from -2000 to 7000ms, and trimmed 1000ms from each end to remove filter warm-up artifacts. Remaining artefacts exceeding ± 100 mV were automatically rejected in an automatic rejection sweep before event-related

desynchronization/synchronization (ERD/ERS) between the reference period (-1000ms to 0ms) and active period (0 to 5000ms) was calculated using the event-related bandpower function in Neuroscan Edit 4.4 (Compumedics, Melbourne, Australia).

Electrodes of interest included: (i) central channels (C3, C1, C2, C4), as it is well established that μ -rhythms are generated in, and recorded over sensorimotor areas (Cheyne et al., 2003; Hari et al., 1998; Rossi et al., 2002); and (ii) occipital channels (O1, O2), as control electrodes to ensure that sensorimotor α reflected motor-related processes and not activity of the visual cortex. α -rhythms originating in the occipital region are associated with visual attention processes (e.g. Foxe et al., 1998) while α -rhythms generated by the sensorimotor cortex are related to motor processes (e.g. Hari et al., 1998).

The bandwidth of interest was α (8 – 12Hz), which was further split into two sub-components: lower (α_{low} : 8 - 10Hz) and upper (α_{high} : 10 - 12Hz) because functions associated with each end of the α spectrum are known to differ (Klimesch et al., 2007; Petsche et al., 1997; Aftanas & Golocheikine, 2001).

Data analysis

Data from all participants were included for analysis. A Kolmogorov–Smirnov test of normality confirmed that the data were normally distributed ($p > .05$). In order to ensure that observing movements from egocentric and allocentric perspectives induced significant change in μ -reactivity, we compared μ -reactivity during observation of perspectives pre and post stimulation for sham and tACS with zero (zero indicating no change between reference period and active period) in one-samples t-tests. For this analysis, given that no difference across hemispheres was found, the factor hemisphere was collapsed to keep comparisons to a minimum.

Subsequently, we investigated the effect of tACS to the IPL on μ -reactivity during hands movements from an egocentric and allocentric perspective separately for sensorimotor and occipital areas (for a similar approach see e.g. Perry, Troje and Bentin, 2010). The rationale for this approach is as follows: it is known that occipital α -power (and suppression) is functionally different (Hari et al., 1998; Pineda, 2005) and demonstrates greater power (and suppression) than sensorimotor α (e.g. Perry, Stein and Bentin, 2011). Consequently, we wanted to ensure that any effects in the sensorimotor region were not shadowed by the spreading of occipital α towards sensorimotor channels. Importantly, we did not expect tACS to affect the occipital region given that occipital α is associated primarily with visual attention (e.g. Foxe, Simpson & Ahlfors, 1998), whereas μ is associated with motor processes (e.g. Hari et al., 1998) and, as more recently shown, with sense of agency (Serino et al., 2015). The ANOVAs conducted included the following factors: “time” (with two levels: pre-stimulation, post-stimulation), “perspective” (with two levels: egocentric, allocentric), “hemisphere” (with two levels: left [C3, C1], right [C2, C4]), and one between-subjects factor “stimulation condition” (with two levels: sham stimulation, active tACS). For the occipital area, the factor hemisphere included two levels: left (O1) and right (O2). It was expected to find an interaction between the factors “time”, “perspective”, and “stimulation condition” in the sensorimotor area only given that occipital regions are not motor in nature. In the event of such a finding, the following pairs were compared within groups: (a) egocentric hands movements pre-stimulation vs. post-stimulation ERD; (b) allocentric pre-stimulation vs. post-stimulation ERD. These comparisons were Bonferroni corrected.

Next, two one-way analysis of covariance (ANCOVA) were conducted to control for the possible confounding influence of pre-stimulation ERD values on post-stimulation ERD values. This analysis was done given that alpha-power demonstrates large inter-individual differences relating to age and cognitive performance (Klimesch et al., 1998). One ANCOVA was conducted for the egocentric hands movements, and the other for the allocentric hands movements. This analysis was conducted with post-stimulation μ -ERD as the dependent variable, stimulation condition as the fixed factor, and ERD values in the pre-stimulation as the covariate.

