Running Head: TDCS of Right and Left TPJ

Functional Lateralization of Temporoparietal Junction: Imitation Inhibition, Visual Perspective Taking and Theory of Mind

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Keywords: bilateral TPJ, tDCS, social cognition, self-other representations

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Total number of pages: 26

Figures: 2

Total number of words:

Whole manuscript: 6426

Abstract: 196

Introduction: 596

Abstract

Although neuroimaging studies have consistently identified the temporoparietal junction (TPJ) as a key brain region involved in social cognition, the literature is far from consistent with respect to lateralization of function. For example, bilateral TPJ activation is found during theory of mind tasks in some studies, but only right hemisphere activation in others. Visual perspective taking and imitation inhibition, which have been argued to recruit the same socio-cognitive processes as theory of mind, are associated with unilateral activation of either left TPJ (perspective taking), or right TPJ (imitation inhibition). The present study investigated the functional lateralization of TPJ involvement in the above three socio-cognitive abilities using transcranial direct current stimulation. Three groups of healthy adults received anodal stimulation over right TPJ, left TPJ or the occipital cortex prior to performing three tasks (imitation inhibition, visual perspective taking and theory of mind). In contrast to the extant neuroimaging literature, our results suggest bilateral TPJ involvement in imitation inhibition and visual perspective taking, while no effect of anodal stimulation was observed on theory of mind. The discrepancy between these findings and those obtained using neuroimaging highlight the efficacy of neurostimulation as a complementary methodological tool in cognitive neuroscience.

Introduction

Within the social domain, the TPJ has been consistently identified as playing a fundamental role in abilities ranging from theory of mind (ToM, an umbrella term for the attribution of mental states to oneself or others; see review by Mar, 2011), visual perspective taking (e.g. Schurz et al., 2013) and the inhibition of imitation (e.g. Brass, Ruby & Spengler, 2009). The range of tasks producing reliable TPJ activation suggests that activity in this area may be related to a basic function, shared by all of the above socio-cognitive abilities. Candidate processes include the distinction between self and other representations (Decety & Sommerville, 2003), the control of self-other representations (i.e. biasing processing towards the self or other, Spengler et al., 2009) according to task relevance (Cook, 2014; Hogeveen et al., 2015), and the representation of transient mental states of others (e.g., beliefs, perspectives, and goals, Van Overwalle & Baetens, 2009). While understanding the specific function of this brain region in social cognition is a worthwhile goal, an equally challenging question relates to the functional lateralization of TPJ activity during social cognition.

Despite the abundant evidence of TPJ involvement in socio-cognitive abilities (e.g. Donaldson, Rinehart & Enticott, 2015), the extant literature is far from consistent when it comes to lateralization of function. For example, with respect to ToM several neuroimaging studies report bilateral TPJ activation (e.g. Gallagher et al., 2000; Jenkins & Mitchell, 2010), while others report unilateral activation of right TPJ ($_{R}$TPJ; e.g. Saxe & Wexler, 2005) or left TPJ ($_{L}$TPJ; (Berthoz, Armony, Blair, & Dolan, 2002). In addition, both visual perspective taking and imitation inhibition have been argued to recruit processes in common with those recruited by ToM (Perner & Rössler, 2012; Santiesteban et al., 2012a; Spengler, von Cramon, & Brass, 2010), yet these tasks activate either $_{L}$TPJ (visual perspective taking; e.g. Schurz et al., 2013) or $_{R}$TPJ (imitation inhibition; e.g. Spengler et al., 2009), exclusively.

Interestingly, where strong claims of lateralization have been made on the basis of neuroimaging data these claims have not always been supported either by data obtained from patients with lesions of the TPJ, or by data obtained from experiments in which the TPJ is stimulated using transcranial magnetic stimulation or transcranial direct current stimulation (tDCS). As an illustration, although it has been suggested that mental state attribution is primarily reliant on $_{R}$TPJ (e.g., Saxe 2010), evidence from brain lesion studies show that $_{L}$TPJ is also necessary for mental state attribution (Apperly, Samson, Chiavarino, & Humphreys, 2004; Samson, Apperly, Chiavarino, & Humphreys, 2004). Furthermore, despite the fact that neuroimaging evidence strongly supports an exclusive role for $_{L}$TPJ in visual perspective taking (see meta-analysis by Schurz et al., 2013), anodal stimulation of $_{R}$TPJ has been shown to result in improved perspective taking (Santiesteban, Banissy, Catmur, & Bird, 2012b). Results of the latter study were interesting, as anodal stimulation of $_{R}$TPJ did not affect ToM, despite the abundant evidence derived from neuroimaging studies of the role of $_{R}$TPJ in ToM (see meta-analysis by Van Overwalle, 2009).

