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Effects of non-invasive brain stimulation on visual perspective taking: A meta-analytic study

Yuan-Wei Yao[a,b,c,1,*], Vivien Chopurian[a,d,1], Lei Zhang[e,*], Claus Lamm[e,f], Hauke R. Heekeren[a,b,c]

[a] Department of Education and Psychology, Freie Universität Berlin, 14195 Berlin, Germany
[b] Einstein Center for Neurosciences Berlin, Charité–Universitätsmedizin Berlin, 10117 Berlin, Germany
[c] Berlin School of Mind and Brain, Humboldt-Universität zu Berlin, 10117 Berlin, Germany
[d] Department of Psychology, Humboldt-Universität zu Berlin, 10099 Berlin, Germany
[e] Social, Cognitive and Affective Neuroscience Unit, Department of Cognition, Emotion, and Methods in Psychology, Faculty of Psychology, University of Vienna, 1010 Vienna, Austria
[f] Vienna Cognitive Science Hub, University of Vienna, 1010 Vienna, Austria

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ABSTRACT

Visual perspective taking (VPT) is a critical ability required by complex social interaction. Non-invasive brain stimulation (NIBS) has been increasingly used to examine the causal relationship between brain activity and VPT, yet with heterogeneous results. In the current study, we conducted two meta-analyses to examine the effects of NIBS of the right temporoparietal junction (rTPJ) or dorsomedial prefrontal cortex (dmPFC) on VPT, respectively. We performed a comprehensive literature search to identify qualified studies and computed the standardized effect size (ES) for each combination of VPT level (Level-1: visibility judgment; Level-2: mental rotation) and perspective (self and other). Thirteen studies (rTPJ: 12 studies, 23 ESs; dmPFC: 4 studies, 14 ESs) were included in the meta-analyses. Random-effects models were used to generate the overall effects. Subgroup analyses for distinct VPT conditions were also performed. We found that rTPJ stimulation significantly improved participants' visibility judgment from the allocentric perspective, whereas its effects on other VPT conditions are negligible. Stimulation of dmPFC appeared to influence Level-1 performance from the egocentric perspective, although this finding was only based on a small number of studies. Notably, contrary to some theoretical models, we did not find strong evidence that these regions are involved in Level-2 VPT with a higher requirement of mental rotation. These findings not only advance our understanding of the causal roles of the rTPJ and dmPFC in VPT, but also reveal that the efficacy of NIBS on VPT is relatively small. Additionally, researchers should also be cautious about the potential publication bias and selective reporting.

1. Introduction

The ability to take another's perspective is crucial for navigating complex social environments. To view the world from the second-person standpoint requires that one distinguish between the self and the other in relation to the environment (Kessler and Thomson, 2010; Lieberman, 2007). One social cognitive process that is closely related to this ability is visual perspective taking (VPT). Dysfunction related to VPT has been observed in multiple clinical disorders, including autism and schizophrenia (Eack et al., 2017). Thus, it is essential to identify cognitive and neural mechanisms underlying the VPT process, as a steppingstone to target interventions for related disorders.

Flavell and colleagues (Flavell, 1977; Flavell et al., 1981) identified two levels of VPT. Level-1 VPT refers to the ability to judge an object's visibility from the perspective of both the self and other. Consider, for example, playing hide-and-seek: you need knowledge about *what* the other person can see to hide from them. Children around the age of 18-24 months (Flavell et al., 1981) as well as chimpanzees (Bräuer et al., 2007), dogs (Hare and Tomasello, 2005) and goats (Kaminski et al., 2005) show the ability to make such line-of-sight judgments.

Level-2 VPT, on the other hand, enables humans to describe *how* an object looks from another's perspective and establishes a shared view of the world by creating a common reference frame for spatial localizations (Flavell, 1977; Kessler and Rutherford, 2010; Michelon and Zacks, 2006). For instance, imagine standing in front of a car while your friend views it from behind: you are aware that although the car is visible to both of you, your friend has a different visual perspective on it (Pearson et al., 2013). In order to figure out how the car looks from your friend's perspective, you might mentally rotate your body into their position. Thus, Level-2 VPT has a higher-level requirement of embodied rotation compared to its Level-1 counterpart (Martin et al., 2020).

* Corresponding authors.
E-mail addresses: yywyao@gmail.com (Y.-W. Yao), lei.zhang@univie.ac.at (L. Zhang).
[1] These authors contributed equally

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In recent years, researchers have conducted a few neuroimaging studies to assess the neural mechanisms underlying VPT. One candidate region identified for this process is the temporoparietal junction (TPJ), as both the right and left parts of this region appear to play a critical role in multiple processes relevant to VPT, including detecting self-other incongruences, controlling self and other representations, and inhibiting the influence of the non-relevant representation via orienting attention (Bahnemann et al., 2009; Lamm et al., 2016; Quesque and Brass, 2019; Wolf et al., 2010). Indeed, the bilateral TPJ has often been reported across different VPT conditions (Bukowski, 2018; Schurz et al., 2013). Another critical region for integrating self-other processing is the dorsomedial prefrontal cortex (dmPFC). The dmPFC has also been implicated in making judgements about others (Denny et al., 2012), social information processing (Lieberman et al., 2019), and in introspection and assessment of mental states (Doré et al., 2015). In VPT tasks, the dmPFC has been reported when requiring egocentric perspective taking and suppressing the influence of the other's perspective, with a proposed process of imagining movement and suppressing the motor response to physically rotate the body (Bukowski, 2018; Mazzarella et al., 2013; Munzert et al., 2009).