RESULTS

Sensorimotor area

The result of the one-samples t-tests indicated that the ERD observed during both egocentric and allocentric hands movements in both pre and post stimulation differed significantly from zero for both the sham and the active tACS in α_{low} (8 – 10 Hz) and α_{high} (10 – 12 Hz): all $ts(20) > 2.53$, $ps < .020$, suggesting that a significant suppression in α -power was observed during observation of hands movements relative to the reference period.

The results of the repeated measures ANOVA revealed a significant interaction between the factors time, perspective, and stimulation condition in α_{high} : $F(1, 19) = 4.72$, $p = .043$, $\eta_p^2 = 0.199$, which was only marginally significant in α_{low} ($p > .057$). Planned comparisons in α_{high} , revealed a significant change explained by a reduced μ -suppression pre to post for the tACS group during observation of egocentric hands movements ($p = .014$), but not during any other pair ($ps > .153$). This result is presented in Figure 4a and suggests that tACS was effective in reducing μ -suppression. Additionally the impact of tACS was selective for egocentric hands movements, suggesting a selective involvement of IPL in egocentric (but not allocentric) hands movements.

The results of the ANCOVA for the egocentric hands movements yielded a significant effect for both the covariate (pre-stimulation ERD values): $F(1, 19) = 6.67$, $p = .019$, $\eta_p^2 = 0.270$, and the stimulation condition: $F(1, 19) = 12.44$, $p = .002$, $\eta_p^2 = 0.409$, further confirming that tACS significantly reduced α_{high} -ERD during observation of egocentric hands movements. The ANCOVA for the allocentric hands movements did not reveal a significant effect for either the covariate or the stimulation condition ($ps > .308$) again confirming previous analysis showing no modulation of ERD in α_{high} by tACS during allocentric hands movements. This result is presented in Figure 4b below.

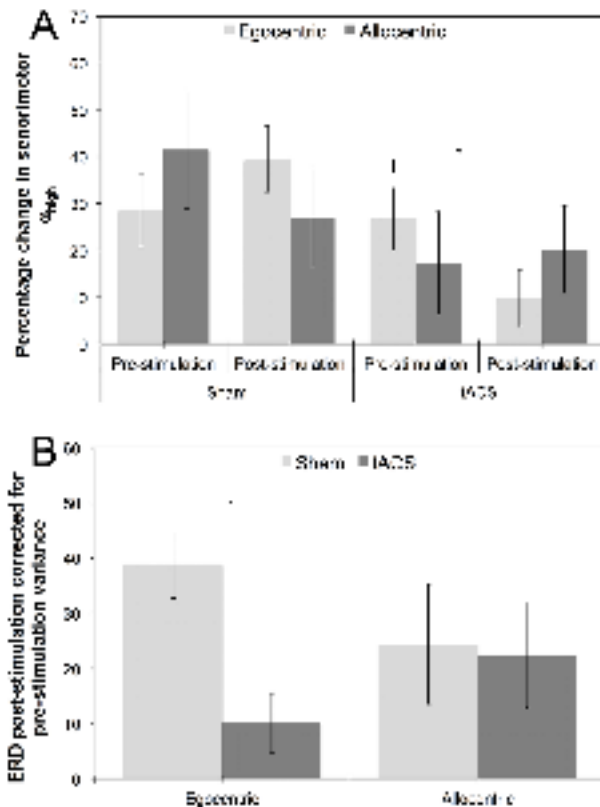


Fig. 4. Sensorimotor (C1/C2/C3/C4) α_{high} percentage change for (a) Interaction between factors time, perspective and stimulation condition (b) post-stimulation ERD corrected for pre-stimulation variance. Bars represent percentage change in α_{high} during observation of hands movements from egocentric and allocentric perspectives, pre and post stimulation for each stimulation group. Error bars indicate standard error. Note: positive values represent ERD. * $p < 0.05$.

Occipital area

The results of the repeated measures ANOVA indicated no significant main effects or interactions in either α_{low} (8 – 10Hz) or α_{high} (10 – 12Hz) ($p_s > .075$), suggesting that occipital α was not affected differentially by either perspective or by tACS.