It is clear that brain stimulation methods such as tDCS can complement neuroimaging data as they allow the direct manipulation of cortical excitability and allow us to infer causal involvement of a specific brain region in the cognitive process under investigation. Accordingly, this study investigated lateralization of function in the TPJ by stimulating either left or right TPJ while participants performed tasks assessing three linked socio-cognitive processes: theory of mind, visual perspective taking, and imitation inhibition. Performance of participants receiving anodal TPJ stimulation was compared to a control group who received anodal stimulation of occipital cortex (Oz).

Method

Participants

Forty-five right-handed adults (25 males, age range 18-39 years, *M* = 23.4, *SD* = 4.5) participated in this study for a small monetary reward. Participants were randomly assigned to the $_{R}$TPJ (*N* =15), $_{L}$TPJ (*N* = 15), or the occipital cortex, Oz (*N* = 15) stimulation condition. The groups were age- ($F_{(2,44)} = 0.10$, $p = 0.91$) and gender- ($\chi^2_{(2, N=45)} = 0.72$, $p = 0.70$) matched. All participants were healthy volunteers, without any known developmental or neurological disorders and no contra-indications to tDCS. They were all naïve with respect to the aims of the study. Ethical approval was granted by Birkbeck's Department of Psychological Sciences Research Ethics Committee and the procedures followed the principles of the Declaration of Helsinki (2013). All participants provided signed informed consent prior to taking part in the study and the tDCS session followed established safety procedures (Nitsche et al., 2003; Poreisz et al., 2007).

Procedure

All participants received active excitatory stimulation. The stimulation was induced with two saline-soaked surface sponge electrodes (5 cm x 7 cm) in size and delivered by a battery-driven, constant current stimulator. For the TPJ stimulation, the anodal electrode was placed vertically over CP6 ($_{R}$TPJ), or CP5 ($_{L}$TPJ), according to the EEG 10/20 system. Oz was chosen as the control site. In our previous tDCS study (Santiesteban et al., 2012b) we used sham stimulation as a control condition. In the present design the inclusion of another anodal stimulation condition upon a brain region that has not been previously identified for its involvement in social processing, allows us to rule out the alternative hypothesis that our previously observed effects in the imitation inhibition and perspective taking tasks were due to the active stimulation *per se*, regardless of where in the cortex the stimulation was applied. The reference electrode was placed horizontally over the vertex, individually measured on each participant. The stimulation was delivered offline, at 1mA, for 20 minutes. Offline (preceding task performance) rather than online (concurrent to task performance) stimulation was chosen in order to, a) keep the design consistent with our previous tDCS study (Santiesteban et al., 2012b), allowing replication of those findings**,** and b) because previous work suggests that effects, at least for anodal stimulation, are more robust for offline than online stimulation (Pirulli, Fertonani, & Miniussi, 2013). Following the stimulation, participants completed the three socio-cognitive tasks described below in a randomised order, counterbalanced across participants. The testing session lasted approximately one hour.

Imitation-inhibition task (Brass, Bekkering, Wohlschläger, & Prinz, 2000): In this task, participants were asked to lift either their index or middle finger in response to a number cue (1 = index; 2 = middle finger – see Figure 1). At the same time, a task-irrelevant stimulus hand lifted either the same (congruent trials) or a different (incongruent trials) finger to that required in response to the number cue. A modified version of the original task was used in which the stimulus hand was rotated around the sagittal and transverse planes with respect to the participant's hand, which rested on the computer keyboard (Cook & Bird, 2011; 2012; Santiesteban et al., 2012a; 2012b). This manipulation allowed imitation to be isolated from spatial compatibility as response movements were spatially orthogonal to stimulus movements. Incongruent trials required participants to inhibit an imitative response and therefore distinguish and control motor representations evoked by the self and the other. On these trials self representations must be enhanced and other representations inhibited. Due to the low number of errors on this task, the ability to control imitation is reflected in reaction times (RTs), with improved imitative control demonstrated by a reduced RT difference between congruent and incongruent trials, which is primarily driven by reduced RTs on incongruent trials (Brass et al., 2000; 2005; Cook & Bird, 2011; 2012; Santiesteban et al., 2012a; 2012b).