While these neuroimaging studies highlight candidate brain hubs for self-other differentiation and integration in VPT, they are mostly based on correlational methods, and thus causal relationships remain to be established (Bell and DeWall, 2018; Lieberman et al., 2019). Fortunately, non-invasive brain stimulation (NIBS) techniques, including transcranial direct current brain stimulation (tDCS) and transcranial magnetic stimulation (TMS), provide an approach to overcome this limitation (Donaldson et al., 2015; Polanía et al., 2018). Specifically, tDCS applies weak direct currents to cortical regions and can either facilitate or inhibit the spontaneous neuronal activity depending on the polarity of the electrode. Typically, anodal and cathodal stimulation has been shown to increase and decrease cortical excitability, respectively (Bell and DeWall, 2018; Brunoni and Vanderhasselt, 2014; Conson et al., 2015). TMS, on the other hand, uses a changing magnetic field to induce an ionic current at a brain region based on the principle of electromagnetic induction. The effects of TMS depend on factors including frequency, intensity, and duration of stimulation. For example, single-pulse TMS can depolarize the targeted neurons, whereas high-frequency (e.g., > 10 Hz) repetitive TMS (rTMS) typically disrupts the cortical function during the stimulation (Kobayashi and Pascual-Leone, 2003).

Researchers have increasingly used NIBS to investigate the causal role of different brain regions in VPT in the past few years. For example, anodal tDCS of the right TPJ (rTPJ) has been shown to improve participants' performance when judging an item's visibility from another's perspective (Santiesteban et al., 2012). Moreover, another study showed that such an improvement could extend to Level-2 allocentric perspective-taking (Martin et al., 2019a). However, there is also opposing evidence in which the rTPJ stimulation increased the impact of perspective discrepancy during Level-1 VPT (Martin et al., 2020). Thus, despite much effort devoted to clarifying the causal relationships between brain regions and VPT, the overall findings to date paint a rather mixed and inconclusive picture.

The inconsistency may be partly due to the complexity and heterogeneity of the existing VPT paradigms (Bukowski, 2018). As mentioned above, participants may be asked to judge the visibility or location of a target from different perspectives (e.g., self or other) in which distinct underlying cognitive mechanisms may be involved. For example, Level-2 VPT typically requires more embodied processing than Level-1 VPT (Martin et al., 2020). However, there is no consensus yet on whether stimulating a brain region would selectively influences any VPT conditions. Moreover, with a few exceptions (Martin et al., 2020, 2019a, 2019b), most NIBS studies in this field only focused on one brain region, making it difficult to investigate different regions' roles in VPT.

The current study aims to clarify the causal roles of key brain regions in VPT. Based on the feasibility of the included studies, we focus on studies targeting rTPJ and dmPFC and quantitatively synthesize the effects of stimulation of these two regions on distinct VPT conditions.

2. Methods

The meta-analysis was conducted following the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2019) and PRISMA guidelines for meta-analyses (Liberati et al., 2009). The literature review and data extraction were performed by two co-authors (Y.W.Y and V.C) independently. Discrepancies were resolved by discussion.

2.1. Search strategy and eligibility criteria

An online literature search was conducted in PubMed, Web of Science, ProQuest, and PsycINFO for full-text articles from January 2000 to June 2020 without language restrictions. The following query syntax was used: ("stimulation" OR "TMS" OR "tDCS" OR "tACS" OR "tPCS" OR "tRNS" OR "TBS") AND ("perspective taking" OR "perspective-taking" OR "VPT"). To be included in the final meta-analysis, studies had to: (1) perform NIBS, (2) include a VPT task, (3) enroll healthy participants, (4) have a control or sham condition. Studies without full text available were excluded. To reduce the effects of publication bias, our literature search covered not only peer-reviewed articles but also unpublished preprints. However, after removing already published duplicates, no additional preprint was eligible for inclusion. Note that, although previous brain stimulation studies mainly focused on rTPJ or dmPFC, we did not explicitly include "rTPJ" OR "dmPFC" during the literature search. However, as a random-effects model requires at least three effect sizes (ESs), the sample size limitation did not allow us to perform a meta-analysis on studies that targeted other brain regions (Cheung and Vijayakumar, 2016).

We first identified 27 potentially related studies by checking the title and abstract. Two authors then independently decided if these studies should be included in the review by reading the full text. The inter-rater reliability for the article selection showed high agreement (Cohen's Kappa = 0.86, $Z = 5.46$, $p < 0.001$). The authors resolved their disagreement about two articles by discussion. The details were listed in Table S1. A total of 16 NIBS studies met the inclusion criteria (Table 1), and 13 studies targeting rTPJ or dmPFC were included in the meta-analyses. Finally, we contacted the authors of these studies for unpublished data/studies. We received some data that were not reported in the original articles (e.g., accuracy data of Martin et al. 2019b), but did not obtain any more unpublished studies for the meta-analyses.

2.2. Quality assessment

We used the Cochrane risk of bias tool to assess the quality of studies (Higgins et al., 2019). Ratings (low, high, or unclear risk of bias) were assigned to each study based on the following six criteria: (1) assessments for sequence generation (e.g., randomization), (2) allocation concealment, (3) blinding of participants and researchers, (4) blinding of outcome assessment (e.g., the use of sham procedures), (5) incomplete outcome data, and (6) selective reporting.

2.3. Data extraction

For each included study, we extracted information regarding the sample size, age, and sex ratio. For intervention characteristics, we extracted the type of NIBS technique, stimulation region, blinding protocol, intensity, duration of active stimulation, valence (excitatory or inhibitory), and study design. For tasks, we extracted the VPT Level (1 or 2) and Perspective (Self or Other) information for each effect and focused on these four conditions in the following analyses.

Table 1
Characteristics of studies using NIBS techniques and VPT paradigms.

