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Review

Are We Right about the Right TPJ? A Review of Brain Stimulation and Social Cognition in the Right Temporal Parietal Junction

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Abstract: In the past decade, the functional role of the TPJ (Temporal Parietal Junction) has become more evident in terms of its contribution to social cognition. Studies have revealed the TPJ as a 'distinguisher' of self and other with research focused on non-clinical populations as well as in individuals with Autism and Type I Schizophrenia. Further research has focused on the integration of self-other distinctions with proprioception. Much of what we now know about the causal role of the right TPJ derives from TMS (Transcranial Magnetic Stimulation), rTMS repetitive Transcranial Magnetic Stimulation), and tDCS (transcranial Direct Cortical Stimulation). In this review, we focus on the role of the right TPJ as a moderator of self, which is integrated and distinct from 'other' and how brain stimulation has established the causal relationship between the underlying cortex and agency.

Keywords: rTPJ; right temporal parietal junction; TMS; transcranial magnetic stimulation; tDCS; transcranial direct cortical stimulation; social cognition

1. The Right Temporal Parietal Junction

The right Temporal Parietal Junction (rTPJ) is a highly innervated cortical region that underlies numerous aspects of social cognition [1,2]. Research focusing on the rTPJ has established correlations with a multitude of critical social functions including self-evaluation and awareness, altruism, Theory of Mind (ToM) and awareness of personal and social functions [2–7]. In moving beyond correlation, researchers have examined the causal role of the rTPJ with patient (i.e., loss of function) data as well as manipulations utilizing brain stimulation. These brain stimulation techniques include Transcranial Magnetic Stimulation (TMS), repetitive Transcranial Magnetic Stimulation (rTMS), and transcranial Direct Cortical Stimulation (tDCS).

Brain stimulation methods are now both routine and critical in all aspects of neuroscience. TMS has been the foundation of brain stimulation techniques, as it was the first focal, non-invasive, and relatively painless investigative tool [8–11]. Much of what is currently known about the causal role of the rTPJ in terms of social cognition is due to the application of TMS [12]. While tDCS and patient data are also main models of causal determinants, we will focus here on TMS. The physics underlying TMS are simple. By passing an alternating current of electricity through metal windings (the primary conductor), a magnetic field is generated that can induce an electrical effect in any potential secondary conductor. Neurons serve as an effective secondary conductor and are easily influenced by the fields generated by the TMS coil. This magnetic field can disrupt the overall neuronal effect immediately (single pulse-TMS) or if pulses are given repetitively (rTMS), the effect can be inhibitory (if pulses are delivered around 1 Hz) or excitatory (if pulses are delivered at 10 Hz or higher). Used in context, one can disrupt/block the rTPJ, inhibit it, or excite it and then measure what the resulting change in behavior is [13–17].

Transcranial Magnetic Stimulation and tDCS are scalp-based techniques. This allows for ease of use from determining timings to having few limitations in terms of the physical restraints found in MRI/fMRI [9,18–26]. Further, logic dictates that if Area X is removed and the behavior under investigation changes, Area X may play a role in that behavior. Unlike neuroimaging, one is directly manipulating the brain. However, the limitations are many including depth of penetration, knowing the exact spread of cortical excitement/inhibition/spread, safety and spatial resolution. However, when employed with other techniques and good experimental design we have now realized that the rTPJ is much more than just a passive player in social behavior.

The TPJ is broadly defined as the posterior/dorsal region of the temporal lobe extending posteriorly to extrastriate regions and dorsally to the lateral inferior parietal sulcus (Figure 1). It includes the posterior portion of the superior temporal sulcus, portions of the supramarginal gyrus, the angular gyrus, and the lateral inferior parietal sulcus [27–29]. A typical TMS study, co-registered into MNI space, gave coordinates as x = 63.4 $\pm$ 0.73, y = -50 ± 1.29, z = 22.7 $\pm$ 0.56 [30]. While there are debates among the definitions, we defer to a broader (i.e., greater area) inclusionary definition. There are asymmetrical anatomical differences (i.e., hemispheric), one of the most notable is the planum temporale, in which we and others have discovered significant structural lateralized differences [31–37], which lead to significant functional differences in non-social domains [38–40]. For example, lesions of the lTPJ (left TPJ) typically lead to aphasias and verbal language disruption [41], visual-spatial neglect, however, is a common outcome of rTPJ damage [42,43].