Perspective-taking task (Keysar, Barr, Balin, & Brauner, 2000): This task required participants to take into account the point of view of a character, introduced as 'the director', who gave them instructions to move objects on a shelf. Crucially, some objects were visible to the participant but not to the director, meaning that on experimental trials there was a conflict between the perspectives of the participant and the director. For example, if the participant was presented with the array shown in Figure 1, and was asked to "move the large candle up", he/she should ignore the largest candle they can see, the 'competitor object' (because the director cannot see it), and instead move the next largest candle, which is visible to the director. In control conditions the director either instructed participants to move an object placed in one of the clear slots (e.g. the mug; C1), or an irrelevant object replaced the 'competitor' item from the experimental trial (C2). Experimental trials required participants to inhibit representation of their own perspective and enhance representation of the other's perspective. Improved perspective taking is indexed by greater accuracy on experimental trials due to the unspeeded nature of the task (Apperly et al., 2010; Dumontheil, Apperly, & Blakemore, 2010; Santiesteban et al., 2012b). In a previous study (Santiesteban et al., 2015), we demonstrated that performance on this task was not determined by theory of mind ability: a group of adults with Autism Spectrum Disorder who all had confirmed theory of mind impairments performed as well as typical adults on the task, and performance was equivalent in a control condition in which perspective taking could not be performed via the representation of mental states. These results suggest that visual perspective taking and theory of mind rely on at least partially non-overlapping cognitive processes.

Theory of mind task: several definitions exist for this socio-cognitive ability (e.g. Apperly, 2010; Samson & Apperly, 2010). Here we use the label theory of mind to describe a situation in which individuals engage in mental state attribution, and assess this ability with the *Movie for the Assessment of Social Cognition* (MASC: Dziobek et al., 2006). The MASC requires comprehension of mental states such as beliefs, emotions and intentions of different valance (positive, negative, neutral). It incorporates classic mentalising concepts such as false belief, faux pas, metaphor, and sarcasm. Participants watched a 15-min film and were required to make inferences about the mental states of the characters. The film showed four people interacting socially – see Figure 1. The video was paused at various points and participants were required to answer a multiple-choice question about the last scene. There were two types of questions: theory of mind (e.g. "what is Betty thinking?") and control questions (e.g. "what was the weather like that evening?"). Errors on the MASC were of three types (complete lack of, insufficient, or excessive/over-interpretative mental state reasoning). Improved theory of mind ability is indexed by greater accuracy when responding to theory of mind questions. Since this is a pen-and-paper task, no RT measures are recorded.

[Insert Figure 1 about here]

Results

Where sphericity assumptions were not met, Greenhouse-Geisser corrected values are reported. Bonferroni corrections were used for post hoc multiple comparisons. In addition to the standard ANOVA analyses, where possible, we also report Bayesian posterior probabilities for the occurrence of the alternative (H_1) hypothesis – based on the obtained data, which was calculated using the open source software JASP (https://jasp-stats.org; Love et al., 2015). This method allows quantifying evidence in favor of the alternative or null hypothesis, with values ranging from 0 (no evidence) to 1 (very strong evidence).

Imitation inhibition

The data from one participant in the Oz group showed extreme scores identified by the 1.5 x IQR (Tukey 1977) rule and were removed from the RT analysis. The remainder of the RT and accuracy data ($_{R}$TPJ: *N*=15; $_{L}$TPJ: *N*=15; Oz: *N*=14) were analysed using ANOVA with Stimulation Site as the between-subjects factor and Trial Type (congruent vs. incongruent) as the within-subject factor.

RT

Figure 2a shows mean RT on congruent and incongruent trials of the imitation-inhibition task. The analysis revealed a significant main effect of Trial Type, $F_{(1,41)} = 97.91$, $p < .001$, $\eta^2_p = .71$, $p(H1|D) > 0.99$; indicating that responses on congruent trials (*M* = 444 ms; *S.E.*M. = 7.4ms) were executed faster than those on incongruent trials (*M* = 479 ms; *S.E.*M. = 7.8ms). The main effect of Stimulation Site failed to reach significance in the standard ANOVA analysis, $F_{(2,41)} = 5.68$, $p = .098$, $\eta^2_p = .11$, however, the Bayesian analysis showed positive evidence [$p(H_1|D) = 0.88$] of a stimulation effect on this task. Therefore, we performed a Post-hoc analysis, which revealed that compared to Oz (*M* = 484 ms; *S.E.*M. = 13ms), responding was (non-specifically) faster following stimulation of $_{R}$TPJ (*M* = 444 ms; *S.E.*M. = 12ms; $p = .035$) but no other contrasts reached significance, all *p*s $\geq .20$.