Study	Target	NIBS type	Electrode/coil size/diameter	Study design	N	NIBS control condition	Intensity	Stimulation setup	Duration/pulse	DV	VPT condition
Conson et al., 2015[a]	Right and left dlPFC	tDCS	5 * 7 cm^2	Within	16	Sham	1.0 mA	Contralateral	15 min	RT	Level 2 Self, Level 2 Other
Gooding-Williams et al., 2017	rTPJ	TMS	7 cm	Within	14	Sham	80% RMT	Repetitive (Inhibitory for 10 Hz)	15 pulses at 6 (not used in meta-analyses) or 10 Hz	RT	Level 2 Other
Guise et al., 2007[a]	Right and left frontal pole	TMS	7 cm	Within	7	Sham (to CZ)	90% RMT	Single pulse (Excitatory)	96 single pulses, 24 per condition	RT	Level 1 Self, Level 1 Other
Martin et al., 2019a	rTPJ, dmPFC	HD- tDCS	Center: 2.5 cm, Return: 7.5/9.8 cm	Within	52	Sham	1.0 mA	Anodal	20 min	RT Accuracy	Level 1 Self, Level 1 Other, Level 2 Self, Level 2 Other
Martin et al., 2019b	rTPJ, dmPFC	HD- tDCS	Center: 2.5cm, Return: 7.5/9.8 cm	Within	52	Sham	1.0 mA	Anodal	20 min	RT Accuracy	Level 1 Self, Level 1 Other, Level 2 Self, Level 2 Other
Martin et al., 2020	rTPJ, dmPFC	HD- tDCS	Center: 2.5 cm, Return: 7.5/9 cm	Within	88	Sham	1.0 mA	Anodal	20 min	RT	Level 1 Other, Level 2 Other
Martin et al., 2017	dmPFC	HD- tDCS	Center: 2.5 cm, Return: 9.2/11.5 cm	Within	40	Sham	1.0 mA	Anodal, cathodal	20 min	RT	Level 1 Self, Level 1 Other, Level 2 Self, Level 2 Other
Nobusako et al., 2017	rTPJ, IFC	tDCS	5 * 7 cm^2	Between	Sham: 10, rTPJ: 10, IFC: 10	Sham	1.0 mA	Anodal	20 min	RT Accuracy	Level 1 Other
Qureshi et al., 2020[a]	Right dlPFC	TMS	7 cm	Within	31	Vertex stimulation	80% RMT	Repetitive (inhibitory)	Three-pulse bursts 50 Hz, repeated every 200 ms for 40s Total: 600 pulses	RT Accuracy	Level 1 Self, Level 1 Other
Santiesteban et al., 2012	rTPJ	tDCS	5 * 7 cm^2	Between	Anodal: 17, Cathodal: 17, Sham: 15	Sham	1.0 mA	Anodal, cathodal	20 min	Accuracy	Level 1 Other
Santiesteban et al., 2015	rTPJ, lTPJ	tDCS	5 * 7 cm^2	Between	rTPJ: 15, lTPJ:15, OZ: 15	OZ stimulation	1.0 mA	Anodal	20 min	Accuracy RT	Level 1 Other
Santiesteban et al., 2017	rTPJ	TMS	7 cm	Within	19	Mid-occipical stimulation	110% RMT	Repetitive (inhibitory)	6 pulses at 10 Hz/trial, 100ms after stimulus onset	RT	Level 1 Self, Level 1 Other
Soutschek et al., 2016	rTPJ	TMS	7 cm	Between	rTPJ: 20, Vertex: 18, S1: 21	Vertex, S1 stimulation	80% RMT	Repetitive (inhibitory)	Three-pulse bursts at 50 Hz, repeated every 200 ms for 40s Total: 600 pulses	Accuracy	Level 1 Other, Level 2 Self
van Elk et al., 2017	rTPJ	tDCS	5 * 7 cm^2	Between	Anodal: 16, Cathodal: 15, Sham: 14	Sham	1.0 mA	Anodal, cathodal	20 min	RT	Level 2 Self, Level 2 Other
Wang et al., 2016	rTPJ	TMS	7 cm	Within	15	Sham	110% RMT	Dual pulse (inhibitory)	80 dual pulses Interval = 100 ms	RT	Level 2 Other
Yang et al., 2020	rTPJ, lTPJ	tDCS	5 * 7 cm^2	Within	45	Sham	2.0 mA	Anodal	30 min	RT Accuracy	Level 2 Self, Level 2 Other

CE: congruency effect; dlPFC: dorsolateral prefrontal cortex; dmPFC: dorsomedial prefrontal cortex; IFC: inferior frontal cortex; lTPJ: left temporoparietal junction; min: minutes; NIBS: Non-invasive brain stimulation; ref: reference site; RMT: resting motor threshold; rTPJ: right temporoparietal junction.

[a] These studies were not included in the meta-analyses because they targeted different regions.

As most VPT tasks had an experimental condition, where the object being judged was incongruent from the Self compared to the Other perspective, and a control condition, where the object was congruent from both perspectives, we extracted the means and standard deviations (SDs) of the congruency effect, for each VPT condition whenever possible. The congruency effect was defined as (*incongruent* − *congruent*) for reaction time (RT) or (*congruent* − *incongruent*) for accuracy, to keep the directions of the effect size in the same direction. If the congruency effect was not available, we extracted the means and SDs of RT or accuracy of the incongruent trials. If the data were only presented in figures, means and SDs were estimated using the WebPlotDigitizer (https://automeris.io/WebPlotDigitizer). If only the standard error (SE) was available, we calculated the SD with the formula: $SD = SE * \mathrm{sqrt}(n)$. We also contacted the authors for the data and related information that was not reported, such as the correlation between repeated measures.

2.4. Data analysis

Data analysis was performed using R (version 4.0.1) and the Metafor package (Viechtbauer, 2010). We used the means and SDs to calculate the standardized ESs for each of the four conditions (VPT Level: 1 or 2, Perspective: Self or Other) and each stimulation target (rTPJ, dmPFC), respectively. For between-subject studies, we calculated the standardized mean difference (i.e., Hedge's *g*). For within-subject studies, we calculated the standardized mean change (Morris and DeShon, 2002). We contacted the authors to ask for the raw data or correlation between repeated measures if the information was not provided in studies.