DISCUSSION

These results provide direct evidence that the IPL is essential in self-other differentiation (Spence et al., 1997; Blanke et al., 2002; Uddin et al., 2006) as μ -suppression during observation of hands movements significantly decreased subsequent to IPL-stimulation. In addition, our results support a neurophysiological

advantage for self-related stimuli (Jackson, Meltzoff, & Decety, 2006; Maeda, Kleiner-Fisman, & Pascual-Leone, 2002) as subsequent to IPL-stimulation, μ -suppression only decreased for the egocentric hands movements. Given that we observed no effect on μ -suppression during observation of allocentric hands movements subsequent to stimulation, we suggest that other neural mechanisms are involved in the processing of allocentric hands movements. The human mirror neuron system (hMNS), which is characterised by neuronal activation during both execution and observation of the same movement, has been associated with self-other differentiation by means of motor simulation (e.g. Jackson, Meltzoff, & Decety, 2006; Kaplan et al., 2008; Uddin et al., 2007). μ -suppression during action observation is a putative index of hMNS activity (e.g. Muthukumaraswamy & Johnson, 2004; Pineda, 2005), and the core areas of the hMNS consists of both IPL and IFG (e.g. Rizzolatti & Craighero, 2004). Therefore, our results may support the involvement of hMNS in self-other differentiation, but more specifically that the IPL is more strongly related to egocentric movements.

Involvement of μ in processing of allocentric hands movements as suggested by Frenkel-Toledo and colleagues (2013) is at odds with previous literature suggesting that greater μ -suppression reflects greater sensory-motor resonance (e.g. Pineda, 2005; Rizzolatti et al., 2001) and has been associated with greater sense of agency (e.g. Serino et al., 2015). However, there is some support for their findings as Fitzgibbon and colleagues' (2014) also reported larger neurophysiological responses to allocentric movements compared to egocentric in the form of TMS induced MEPs. Our results demonstrated μ -suppression during both egocentric and allocentric movements, however, after tACS we only observed reduced μ -suppression during observation of egocentric movements. Given that we stimulated IPL, and observed no modulation of μ -suppression during allocentric movements, it is conceivable that the pattern of μ -suppression reported by Frenkel-Toledo and colleagues reflected cortical activity originating from another region. The IFG is involved in self-other differentiation (e.g. Kaplan et al., 2008; Devue et al., 2007), and also influences μ -reactivity (Arnstein et al., 2011; Babiloni et al., 2016; Braadbaart, Williams, & Waiter, 2013). Therefore, it is plausible that μ -suppression as reported by Frenkel-Toledo and colleagues could originate from a different area than IPL, such as IFG. While

further research should investigate the role of the IFG in processing allocentric movements, here we already causally demonstrate that μ -suppression during allocentric hands movements was not affected by tACS to the IPL, suggesting that the IPL is not involved in processing allocentric hands movements. Thus, the IPL's role in self-other differentiation may be to recognize self-related stimuli. It is possible that the modulation of IPL activity could impact perception of hands movements from both egocentric and allocentric perspectives given that interfering with IPL has been shown to selectively disrupt performance on self-other discrimination (Uddin et al., 2006). This possibility should be more directly tested in the future.

Previous literature has suggested that the right hemisphere is involved in processing self-related and egocentric stimuli, while the left hemisphere is involved in processes relating to other agents and allocentric stimuli (e.g. Kaplan et al., 2008; Uddin et al., 2006); although not consistently as the reverse has also been reported (Chaminade & Decety, 2002; Decety et al., 2002; Farrer & Frith, 2002). We observed no interaction between perspective and hemisphere in our data, and therefore, our results do not enlighten previous inconsistencies. This failure may however be related to the fact that we presented both hands (left and right hand) rather than one hand (left or right), because presentation of both hands is likely to induce bilateral activity in the motor cortex rather than activity in the contralateral hemisphere to the observed movement. Some of the inconsistencies reported in relation to hemisphere may be related to the way in which self-other relations have been investigated, as different experimental protocols have been employed to examine this issue. For example, some studies investigated neural correlates of agency i.e. the experience of oneself as the cause of an action (Farrer et al., 2002; 2003), while others explored reciprocal imitation (e.g. Decety et al., 2002) or recognition of self vs. others' faces and voices (e.g. Kaplan et al., 2008). Future studies should aim to clarify under which conditions hemisphere is relevant in self-other differentiation or rather conveys other, second-order components unrelated to self-other relations per se.