Crucially, the Stimulation Site × Trial Type interaction was significant, $F_{(2,41)} = 5.68$, $p = .007$, $\eta^2_p = .22$, $p(H_1|D) = 0.75$; reflecting a reduced difference between RTs on congruent trials and incongruent trials for both the $_{L}$TPJ and $_{R}$TPJ groups compared to the Oz group. Post-hoc analysis showed that this interaction was driven by differences in the incongruent trials between the Oz vs. $_{R}$TPJ (p = .011) and the Oz vs. $_{L}$TPJ (p = .044) stimulation groups. Neither the $_{R}$TPJ vs. $_{L}$TPJ (p = .564) comparison in the incongruent trials, nor any of the comparisons in the congruent trials (all ps >. 12) were significant. As a further check on the specificity of stimulation, we analysed RT on incongruent trials including RT on congruent trials as a covariate. This analysis revealed that compared to Oz stimulation, tDCS of either $_{L}$TPJ ($F_{(1,26)}$ = 10.10, p = .004, η^2_p= .28) or $_{R}$TPJ ($F_{(1,26)}$ = 4.71, p = .039, η^2_p= .15) resulted in stronger imitation inhibition. The $_{R}$TPJ vs. $_{L}$TPJ comparison was not significant, (p = .56, η^2_p=.012).

Accuracy

The main effect of Trial Type was significant, $F_{(1,41)}$ = 23.0, p < .001, η^2_p= .36, $p(H_1|D)$ > 0.99; participants made more errors on incongruent (M = 6.7%, *S.E.M.* = 0.8%) than on congruent (M = 2.3%, *S.E.M.* = 0.4%) trials. However, neither the main effect of Stimulation Site, $F_{(2,41)}$ = 2.77, p = .001, η^2_p = .12, $p(H_1|D)$ = 0.41 nor the Stimulation Site × Trial Type interaction, $F_{(2,41)}$ = 0.87, p = .43, η^2_p = .04, $p(H_1|D)$ = 0.11 were significant, indicating no specific effect of anodal stimulation on accuracy of imitation inhibition.

Visual Perspective taking

Due to faulty equipment, the perspective taking data from one participant in the Oz group were not recorded. The remaining data were analysed using ANOVA with Stimulation Site as a between-subject factor and Trial Type (Experimental vs. C1 vs. C2) as the within-subjects factor.

Accuracy

Figure 2b shows accuracy data from the experimental trials of the visual perspective-taking task. The ANOVA revealed a main effect of Trial Type, $F_{(1.05,43.2)} = 16.27$, $p < 0.001$, $\eta^2_p = .28$, $p(H_1|D) > 0.99$. Overall, performance was better on C1 trials (*M* = 97.1%, *S.E.M* = 1.2%) than on experimental (*M* = 81.6%, *S.E.M*. = 3.2%; $p < .001$) and on C2 trials (*M* = 94.3%, *S.E.M*. = 1.8%; $p = .003$). The interaction of most theoretical interest, the interaction between Stimulation Site and Trial Type was significant, $F_{(2.1,43.2)} = 7.24$, $p = .002$, $\eta^2_p = .26$, $p(H_1|D) = 0.99$. Post-hoc analysis showed that while no effects of Stimulation Site were found on control trials (all *ps* > .16), on experimental trials (trials on which perspective taking was required), participants in both $_R$TPJ and $_L$TPJ stimulation groups performed significantly better than those in the Oz group ($_R$TPJ vs. Oz, $p < .001$; $_L$TPJ vs. Oz, $p = .004$); whereas the comparison between $_R$TPJ vs. $_L$TPJ groups was not significant ($p = .28$). Thus, participants were better able to adopt the Director's perspective following stimulation of either $_R$TPJ or $_L$TPJ.

The main effect of Stimulation Site was also significant $F_{(2,41)} = 5.79$, $p = .006$, $\eta^2_p = .22$, $p(H_1|D) > 0.99$. Post-hoc analysis showed that $_R$TPJ stimulation resulted in better overall performance compared to Oz stimulation ($p = .005$), whereas the comparison $_L$TPJ vs. Oz ($p = .31$) and $_R$TPJ vs. $_L$TPJ ($p = .26$) failed to reach significance. However, it should be noted that this effect applies to performance on all three trial types; therefore, it is not specific to perspective taking.