If a study reported both RT and accuracy, we calculated a combined ES and variance (i.e., ES_{comb} and var_{comb}) using the following equations:

$$ES_{comb} = \frac{1}{2}\left(ES_{RT} + ES_{accuracy}\right)$$
$$var_{comb} = \frac{1}{4}\left(var_{RT} + var_{accuracy} + 2corr\sqrt{var_{RT}}\sqrt{var_{accuracy}}\right)$$

Where *corr* is the correlation between RT and accuracy. If it was not provided in studies, we used an assumed $corr = 1$, which was a conservative approach according to Borenstein et al. (2009) and Scammacca et al. (2014).

For three studies (Gooding-Williams et al., 2017; Martin et al., 2020; Wang et al., 2016) that reported effects for different rotation angles and body postures during VPT, we focused on the 160-degree condition and calculated a combined ES for both body postures. For one study (van Elk et al., 2017), which examined the effects of complex mental body transformation and stimulation sessions (online and offline) on VPT, we focused only on the z-axis 180-degree condition and combined the ESs of both stimulation sessions, to ensure its comparability with other studies. Moreover, the studies by Martin et al., 2019b and Martin et al., 2019a reported the same data from the Australian participant group, so we only used the data from the South-East Asian group for Martin et al., 2019b.

For consistency, the direction of the ES was defined as positive if the excitatory stimulation increased the RT or decreased the accuracy congruency effect (or that of the incongruent trials), and negative for the inhibitory stimulation. For between-subject tDCS studies that included anodal, cathodal, and sham stimulation groups, only the anodal > sham comparison was used for the main meta-analysis to avoid the data of the sham group being used repeatedly. One within-subject TMS study (Gooding-Williams et al., 2017) used two types of active stimulation (6 and 10 Hz). We only included the sham > 10 Hz contrast for the meta-analysis, because it is generally agreed that high-frequency online rTMS could lead to disruptive effects (Kobayashi and Pascual-Leone, 2003). Additionally, it should be noted that the anodal stimulation group of Martin et al., 2017 is a subset of Martin et al., 2019a, so we only included sham > cathodal comparison for this study.

We first performed two separate meta-analyses to examine the overall effect of rTPJ and dmPFC stimulation on VPT, respectively. As some studies included multiple VPT conditions, we used both the two-level and three-level random-effects model with the restricted maximum-likelihood estimator (Cheung, 2014; Konstantopoulos, 2011). A critical difference between the two models is that the former ignored the within-sample variance and treated ESs from the same study as independent, whereas the latter accounted for potential dependence between ESs from the same study. Model comparison based on Akaike's information criteria (AIC) was conducted to test which model was better given the data. Heterogeneity among the included ESs was assessed using the *Q* and I^2 tests (Cheung and Vijayakumar, 2016). The funnel plot and Egger's test were used to assess publication bias (Egger et al., 1997). If an Egger's test revealed significant publication bias, the trim-and-fill method (Duval and Tweedie, 2000) was used to generate a corrected estimate after accounting for the effects of unpublished studies.

To investigate how rTPJ and dmPFC stimulation influence specific VPT conditions, we further conducted subgroup analyses for each of the conditions and each stimulation target (except for rTPJ stimulation on Level-2 VPT Self condition because of insufficient ESs). The meta-regression (with the task condition as a moderator) and Wald tests were used to statistically compare the aggregate ESs of different subgroups.

To assess the reliability of the results, we conducted a few control analyses. First, we used a leave-one-study-out analysis to examine the influence of individual ESs. Second, we conducted a control analysis for the dependent variable measure by replacing each of the combined RT and accuracy ESs with ESs for only RT or accuracy and comparing the effect sizes. In addition, we explored the effects of stimulation timepoint (offline or online), study design (between- or within-subject design), and tDCS electrode size on results for TPJ stimulation. For studies using dmPFC stimulation, we examined the effects of contrast selection (cathodal or anodal) on results, because the studies were otherwise similar in their design.

3. Results

3.1. Overview

A total of 16 studies met the inclusion criteria for the qualitative review (Fig 1). Since a random-effects model requires at least three ESs (Cheung and Vijayakumar, 2016), three studies were excluded from the meta-analysis because they stimulated regions not tested for in other studies and thus did not provide sufficient ESs required by a meta-analysis.

Among the remaining 13 studies, nine stimulated rTPJ only, one stimulated dmPFC only, and three stimulated both regions. After distinguishing four unique combinations of VPT Level and Perspective, we obtained 23 effect sizes for the rTPJ and 14 effect sizes for the dmPFC targets. An overview of selected studies and variables for the analyses can be found in Table S2.

3.2. Quality assessment

The quality assessment showed that all the 16 studies used a random assignment to allocate participants to different stimulation conditions (Fig 2). A total of six tDCS and five TMS studies used the within-subject design, whereas the remaining four tDCS and one TMS studies used the between-subject design. However, none of the studies included an explicit statement about the allocation concealment, yielding potential biases related to this criterion.

Regarding blinding of participants and researchers, six studies were double-blinded. The remaining 10 studies did not report if blinding was used, resulting in the unclear risk of bias regarding this criterion.