It is conceivable that 'familiarity' confounded our results, as the visual presentation of hands from an egocentric perspective is more visually similar to our own hands than

we see more frequently than we see other peoples' hands. To this extent, it has been demonstrated that neuronal responses to a movement increases with exposure or training (e.g. Calvo-Merino et al., 2005). However, given that the opposite effect of 'familiarity' has also been reported (e.g. Babiloni et al., 2010), this possibility remains speculative. One may also question whether observation of a movement from the egocentric perspective can be perceived as belonging to the self more than to others. It has been demonstrated that observation of a virtual morphed face can be processed and perceived as more similar to one's own face if it moves in synchrony with the observer's self-initiated movements (Serino et al., 2015). It is assumed that this effect is due to matching between predicted proprioceptive and somatosensory consequences of executed movements and visual feedback. However, participants in our study only observed movements and therefore it is unlikely that they perceived the observed movement as belonging to themselves, as voluntary movement results in somatosensory feedback (Blakemore et al., 1998) that is not experienced when observing movements. Nevertheless, it is known that mirror neurons fire during execution and observation of the same movements (Mukamel et al., 2010), and therefore, the neurophysiological response during self-produced movements overlaps with observation of self-related movements. This effect has however only been recorded during observation of egocentric simple hands movements. There is no direct evidence in the human cortex to suggest that allocentric hands movements trigger the same mirror neuron response, although there is indirect evidence (e.g. Frenkel-Toledo et al., 2013). However, this purported link requires further investigation. Little is known about the link between IPL activity and perception of movements from perspectives. Future studies should aim to investigate whether there is perceptual dissociation between egocentric and allocentric perspectives that is related to activity in IPL.

Another consideration is that observation of allocentric movements may be processed as the rotated version of the egocentric movement rather than belonging to someone else per se. This rotation would arguably require a greater level of processing, and may explain Frenkel-Toledo and colleagues' (2013) finding that an allocentric perspective of a movement induced greater μ -suppression compared to

an egocentric perspective, as it is known that sensorimotor suppression is enhanced by task demands and cognitive load (Klimesch, Schimke, & Pfurtscheller, 1993; Klimesch et al., 1998; Brinkman et al., 2014). However, we did not observe a significant effect for the factor perspective, suggesting that this possibility is unlikely. The effects observed in the current study are rather attributed to the expression of self and other-related perspective.

There are a small number of potential limitations of our study as well as additional considerations in regards to the effect of tACS as reported here. First of all, despite the fact that our results demonstrated a reduction in α_{high} -ERD subsequent to tACS, we cannot ascertain the exact neurophysiological mechanism of action of our offline approach. The mechanism behind tACS after-effects is assumed to be different from online entrainment effects, but this is currently debated (see Veniero et al., 2015 & Vossen et al., 2015). Secondly, it is known that the effects of transcranial electrical stimulation (including tACS) become more dispersed before reaching brain tissue as a consequence of passing through scalp and skull (e.g. Antal & Paulus, 2013). Therefore, the effect of the stimulation may have also influenced other nearby regions. However, as the IPL is a broad area including several regions implicated in self-other discrimination such as the angular gyrus and temporo-parietal junction (Blanke et al., 2002; Blanke et al., 2005), this lack of spatial focality may have played at advantage of the manipulation efficacy by ensuring frequency-specific targeting of the relevant areas relating to self-other differentiation (see Romei et al., 2016 for a recent review on information-based approaches of non-invasive transcranial brain stimulation). Third, it should be noted that we did apply tACS exclusively over IPL. Therefore we cannot ascertain whether the effects reported here are site specific (but see above regarding spatial focality of tACS). Future research should test whether stimulation of other areas such as the IFG or another control site would lead to a different outcome. For example a differential impact of IFG stimulation relative to IPL on μ -suppression for allocentric vs. egocentric perspective could be an intriguing working hypothesis to be tested also in relation to previous contradicting findings (Frenkel-Toledo et al., 2013; Fitzgibbon et al., 2014).