RT

This analysis revealed a significant main effect of Trial Type, $F_{(2,82)} = 54.1$, $p < .001$, $\eta^2_p = .57$, $p(H_1|D) > 0.99$. Overall, participants responded faster in C1 trials (*M* = 2.4 s, *S.E.M.* = .03) than in Experimental (*M* = 2.8 s, *S.E.M.* = .05; $p < .001$) and C2 trials (*M* = 2.7 s, *S.E.M.* = .06; $p < .001$). Neither the main effects of Stimulation Site, $F_{(2,41)} = 2.53$, $p = .091$, $\eta^2_p = .11$, $p(H_1|D) =$

0.69, nor the Stimulation Site × Trial Type interaction, $F_{(4,82)} = 1.88$, $p = .12$, $\eta^2_p = .08$, $p(H_1|D) = 0.22$, reached significance.

Theory of mind task

Figure 2c shows accuracy data for the theory of mind task. Two separate analyses were performed on data from this task. The first analysis included the accuracy rate for theory of mind and control questions and the second sought to investigate if there were group differences in the type of errors participants made. The first analysis revealed that overall, participants' accuracy was higher for control questions (*M* = 89.2%, *S.E.M.* = 1.4%) than for questions requiring mental state attribution (*M* = 78.8%, *S.E.M.* = 1.1%), $F_{(1,42)} = 51.69$, $p < .001$, $\eta^2_p = .55$, $p(H_1|D) > 0.99$; Figure 2C. Neither the main effect of Stimulation Site ($F_{(1,42)} = 2.39$, $p = .10$, $\eta^2_p = .10$, $p(H_1|D) = 0.51$), nor the Stimulation Site × Question Type interaction ($F_{(1,42)} = 0.87$, $p = .43$, $\eta^2_p = .04$, $p(H_1|D) = 0.12$) were significant. Additionally, we performed a separate analysis with the theory of mind trials only and no effects of stimulation were found, $F_{(2,42)} = 1.395$, $p = .26$, $\eta^2_p = .06$, $p(H_1|D) = 0.30$.

Error analysis. A 3 (Stimulation Site) x 3 (Error Type) ANOVA revealed a significant main effect of Error Type, $F_{(1.5,64.8)} = 22.09$, $p < .001$, $\eta^2_p = .34$, $p(H_1|D) > 0.99$. Post-hoc analysis showed that overall, participants made fewer errors reflecting a lack of theory of mind ability (*M* = 3.7%, *S.E.M.* = 0.5, than errors reflecting either insufficient theory of mind (*M* = 7.4%, *S.E.M.* = 0.7; $p < .001$, or excessive theory of mind (*M* = 9.9%, *S.E.M.* = 0.8; $p < .001$). Neither the main effect of Stimulation Site, $F_{(2,42)} = 1.28$, $p = .28$, $\eta^2_p = .06$, $p(H_1|D) = 0.22$; nor the Stimulation Site × Error Type interaction, $F_{(3.04,63.9)} = 1.32$, $p = .27$, $\eta^2_p = .06$, $p(H_1|D) = 0.06$ reached significance.

[Insert Figure 2 about here]

Comparison Across Tasks: In order to test whether stimulation of TPJ had a differential effect on the three tasks, an additional analysis was conducted which compared performance across tasks. The variables of interest (imitation effect [RT incongruent – RT congruent trials]) on the imitation-inhibition task, accuracy of experimental trials in the perspective-taking task and accuracy of theory of mind trials in the MASC) were each converted into Z scores and were analysed using a 3 × 3 ANOVA with the factors Task and Stimulation Site. We found no main effects of Task ($F_{(2,80)}$ = 0.03, p = .97, η^2_p = .001, $p(H_1|D)$ =0.01) or Stimulation Site ($F_{(2,40)}$ = 1.03, p = .37, η^2_p = .05, $p(H_1|D)$ = 0.02), but the Stimulation Site × Task interaction was significant, $F_{(2,80)}$ = 6.16, p < .001, η^2_p= .24, $p(H_1|D)$ = 0.87. We explored this interaction further by comparing the performance of the stimulation groups on the three tasks. The analysis including the $_R$TPJ and Oz groups revealed a significant interaction between Stimulation Site and Task ($F_{(2,52)}$ = 10.04, p < .001, η^2_p= .28). Post-hoc analysis confirmed that the $_R$TPJ group outperformed the Oz group in both imitation inhibition (p= .027) and visual perspective taking (p = .002), but that no effect of stimulation was found on the theory of mind task (p = .22). Similarly, the analysis including the $_L$TPJ and Oz groups revealed a significant Stimulation Site × Task interaction ($F_{(2,52)}$ = 7.47, p = .001, η^2_p= .22). Again, Post-hoc analysis confirmed that the $_L$TPJ group outperformed the Oz group in both imitation inhibition (p= .004) and visual perspective taking (p = .035), but that there was no effect of stimulation on theory of mind (p = .21). Finally, in the analysis including the $_R$TPJ and $_L$TPJ groups we found a significant main effect of task, $F_{(1.6,46.4)}$ = 5.54, p = .01, η^2_p= .17. Post-hoc analysis revealed that z scores on the perspective-taking task and imitation tasks were significantly different (p = .001), while the difference between z scores on the imitation and theory of mind tasks approached significance (p = .051). However, neither the main effect of Stimulation Site (p = .16) nor the Stimulation Site × Task interaction (p = .82) were significant. In sum, the results from the comparison across tasks support our previous analyses and confirm that compared to Oz stimulation, stimulating either $_{R}$TPJ or $_{L}$TPJ results in differential performance on the imitation inhibition and perspective taking tasks, but not on the theory of mind task.