All studies used sham procedures. Specifically, nine tDCS studies used a procedure by turning off the electric current shortly after stimulation onset, with a length ranging from 15 to 60 seconds. The remaining one tDCS study used anodal stimulation of the occipital cortex with the same duration and intensity as an active control condition (Santiesteban et al., 2015). For TMS studies, two used a sham

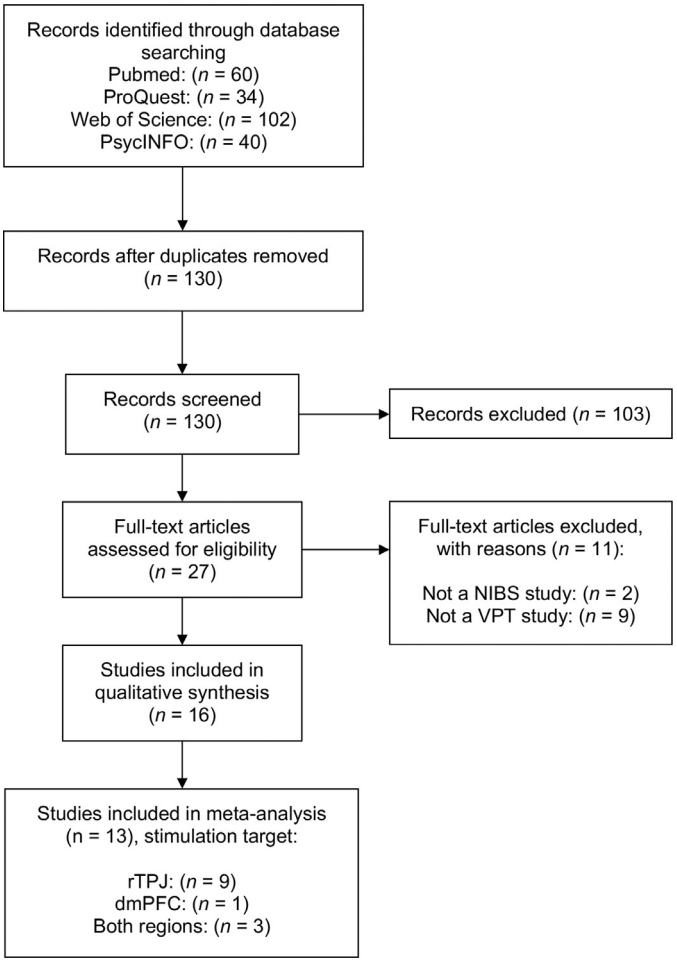

Fig. 1. PRISMA flow diagram of literature search strategy.

coil and played loud sounds mimicking TMS discharges via earphones during both active and sham stimulation (Gooding-Williams et al., 2017; Wang et al., 2016). Another three studies stimulated the vertex (Guise et al., 2007; Qureshi et al., 2020; Soutschek et al., 2016) and one study stimulated the occipital cortex for control (Santiesteban et al., 2017).

The risk of incomplete outcome data (e.g., attrition bias) was low for all of the included studies except one, in which 11 participants were excluded due to technical issues related to tDCS (van Elk et al., 2017), although it included a relatively large sample of participants (n = 58).

Finally, regarding selective reporting, seven studies reported both RT and accuracy measures, while seven and two studies only reported RT or accuracy respectively. Thus, the nine studies that only reported one dependent variable may be associated with a high risk of selective reporting. Moreover, five studies reported congruency effects, whereas the remaining 11 studies reported data from specific conditions (e.g., incongruent trials). Therefore, the research degrees of freedom in data analysis and results reporting appears to be high.

4. Meta-analyses

4.1. Effects of rTPJ stimulation

The two-level random-effects model showed that the overall effect of rTPJ stimulation on VPT was not significant (ES = -0.10, 95% CI: [-0.22, 0.03], Z = -1.49, p = 0.14), with high dispersion and residual heterogeneity ($I^2_{\text{Level-2}}$= 62.34%, $Q(22)$ = 60.08, $p < 0.001$). Egger's test (Z = -1.75, p = 0.08) indicated that the publication bias was not significant (Fig S1). The three-level random-effects model considering the dependence between ESs from the same study showed a slightly larger but not significant effect (ES = -0.18, 95% CI: [-0.44, 0.08], Z = -1.40, p = 0.17). In this model, 76.12% ($I^2_{\text{Level-3}}$) of the total variation can be attributed to between-study, 5.10% to within-study heterogeneity ($I^2_{\text{Level-2}}$), and 18.77% to sampling variance ($I^2_{\text{Level-1}}$). Model comparison slightly preferred the three-level random-effects model (AIC = 25.23) over the two-level model (AIC = 27.04), reflecting the dependency between ESs from the same study.

To test the effects of rTPJ stimulation on specific task conditions, we further ran four subgroup meta-analyses for each unique combination of VPT Level and Perspective (Fig 3). Our results showed that rTPJ stimu-