Fourth, we did not assess blinding directly. However it has to be noted that our tACS protocol was run offline, therefore ruling out any direct potential impact of phosphenes that might have been perceived during the stimulation. It might be argued that tACS induced retinal phosphenes that may consequently entrained oscillatory activity rather than the actual cortical stimulation. Nonetheless, this occurrence would hardly explain the selective sensorimotor (vs. occipital) impact induced by our tACS manipulation. Therefore, we can confidently exclude that any potentially induced tACS retinal phosphenes might have had a significant impact under our experimental design. Lastly, our sample size was based on previous and comparable tACS work eliciting significant effects (e.g. Moliadze et al., 2012; Neuling, Rach, & Hermann, 2013). Although we found a sizeable effect as in previous reports, we also observed a different ERD pattern between groups prior to stimulation, and thus we recognize that a larger sample size would be beneficial and could reduce inter-individual variance in α -power.

In summary, we demonstrated a causal relationship between cortical activity in IPL and processing self-related stimuli, as tACS to the IPL lead to reduced μ -suppression during observation of egocentric hands movements only. This finding suggests that the IPL is directly involved in processing self-related stimuli and to a greater extent than stimuli relating to others.

References

- Aftanas LI, Golocheikine, SA (2001) Human anterior and frontal midline theta and lower alpha reflect emotionally positive state and internalized attention: high-resolution EEG investigation of meditation. *Neurosci Lett*, 310: 57 – 60.
- Alaerts K, Heremans E, Swinnen SP, Wenderoth N (2009) How are observed actions mapped to the observer's motor system? Influence of posture and perspective. *Neuropsychologia*, 47: 415-422.
- Antal A, Paulus W (2013) Transcranial alternating current stimulation (tACS). *Front Hum Neurosci*, 7:317.
- Arnstein D, Cui F, Keysers C, Maurits NM, Gazzola V (2011) Mu suppression during action observation and execution correlates with BOLD in dorsal premotor, inferior parietal, and SI cortices. *J Neurosci*, 31: 14243-14249.
- Babiloni C, Marzano N, Infarinato F, Iacoboni M, Rizza G, Aschieri P, Cibelli G, Soricelli A, Eusebi F, Del Percio C (2010) "Neural Efficiency" of experts' brain during judgment of actions: A high-resolution EEG study in elite and amateur karate athletes. *Behav Brain Res*, 207: 466-475.
- Babiloni C, Percio C, Vecchio F, Sebastiano F, di Gennaro G, Quarato PP, Morace R, Pavone L, Soricelli A, Noce G, Esposito V, Rossini PM, Gallese V, Mirabella G (2016) Alpha, beta and gamma electrocorticographic rhythms in somatosensory, motor, premotor and prefrontal cortical areas differ in movement execution and observation in humans. *Clin Neurophysiol*, 127: 641 – 654.
- Berlucchi G, Aglioti S (1997) The body in the brain: Neuronal bases of corporeal awareness. *Trends Neurosci*, 20: 560-564.
- Bernier R, Dawson G, Webb S, Murias M (2007) EEG mu rhythm and imitation impairments in individuals with autism spectrum disorder. *Brain Cognition*, 64: 228-237.
- Blakemore SJ, Wolpert DM, & Frith CD (1998) Central cancellation of self-produced tickle sensation. *Nat Neurosci*, 1: 635-640.
- Blanke O, Mohr C, Michel CM, Pascual-Leone A, Brugger P, Seeck M, Landis T, Thut G (2005) Linking out-of-body experience and self-processing to mental own-body imagery at the temporoparietal junction. *J Neurosci*, 25: 550-557.
- Blanke O, Ortigue S, Landis T, Seeck M (2002) Stimulating illusory own-body perceptions. *Nature*, 419: 269-270.
- Bortoletto M, Mattingley JB, Cunnington R (2013) Effects of context on visuomotor interference depends on the perspective of observed actions. *PLOS one*, 8: e53248.

Braadbaart L, Williams JH, Waite GD (2013) Do mirror neuron areas mediate mu rhythm suppression during imitation and action observation? *Int J Psychophysiol*, 89: 99 – 105.