Discussion

This study aimed to investigate lateralization of function in the TPJ within the socio-cognitive domain. Results indicated that anodal stimulation of both $_{R}$TPJ and $_{L}$TPJ modulated imitation inhibition and visual perspective taking, while stimulation of TPJ, in either hemisphere, did not affect theory of mind. The data are consistent with previous neurostimulation studies demonstrating $_{R}$TPJ involvement in the control of imitation and visual perspective taking (Santiesteban et al., 2012b; Hogeveen et al., 2015), and extend such findings by showing that $_{L}$TPJ is also recruited during these socio-cognitive processes. Our findings are also consistent with neuropsychological evidence showing impairment of imitation inhibition and visual perspective taking in patients with lesions to either right, left or bilateral TPJ (Spengler, von Cramon & Brass, 2010). However, the finding of bilateral TPJ involvement across these tasks is not entirely consistent with the evidence available from neuroimaging studies of imitation inhibition and visual perspective taking. A recent meta-analysis of fMRI studies of visual perspective taking and false belief reasoning by Schurz et al., (2013) found common activation in the $_{L}$TPJ but not $_{R}$TPJ. In a different socio-cognitive domain, inhibition of imitation, previous fMRI studies have reported activation of $_{R}$TPJ but not $_{L}$TPJ (Brass et al., 2005; Spengler et al., 2009). Several factors could account for these contrasting findings.

One likely source of the discrepancy between results of fMRI and neurostimulation studies is the use of what have been argued to be over-conservative statistical thresholds in fMRI research (Lieberman & Cunningham, 2009). Statistical thresholds are conservative as a result of correction for the large number of comparisons made across the brain (typically in the region of tens or hundreds of thousands) in order to avoid a Type I error. Lieberman and Cunningham (2009) have argued that as a result of the conservative thresholds adopted, Type II errors frequently occur. Perhaps of greater concern, however, is the manner in which the corrected threshold is derived. One widely used multiple comparison correction method in the most-extensively used analysis package for fMRI data (SPM 12) is a False Discovery Rate correction based on cluster extent. In essence, this technique adopts a voxel-level uncorrected threshold to perform an initial analysis and then determines the significance of each resulting cluster based on its spatial extent. Clusters are arranged in order of significance and then the most significant clusters are determined to be 'truly significant'. While a logical approach, it has the disadvantage of discriminating against small clusters of activation, particularly when in the presence of large areas of activation. Therefore should a large area of, for example, $_{R}$TPJ be activated by imitation inhibition then smaller clusters in $_{L}$TPJ would be unlikely to survive correction. Given that the functional consequences of the spatial extent of activity are currently unknown, this gives cause for concern when making strong claims about a greater involvement of $_{R}$TPJ or $_{L}$TPJ in any cognitive process. The use of functional localisers within fMRI paradigms may go some way to address this problem (Fedorenko et al., 2010).

A second possible cause of the discrepant findings between neurostimulation and fMRI studies is the combination of the greater spatial resolution of fMRI coupled with the reliance on spatial consistency across participants. If all 12 members of a group show significant $_{R}$TPJ activation, but the exact area of the $_{R}$TPJ only partially overlaps across group members, then it is unlikely that significant $_{R}$TPJ activity will be observed at the group level in an fMRI study. While the same requirement of spatial consistency holds for neurostimulation studies, the large spatial extent of stimulation effects (particularly with the large electrodes used in the current study) means that the degree of tolerance for spatial variability is higher than for fMRI.