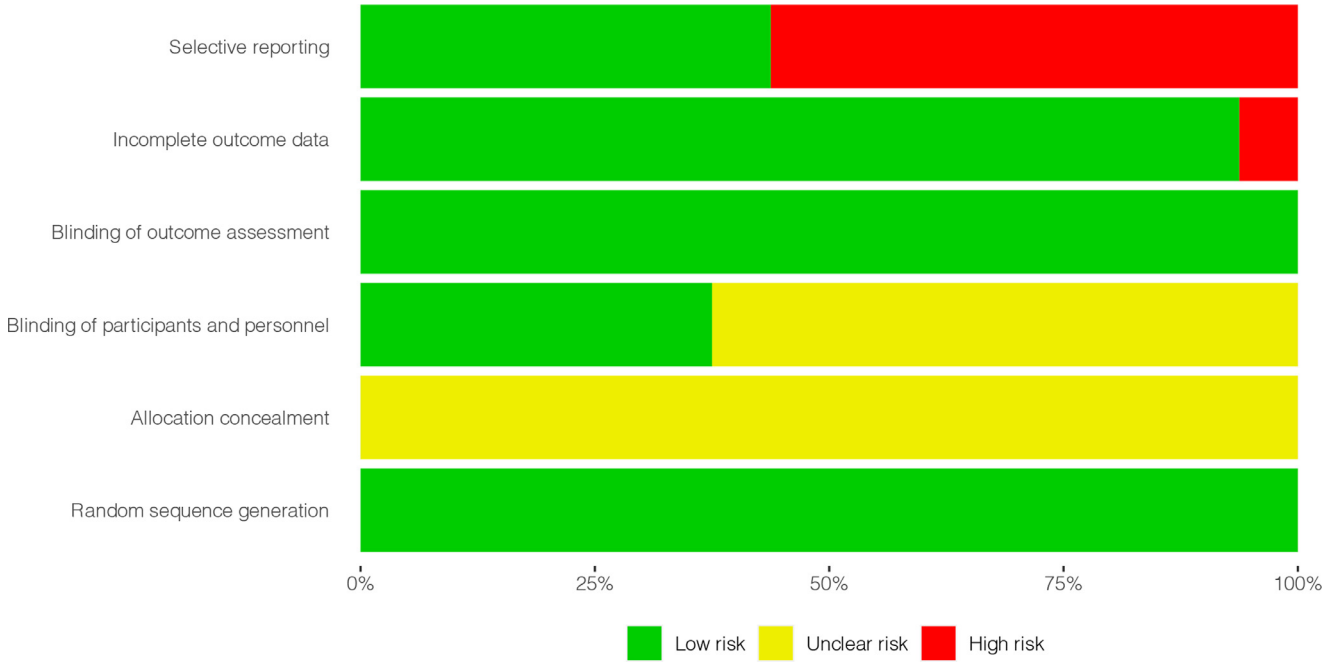

Fig. 2. Risk of bias graph of included studies.

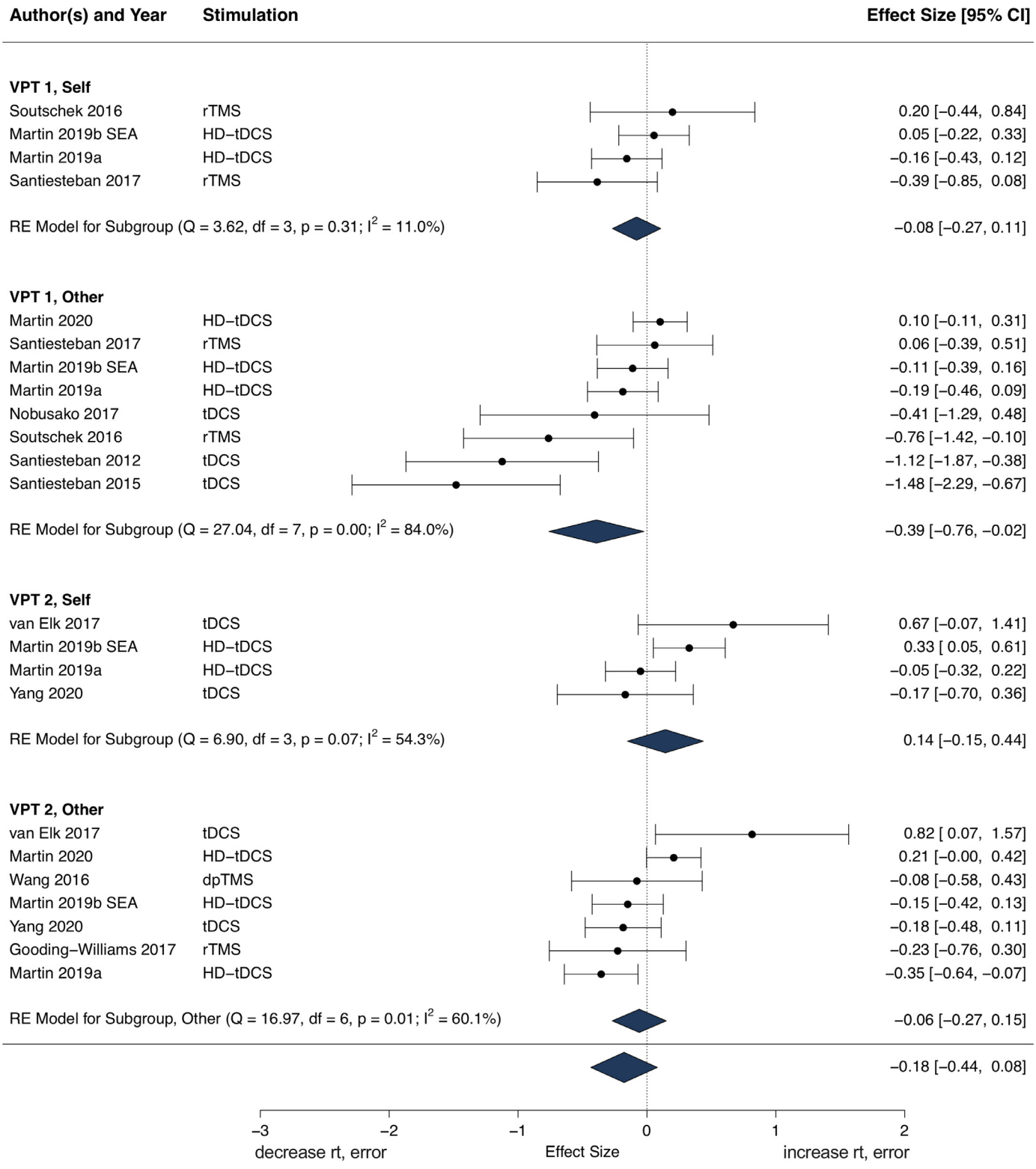

Fig. 3. The effect of rTPJ stimulation on different VPT conditions. The excitatory stimulation of the rTPJ (vice versa for the inhibitory stimulation) significantly increased participants' performance (i.e., shorter RT or lower error rate) in Level-1 VPT Other condition (ES = -0.39). The effects of rTPJ on other VPT conditions are negligible.