Brinkman L, Stolk A, Dijkerman C, de Lange FP, Toni I (2014) Distinct roles for alpha- and beta-band oscillations during mental simulation of goal-directed actions. *J Neurosci*, 34: 14783 – 147492.

Burgess JD, Arnold SL, Bernadette M, Fitzgibbon PB, Enticott PG (2013) A transcranial magnetic stimulation study of the effect of visual orientation on the putative human mirror neuron system. *Front Hum Neurosci*, 7: 679.

Calvo-Merino B, Glaser DE, Grezes J, Passingham RE, Haggard P (2005) Action observation and acquired motor skills: An fMRI study with expert dancers. *Cereb Cortex*, 15:1243 – 1249.

Cecere R, Rees G, Romei V (2015) Individual differences in alpha frequency drive crossmodal illusory perception. *Curr Biol*, 25: 231-235.

Chaminade T, Decety J (2002) Leader or follower? Involvement of the inferior parietal lobule in agency. *NeuroReport*, 13: 1975-1978.

Cheyne D, Gaetz W, Garnero L, Lachaux JP, Ducorps A, Schwartz D, Varela FJ (2003) Neuromagnetic imaging of cortical oscillations accompanying tactile stimulation. *Cognitive Brain Res*, 17: 599-611.

Croft RJ, Barry RJ (2000) Removal of ocular artifact from the EEG: a review. *Clin Neurophysiol*, 30: 5 – 19.

David N, Bewernick BH, Cohen MX, Newen A, Lux S, Fink GR, Shah NJ, Vogeley K (2006) Neural representations of self versus other: Visual-spatial perspective taking and agency in a virtual ball-tossing game. *J Cognitive Neurosci*, 18: 898-910.

Decety J, Chaminade T (2003) When the self represents the other: A new cognitive neuroscience view on psychological identification. *Conscious Cogn*, 12: 577-596.

Decety J, Chaminade T, Grèzes J, Meltzoff AN (2002) A PET exploration of the neural mechanisms involved in reciprocal imitation. *NeuroImage*, 15: 265–272.

Devue C, Collette F, Balteau E, Degueldre C, Luxen A, Maquet P, Bredart S (2007) Here I am: the cortical correlates of visual self-recognition. *Brain Res*, 1143: 169-182.

Farrer C, Frith CD (2002) Experiencing oneself vs. another person as being the cause of an action: The neural correlates of the experience of agency. *NeuroImage*, 15: 596-603.

Farrer C, Franck N, Georgieff N, Frith CD, Decety J, Jeannerod M (2003) Modulating the experience of agency: a positron emission tomography study. *NeuroImage*, 18: 324-333.

Fitzgibbon, BM, Fitzgerald PB, Enticott PG (2014) An examination of the influence of visuomotor associations on interpersonal motor resonance. *Neuropsychologia*, 56: 439-446.

Foxe JJ, Simpson GV, Ahlfors SP (1998) Parieto-occipital approximately 10Hz activity reflects anticipatory state of visual attention mechanisms. *NeuroReport*, 9: 3929 – 3933.

Frenkel-Toledo S, Bentin S, Perry A, Liebermann DG, Soroker N (2013) Dynamics of the EEG power in the frequency and spatial domains during observation and execution of manual movements. *Brain Res*, 1509: 43-57.

Gallagher S, Meltzoff AN (1996) The earliest sense of self and others: Merleau-Ponty and recent developmental studies. *Philos Psychol*, 9: 211-233.

Goldenberg G, Karnath H (2006) The neural basis of imitation is body part specific. *J Neurosci*, 26: 6282 – 6287.

Goldenberg G (1995) Imitating gestures and manipulating a manikin – the representation of the human body in ideomotor apraxia. *Neuropsychologia*, 33: 63 – 72.

Grandy TH, Werkle-Bergner M, Chicherio C, Lovden M, Schmiedek F, Lindenberger U (2013) Individual alpha peak frequency is related to latent factors of general cognitive abilities. *NeuroImage*, 79: 10 – 18.