A further potential explanation of the discrepancy between the current findings and those reported in the neuroimaging literature is that effects of stimulation in one hemisphere may be propagated to the other hemisphere, resulting in bilateral stimulation regardless of electrode positioning. However, given that interhemispheric connections between the stimulated TPJ areas are inhibitory (Koch et al., 2011) these effects should be antagonistic in nature. Furthermore, two previous TMS studies (Heinisch, Dinse, Tegenthoff, Juckel, & Brüne, 2011; Uddin, Iacoboni, Lange, & Keenan, 2007) stimulated both $_{R}$TPJ and $_{L}$TPJ and found selective effects of $_{R}$TPJ stimulation. Therefore, these findings do not support the hypothesis that propagation of stimulation caused the bilateral effects observed here.

While the above factors seek to explain why effects may be observed using brain stimulation but not using fMRI, an interesting feature of the current data is the *absence* of stimulation effects on the ToM task even though TPJ activation during ToM tasks has been consistently demonstrated using fMRI, including a study utilising the same ToM task as used here ($_{L}$TPJ, Wolf, Dziobek, & Heekeren, 2010). The absence of a stimulation effect in this task was supported using a Bayesian analysis. The absence of effects of TPJ stimulation on ToM performance has been reported previously using an alternative ToM test (Santiesteban et al., 2012b; but see Young, Camprodon, Hauser, Pascual-Leone, & Saxe, 2010 for conflicting findings with a third type of ToM test). These findings open up the possibility that the TPJ activation observed in response to ToM tasks in fMRI studies may not reflect ToM processing itself, but may instead reflect processing which is reliably associated with, but not exclusive to ToM (see Corbetta, Patel, & Shulman, 2008; Mitchell, 2008). An alternative, and perhaps more likely, explanation is that most ToM tasks are insensitive to the performance variation induced by stimulation in typical adults, able only to identify the more marked deficits in ToM exhibited by clinical populations. For example, previous studies using the MASC have reported performance variability on ToM by individuals with autism (Dziobeck et al., 2006) and schizophrenia (Montag et al., 2011). It is worth noting that none of the above potential explanations for the discrepancy between our current tDCS results and previous fMRI studies imply that the two methodologies tap into different processes. Future research in this area could help providing more definitive clues about these discrepancies.

Ultimately, our findings could contribute to a better understanding of the neurocognitive architecture of different socio-cognitive abilities and the role of TPJ in them (Cook, 2014; Donaldson et al., 2015). If both right and left TPJ are engaged in some social cognition tasks but not others, this would allow novel predictions that deviate from previous, more strongly lateralized accounts (e.g. Aichhorn et al., 2009; Saxe, 2010; Schurz et al., 2013). Furthermore, these data support claims that imitation and visual perspective-taking share a common process (Santiesteban et al., 2012a), potentially that of self-other control, which is unlikely to be explained under previous accounts of strong, and opposite, lateralization of these two processes.

Our data could also pave the way to a future line of research concerning the role of TPJ in self-other representations. The dynamics of enhancing vs. inhibiting self-other representations differ in both imitation inhibition (enhance self – inhibit other) and visual perspective taking (inhibit self – enhance other). A recent account suggests that rather than distinguishing between self and other, the TPJ might discriminate between an action that is relevant vs. irrelevant to the actual task (Cook, 2014; see also Nicolle et al., 2012).

Understanding the mapping of brain involvement to cognitive models of social cognition is likely to necessitate the use of multiple techniques, using multiple tests, across multiple socio-cognitive domains within the same individuals. Tools such as fMRI, electroencephalography (EEG) and magnetoencephalography (MEG) have a number of strengths, many of which are not shared by brain stimulation techniques, therefore, future research could benefit from employing combined methodologies. Indeed, such combined approaches could help overcome the low spatial resolution inherent to tDCS, and provide a better insight into the specific role of the TPJ in the social domain.

In conclusion, our findings a) challenge the assumption of lateralization of function within TPJ of socio-cognitive processes such as the inhibition of imitation and perspective taking, b) highlight the potential contribution of brain stimulation methods such as tDCS to the field of social cognitive neuroscience, and c) show that by relying on fMRI data alone, our understanding of functional specialization could be limited.

Acknowledgements

The authors with to thank Dr Isabel Dziobek for kindly sharing the MASC with us and Sophia Androu and Cristina Cioffi for assistance in data collection.