Congruency Effect: incongruent – congruent trials for RT, congruent – incongruent trials for accuracy; SEA: South-East Asian participants.

lation significantly improved participants' performance on Level-1 VPT Other condition (ES = -0.39, 95% CI: [-0.76, -0.02], $Z = -2.09$, $p = 0.04$). Egger's test ($Z = -4.24$, $p < 0.001$) indicated a high risk of publication bias in these studies. The trim-and-fill method that considered this bias yielded a negligible effect (ES = -0.07). The effects on Level-1 VPT Self (ES = -0.08, 95% CI: [-0.27, 0.11], $Z = -0.84$, $p = 0.40$), Level-2 VPT Self (ES = 0.14, 95% CI: [-0.15, 0.44], $Z = 1.01$, $p = 0.34$) and Level-2 VPT Other condition (ES = -0.06, 95% CI: [-0.27, 0.15], $Z = -0.56$, $p = 0.58$) are small and insignificant. Egger's tests for these three subgroups did not show significant publication bias either ($ps > 0.25$). To further test if the effects on Level-1 VPT were stronger than the other three conditions, we conducted a three-level meta-regression with the task condition as a moderator. The Wald tests only showed a significant difference between Level-1 Other and Level-2 Self conditions ($Z = 2.36$, $p = 0.02$).

4.2. Effects of dmPFC stimulation

The two-level random-effects model showed that the overall effect of dmPFC on VPT was significant, showing an slight increase in RT or error rate after stimulating the dmPFC (ES = 0.09, 95% CI: [0.02, 0.17], $Z = 2.41$, $p = 0.02$, Fig S2), with very low heterogeneity ($I^2_{\text{Level-2}} < 0.01\%$, $Q(13) = 9.29$, $p = 0.75$). Egger's test ($Z = 1.20$, $p = 0.22$) suggests that the risk of the potential publication bias was low (Fig S1). The three-level model yielded similar results (ES = 0.09, 95% CI: [0.01, 0.18], $Z = 2.42$, $p = 0.03$). As expected, the model comparison preferred two-level random-effects model (AIC = -11.20) over the three-level model (AIC = -9.19).

Again, we ran subgroup meta-analyses for each VPT condition respectively (Fig S2). We found a significant effect of dmPFC stimulation in the Level-1 VPT Self condition (ES = 0.18, 95% CI: [0.004, 0.36], SE = 0.09, $Z = 2.01$, $p = 0.04$). None of the other three conditions showed a significant effect: Level-1 VPT Other (ES = 0.05, 95% CI: [-0.09, 0.21], $Z = 0.69$, $p = 0.49$), Level-2 VPT Self (ES = 0.16, 95% CI: [-0.02, 0.34], $Z = 1.75$, $p = 0.08$), and Level-2 VPT Other condition (ES = 0.04, 95% CI: [-0.09, 0.18], $Z = 0.67$, $p = 0.50$). Egger's tests for these subgroups did not show significant publication bias ($ps > 0.50$). We also conducted the three-level meta-regression and Wald tests as above but found no significant difference between the subgroups ($ps > 0.23$).

4.3. Supplementary analyses

We first performed sensitivity analyses regarding the selection of the dependent variable for rTPJ stimulation studies. In the analyses mentioned above, we used the combined RT and accuracy ESs for studies that reported both measures. The sensitivity analyses showed that the results of the meta-analyses remained similar if we only used RT or accuracy ESs for those studies (Table S3). Moreover, we conducted stricter sensitivity analyses by doing the above analyses only based on RT or accuracy data, which did not show significant differences between models based on different dependent variables (Table S3). However, it should be noted that the effects of rTPJ stimulation on Level-1 VPT Other condition became negligible in the RT-only model (ES = -0.10, $p = 0.32$). Since the sample sizes were smaller when focusing on a single dependent variable, more evidence is needed to confirm these findings.

Additionally, we compared the overall effects of studies using different stimulation timepoints (online and offline), tDCS electrode sizes, and study designs (within- and between-subject designs). We did not find significant differences here either (see Table S4 for details). Finally, the leave-one-study-out analyses showed that the overall effects of the main and subgroup analyses were relatively stable. The key findings were not driven by any individual studies. The detailed results were listed in Table S5.

5. Discussion

This meta-analytic study examined how rTPJ and dmPFC stimulation influenced VPT across 13 studies. The results showed that the rTPJ was mainly involved in allocentric visibility judgment. The dmPFC appeared to play a role in processes related to the egocentric perspective. Importantly, the overall effects of rTPJ and dmPFC stimulation on most VPT conditions were negligible. These findings not only advance our understanding of the neural mechanisms underlying VPT but also systematically demostrate the efficacy of NIBS on VPT and the implications for its practical use.

One main finding of our meta-analysis is that excitatory stimulation of the rTPJ increased performance in Level-1 VPT Other condition: participants' error rate and RT decreased during line-of-sight or visibility judgements when their own perspective was incongruent with the other's perspective. Level-1 VPT requires participants to trace the line of sight between the self and target object and does not rely on deliberate movement simulation (Kessler and Rutherford, 2010). Our findings thus suggest that rTPJ plays a critical role in suppressing the egocentric perspective when taking the other's perspective (Santiesteban et al., 2012). Notably, the ability to overcome one's self-centered perspective implemented in the posterior TPJ was also recruited in choosing delayed and prosocial rewards (Soutschek et al., 2016). Moreover, two subprocesses have been proposed in Level-1 VPT: (1) perspective calculation, which is the fast, automatic, and cognitively efficient calculation of someone else's perspective, and (2) perspective selection, which is the effortful selection of either representation, depending on task demands (Apperly and Butterfill, 2009; Qureshi et al., 2020; Todd et al., 2019). Therefore, a promising direction for future studies is to elucidate the effects of rTPJ stimulation on these two subprocesses of Level-1 VPT.