Gutman B, Mierau A, Hulsdunker T, Hildebrand C, Przyklenk A, Hollmann W, Struder HK (2015) Effects of physical exercise on individual resting state EEG alpha peak frequency. *Neural Plast*, 717312

Haegens S, Cousijn H, Wallis G, Harrison JH, Nobre AC (2014) Inter- and intra-individual variability in alpha peak frequency. *NeuroImage*, 92: 46 – 55.

Hari R, Forss N, Avikainen E, Kirveskari E, Salenius S, Rizzolatti G (1998) Activation of human primary motor cortex during action observation: A neuromagnetic study. *PNAS*, 95: 15061 - 15065.

Iyer MB, Mattu U, Grafman J, Lomarev M, Sato S, Wassermann EM (2005) Safety and cognitive effects of frontal DC brain polarization in healthy individuals. *Neurology*, 64: 872 – 875.

Jackson PL, Meltzoff AN, Decety J (2006) Neural circuits involved in imitation and perspective-taking. *NeuroImage*, 31: 429-439

Kaplan JT, Aziz-Zadeh L, Uddin LQ, Iacoboni M (2008) The self across the senses: an fMRI study of self-face and self-voice recognition. *SCAN*, 3: 218-223.

Keel JC, Smith MJ, Wassermann EM (2001) A safety screening questionnaire for transcranial magnetic stimulation. *Clin Neurophysiol*, 112: 720.

Keuken MC, Hardie A, Dorn BT, Dev S, Paulus MP, Jonas KJ, Van Den Wildenberg WPM, Pineda JA (2011) The role of the left inferior frontal gyrus in social perception: an rTMS study. *Brain Res*, 1383: 196-205.

Klimesch W, Doppelmayr, M, Russegger H, Pachinger T, Schwaiger J (1998) Induced alpha band power changes in the human EEG and attention. *Neurosci Lett*, 244: 73 – 76.

Klimesch W (1999) EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. *Brain Res Rev*, 29: 169 – 195.

Klimesch W, Sauseng P, Hanslmayr S (2007) EEG alpha oscillations: the inhibition–timing hypothesis. *Brain Res Rev*, 53: 63 – 88.

Klimesch W, Schimke H, Pfurtscheller G (1993) Alpha frequency, cognitive load and memory performance. *Brain Topogr*, 5: 241 – 251.

Maeda F, Kleiner-Fisman G, Pascual-Leone A (2002) Motor Facilitation While Observing Hand Actions: Specificity of the Effect and Role of Observer's Orientation. *J Neurophysiol*, 87: 1329-1335.

Meltzoff AN, Decety J (2003) What imitation tells us about social cognition: a rapprochement between developmental psychology and cognitive neuroscience. *Philos T R Soc Lond B Biol Sci*, 358: 491-500.

Miniussi C, Ambrus GG, Pellicciari MC, Walsh V, Antal A (2012) Transcranial magnetic and electric stimulation in perception and cognition research. In: Miniussi, C., Paulus, W., Rossini, P. M. (Eds). *Transcranial Brain Stimulation*. CRC Press Taylor & Francis Group: FL.

Moliadze V, Atalay D, Antal A, Paulus W (2012) Close to threshold transcranial electrical stimulation preferentially activates inhibitory networks before switching to excitation with higher intensities. *Brain Stimul*, 5: 505 – 511.

Moliadze V, Antal A, Paulus W (2010) Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic reference electrodes. *Clin Neurophysiol*, 121: 2165-2171.

Mukamel R, Ekstrom AD, Kaplan J, Iacoboni I, Fried I (2010) Single-Neuron Responses in Humans during Execution and Observation of Actions. *Curr Biol*, 20: 750 – 756.

Muthukumaraswamy SD, Johnson BW (2004) Primary motor cortex activation during action observation revealed by wavelet analysis of the EEG. *Clin Neurophysiol*, 115: 1760 – 1766.

Neuling T, Rach S, Herrmann CS (2013) Orchestrating neuronal networks: Sustained after-effects of transcranial alternating current stimulation depend upon brain states. *Front Neurosci*, 7: 161.

Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol*, 527: 633 – 639.

Nitsche MA, Liebetanz D, Antal A, Lang A, Tergau F, Paulus W (2003) Modulation of cortical excitability by weak direct current stimulation-technical, safety, and functional aspects. *Suppl Clin Neurophys*, 56: 255 – 276.