This work was supported by an Economic and Social Research Council (ESRC) studentship [ES/H013504/1] awarded to IS and ESRC grants awarded to MJB [ES/K00882X/1] and to CC [ES/K00140X/1]. GB contributed to the paper while a Senior Fellow at the Netherlands Institute of Advanced Study in the Humanities and Social Sciences.

Conflict of Interests

The authors declare no conflict of interests.

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Figure Legends

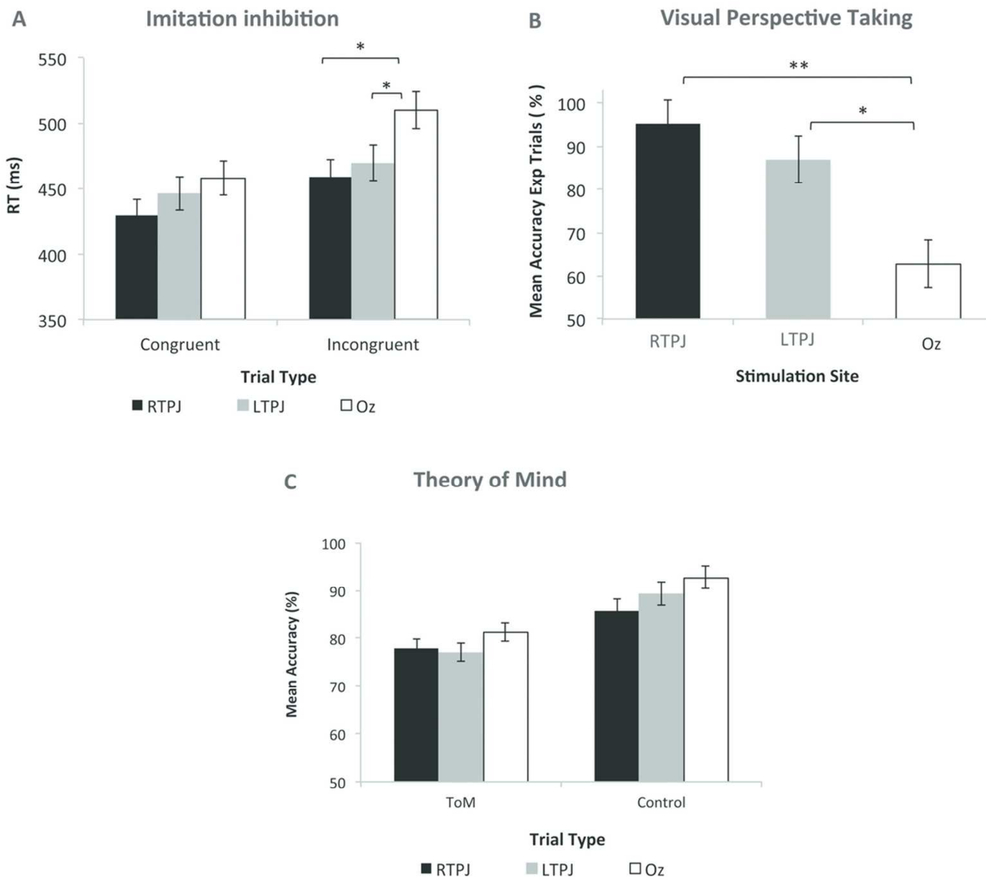
Figure 1. Experimental tasks. In the imitation-inhibition task participants responded to a number cue by lifting either the index finger – upon appearance of the number 1 – or the middle finger – upon appearance of the number 2, while ignoring a task-irrelevant finger movement that was either the same (congruent trials, left frame) or different from (incongruent trials, right frame), that performed by the participant. Imitation inhibition was required during incongruent trials.

In the visual perspective-taking task participants were required to adopt the perspective of another individual, the 'director'. For example, when instructed to "move the large candle", participants had to ignore the largest candle (dashed circle) which was invisible to the director and choose the medium-sized candle (solid circle), which the director could see.

In the theory of mind task participants watched a movie of four people interacting and were required to answer questions concerning either the characters' mental states or a physical aspect of the scene – see Methods.

Figure 2. Anodal tDCS of either $_{R}$TPJ or $_{L}$TPJ (but not Oz) reduced the imitation effect in the imitation-inhibition task (A) and improved performance in the visual perspective-taking task (B) but had no effect on theory of mind (C). Error bars represent S.E.M. ** ($p < .01$); * ($p < .05$)

Figure 1
42x10mm (300 x 300 DPI)



99x90mm (300 x 300 DPI)