Notably, the subgroup analysis showed that the aggregate effect of rTPJ stimulation on Level-2 VPT Other condition was negligible. Because of the proposed role of the rTPJ in Theory of Mind (Krall et al., 2015; Saxe and Wexler, 2005) and its implications in multisensory integration between proprioceptive and visual inputs (Blanke and Mohr, 2005; Ionta et al., 2011), it was suggested that the rTPJ might be critical for Level-2 allocentric perspective taking, which has a high-level requirement of embodied rotation (Martin et al., 2020). The current study, however, did not provide strong evidence for the rTPJ's involvement in embodied processes during VPT. A plausible explanation is that the relative contribution of the rTPJ-centered network to Level-2 VPT is smaller than its Level-1 counterpart, as Level-2 VPT is more complex and may rely on the coordinated effort of more distinct networks, although this finding remains to be confirmed due to relatively small sample size and high heterogeneity in NIBS methods. Moreover, Bayesian statistics (Schmalz et al., in press; van de Schoot et al., 2021) can provide a more thorough investigation into null results when more VPT studies are accumulated in the future.

In addition to the rTPJ, the dmPFC is also closely related to complex social cognition (Lieberman et al., 2019), particularly in merging the self- and other-related information to guide social decision-making (Schurz and Perner, 2015; Wittmann et al., 2016). In the context of VPT, we found that the dmPFC stimulation significantly decreased participants' performance during Level-1 egocentric perspective taking, possibly by increasing the salience of irrelevant information from the allocentric perspective (Martin et al., 2019a). The effects of dmPFC stimulation on allocentric perspective taking are rather negligible. Taken together, the dmPFC might be recruited to integrate the external information into one's own perspective, especially when embodied rotation is less required (i.e., Level-1). This interpretation is consistent with findings that the excitatory dmPFC stimulation decreased the self-reference effect in episodic memory (Martin et al., 2019a). However, findings should be regarded as preliminary and interpreted with caution, because they are based on a relatively small number of studies from the same research group.

The current study also revealed some general problems related to NIBS studies in this field. First, there is no consensus on the selection of dependent variables. Both RT and accuracy were widely used to reflect VPT performance. Moreover, some studies calculated the differences between incongruent and congruent trials, whereas others just analyzed

data from specific conditions (e.g., incongruent trials). This flexibility may increase the risks of selective reporting. Therefore, we recommend researchers report both RT and accuracy measures for all task conditions and perform a multiverse analysis (Steegen et al., 2016) to comprehensively evaluate the effects of NIBS on VPT. Second, previous studies showed that trait factors, such as baseline perspective-taking ability (Fini et al., 2017) or empathetic understanding (Bukowski et al., 2020), may modulate the effect of NIBS (of other brain regions) on spatial or emotional perspective taking. However, most studies only focused on the stimulation effects at the group level without taking individual differences into account. This is particularly important for between-subject studies since the effects may be attributed to differences on a dispositional factor rather than stimulation itself. Finally, although the potential of NIBS as an intervention for VPT-related disorders has been proposed by some researchers (Martin et al., 2020; Santiesteban et al., 2012), our findings raise challenges on its efficacy. For example, even the largest effect we found (i.e., rTPJ stimulation on Level-1 VPT Other condition) is relatively small and may be associated with publication bias. Therefore, it appears still premature to apply this approach to practical use at the current stage.

As one of the first meta-analytic studies that examines NIBS on VPT tasks, the present study has some limitations. First, the sample sizes for some subgroup analyses are limited. Thus, the current findings should be interpreted with caution. Results are expected to be more robust and reliable with future NIBS studies on VPT. Second, the meta-analyses are mainly based on the evidence from tDCS studies. Due to the sample size limitation, we are unable to directly compare the effects of different NIBS techniques (e.g., tDCS vs. TMS) on a certain VPT condition in the current study. This issue is likely to be addressed when more TMS studies are available. Third, both the rTPJ and dmPFC are heterogeneous regions. At least three subregions have been identified in the TPJ (Mars et al., 2012). The posterior region might be recruited during control of self and other representations and the anterior region during attentional reorientation (Corbetta et al., 2008; Krall et al., 2015; Scholz et al., 2009). Similarly, the dorsal and ventral parts of the dmPFC appear to mainly involve in other- and self-related processes, respectively (Lieberman et al., 2019). Due to the spatial precision limitation of stimulation (e.g., two-electrode tDCS), most studies did not specify which subregions of the rTPJ or dmPFC were stimulated. Future studies may address this issue with the assistance of neuronavigation and more focal NIBS techniques (Donaldson et al., 2015). Finally, most of the included studies focused on the role of an individual brain region in VPT. However, neuroimaging evidence suggests that complex social cognitive processes, such as VPT, depend on the interactions of multiple brain areas (Schurz et al., 2013). Particularly, the effects of tDCS may be not limited to the targeted area either, because the current travels along the path between anodal and cathodal electrodes (Stagg and Nitsche, 2011). Therefore, another future avenue for research is to elucidate how NIBS influences interactions between brain networks during VPT.

6. Conclusion

The current meta-analytic study found that the rTPJ and dmPFC appeared to be causally involved in allocentric and egocentric Level-1 VPT, respectively. The effects of the stimulation of both regions on Level-2 VPT were negligible, suggesting that neither was necessary for embodied processing. These findings contribute to a better understanding of the neural mechanisms of VPT and show the limitations and future directions of the NIBS technique as a potential intervention for patients with related deficits.

Declaration of Competing Interest

None

Credit authorship contribution statement

Yuan-Wei Yao: Conceptualization, Methodology, Validation, Data curation, Writing – original draft, Project administration. **Vivien Chopurian:** Conceptualization, Methodology, Formal analysis, Data curation, Writing – original draft, Visualization. **Lei Zhang:** Conceptualization, Methodology, Writing – original draft. **Claus Lamm:** Writing – review & editing, Supervision. **Hauke R. Heekeren:** Writing – review & editing, Supervision.

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Data and code availability statement

The data related to this study are available on an OSF repository (https://osf.io/vraun/). Other materials and analysis code are available on reasonable request to Y.W.Y.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.118462.

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