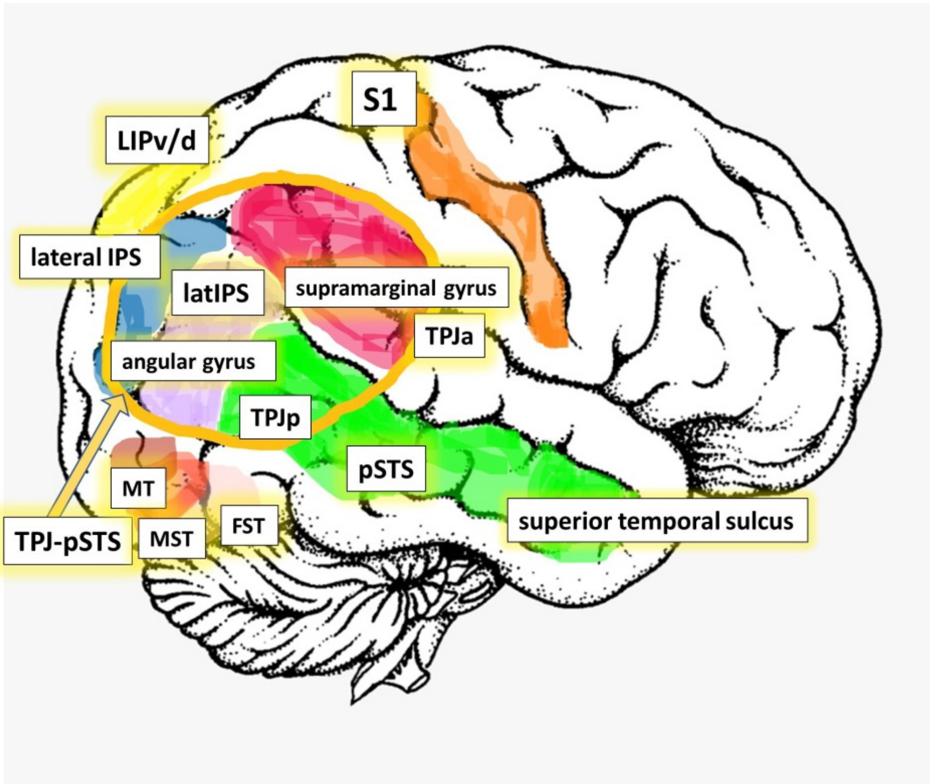

Figure 1. The rTPJ is the junction between the Temporal and Parietal Lobes. It includes the posterior portion of the superior temporal sulcus, portions of the supramarginal gyrus, the angular gyrus, and the lateral inferior parietal sulcus.

The TPJ networks with a number of systems in the brain that are critical for higher-order cognition including the Fronto-Parietal network [27]. This includes the PFC, the

Precuneus, and the insula which are all highly involved in social cognition [44–46]. These regions overlap with the Default Mode Network (DFM), which innervate with the TPJ [47–49]. These regions sustain numerous social abilities including self-awareness [50] (readers are directed to Igelstrom & Graziano, 2017 [27]).

2. TMS and rTMS

There is agreement that the self is critical to social cognition [51]. While there are a plethora of ways to examine self-brain connections [52–57], the awareness of the self and the ability to differentiate self from other has become a cornerstone of social neuroscience [58,59]. Neuroimaging studies have found correlations between the rTPJ and all manners of the self [60–63]. While we have gained much from imaging, TMS has demonstrated that alterations of the self can be induced via rTPJ stimulation.

One of the most interesting applications of TMS to investigate the self is in terms of body illusion. Tsakiris et al. [30] sought out to investigate the right TPJ on the basis of its involvement in maintaining and processing multisensory stimuli related or unrelated to one's own body by carrying out experiments employing TMS. By the induction of a bodily illusion, the investigators utilized the representation of external stimuli and controlled whether these objects presented were correlated with the participants' bodies or not. RTPJ stimulation significantly disrupted the sense of self-body perception.

Of interest, is that this paper revealed that the timing of 350ms was effective in disrupting rTPJ functioning. These data are similar to those of Blanke (see below) and match late P300 potentials indicating ample time for higher-level cognitive processes to form and thus be disrupted via TMS. Whereas the spatial resolution of TMS and other scalp stimulation techniques are lacking, the temporal resolution remains excellent which is an often-overlooked benefit of stimulation (most studies reported here report a similar timing when single-pulse TMS was employed). The authors concluded that the role of the rTPJ at some level compares the current sensory information of the self with a previously stored representation and disruptions of this ability to compare accurately lead to difficulties in self (and self-other) processing [64].