Oberman LM, Hubbard EM, McCleery JP, Altschuler EL, Ramachandran VS, Pineda JA (2005) EEG evidence for mirror neuron dysfunction in autism spectrum disorders. *Cognitive Brain Res*, 24: 190-198.

Petsche H, Kaplan S, von Stein A, Filz O (1997) The possible meaning of the upper and lower alpha frequency ranges for cognitive and creative tasks. *Int J Psychophysiol*, 1: 77 – 97.

Pineda JA (2005) The functional significance of mu rhythms: Translating “seeing” and “hearing” into “doing”. *Brain Res Rev*, 50: 57-68.

Puzzo I, Cooper NR, Cantarella S, Russo R (2011) Measuring the effects of manipulating stimulus presentation time on sensorimotor alpha and low beta reactivity during hand movement observation. *NeuroImage*, 57: 1358 – 1363.

Puzzo I, Cooper NR, Cantarella S, Fitzgerald BP, Russo R (2013) The effect of rTMS over the inferior parietal lobule on EEG sensorimotor reactivity differs according to self-reported traits of autism in typically developing individuals. *Brain Res*, 1541: 33 – 41.

Raymaekers R, Wiersema JR, Roeyers H (2009) EEG study of the mirror neuron system in children with high functioning autism. *Brain Res*, 1304: 113 – 121.

Rizzolatti G, Fogassi L, Gallese V (2001) Neurophysiological mechanisms underlying the understanding and imitation of action. *Nat Rev Neurosci*, 2: 661-70.

Rizzolatti G, Craighero C (2004) The mirror neuron system. *Ann Rev Neurosci*, 27: 169 – 192.

Romei V, Thut G, Silvanto J (2016) Information-Based Approaches of Noninvasive Transcranial Brain Stimulation. *Trends Neurosci*, 39: 782 – 795.

Rossi S, Tecchio F, Pasqualetti P, Ulivelli M, Pizzella V, Romani GL, Rossini PM (2002) Somatosensory processing during movement observation in humans. *Clin Neurophysiol*, 113: 16-24.

Ruby P, Decety J (2001) Effect of subjective perspective taking during simulation of action: a PET investigation of agency. *Nat Neurosci*, 4: 546-550.

Serino A, Sforza AL, Kanayama N, van Elk M, Kaliuzhna M, Herbelin B, Blanke O (2015) Tuning of temporo-occipital activity by frontal oscillations during virtual mirror exposure causes erroneous self-recognition. *Eur J Neurosci*, 42: 2515 – 2526.

Spence SA, Brooks DJ, Hirsch SR, Liddle PF, Meehan J, Grasby PM (1997) A PET study of voluntary movement in schizophrenic patients experiencing passivity phenomena (delusions of alien control). *Brain*, 120: 1997 – 2011.

Uddin LQ, Molnar-Szakacs I, Zaidel E, Iacoboni M (2006) rTMS to the right inferior parietal lobule disrupts self-other discrimination. *SCAN*, 1: 65-71.

Uddin LQ, Iacoboni M, Lange C, Keenan JP (2007) The self and social cognition: the role of cortical midline structures and mirror neurons. *Trends Cogn Sci*, 11: 153-157.

Veniero D, Vossen A, Gross J, Thut G (2015) Lasting EEG/MEG after-effects of rhythmic transcranial brain stimulation: Level of control over oscillatory network activity. *Front Cell Neurosci*, 9: 477.

Vogt S, Taylor P, Hopkins B (2003) Visuomotor priming by pictures of hand postures: perspective matters. *Neuropsychologia*, 41: 941 – 951.

Vossen A, Gross J, Thut G (2015) Alpha power increase after transcranial alternating current stimulation at alpha frequency (α -tACS) reflects plastic changes rather than entrainment. *Brain Stimul*, 8: 499-508.

Wach C, Krause V, Moliadze V, Paulus W, Schnitzler A, Pollok B (2013) Effects of 10Hz and 20Hz transcranial alternating current stimulation (tACS) on motor functions and motor cortical excitability. *Behav Brain Res*, 241: 1 – 6.