These data are similar to those of Blanke [65] and colleagues. He and his colleagues have established the role of the TPJ [66–70] as a causal agent in self/body connections, specifically the rTPJ in OBE (Out of Body Experiences) and autoscopic phenomena [71–73]. In these studies, rTPJ stimulation resulted in individuals seeing themselves from a different person's point of view in one case, as well as the person's own limbs distorted in another case. When mapped back on to other self-illusion data obtained via fMRI, these data indicate that the 'lighting up' of the rTPJ is likely causal rather than just correlational [60]. In other words, a normally functioning rTPJ is required to maintain our accurate sense of self in terms of space and proprioception. Disruption of this region leads to self-body distortions which lead to the conclusion that the rTPJ is needed for the maintenance of an accurate physical self-perception.

In addition to body ownership and making self-other distinctions, the right TPJ has been connected to the reorienting of attention in humans, where focus can be rapidly redirected from and to specific stimuli in certain situations and environments. The ability to distinguish between oneself and individuals and objects around them is a phenomenon known as contingent orienting. This explains how one can redirect their attention and focus to a certain object or person, due to "top-down and stimulus-driven control" [6]. However, bottom-up stimuli have been linked to attention being captured [74] and evidence has shown that the reorienting of attention is connected to the response of the integration of both the bottom-up stimuli as well as top-down [75,76]. With the use of TMS to interfere with the function of the TPJ of participants, research has pointed to the right TPJ's involvement in attentional reorienting, visual and social cognition, finding that TMS to the right TPJ modified and had a control on contingent orienting when participants were presented with specific stimuli.

Krall et al. went further confirming the anterior rTPJ's cognitive role in attention shifting using the application of TMS [77]. The Posner task was utilized to observe the reorienting of the participants' spatial attention and false belief was also investigated using Gallagher's cartoon task. The researchers stated that due to the restricted spatial precision of TMS, they were able to stimulate only the anterior rTPJ; therefore, we must not necessarily conclude that the posterior rTPJ has no role in these tasks. Observing how participants respond to these tasks when TMS is delivered to the posterior rTPJ would provide further insight into the neural correlates of the rTPJ and its importance in these processes. Additionally, the data were collected from a total of 20 participants, perhaps having a larger number of subjects would yield more accurate results- especially since the researchers were aware that cortical excitability wasn't inhibited in some of their participants, causing some uncertainty. Ultimately, the authors conclude that the rTPJ is a critical brain region involved in cognitive, social processes, such as attention reorienting. Overall, these data suggest that visual cognition is a key factor that partakes in an individual's ability to encode information from the surrounding environment and reorient that attention quickly, from any object or person that present key features that allow the visual system to recognize and process them. Krall et al. [77] also found and confirmed the right TPJ's cognitive role in attention shifting, while employing TMS. This all suggests that visual cognition is a key factor that partakes in an individual's ability to take in information from the surrounding environment and reorient that attention quickly, from any object or person that present key features that allow the visual system to recognize and process them.

Attention reorienting is a crucial part of social cognition, as it allows us to understand our surroundings and more importantly, can allow us to empathize with others as well. Previous research has provided evidence for multiple neural systems and networks behind the processes regarding empathy and morale, Miller et al. [78] designed a TMS study aimed to find the exact role of the right TPJ in participant psychophysiological responses when presented with the suffering of another individual (more specifically, a young child experiencing sadness) to truly understand the importance of the rTPJ in the way we as humans, process and approach the suffering of others. The researchers observed decreased activity of the parasympathetic nervous system when disrupting the activity of the rTPJ, providing further evidence that empathy is regulated by the rTPJ, along with playing a certain role in autonomic and affective responses to others' suffering [78]. These data again confirm that the fMRI data that has linked the rTPJ to empathy is likely causal [79–82].

Moral judgments and being able to make a clear distinction between right and wrong have also been connected to the rTPJ. Young et al. [83] found that when the activity of the rTPJ was disrupted by TMS, in comparison to control TMS, the role of beliefs in moral judgments of the participants was drastically reduced. Participants, when judging attempted harms throughout the study, tended to infer that the attempted harms they were presented with were morally acceptable and less morally prohibited. In other words, disrupting one's rTPJ using TMS caused a change in the participants' abilities to utilize their full mental state capacities and judge moral situations. A recent single-pulse TMS study disrupting rTPJ activity found that TMS again increased participant moral judgment. The participants became more restrictive and "adopted a more prohibitive attitude" in respect to certain conditions in the stories narrated during the experiments of either intentional or accidental harms [84].

As one may suspect, there is rich literature regarding neuroimaging studies that have linked the Theory of Mind (ToM) with the rTPJ [46,85–93]. Temporary inhibition via application of TMS to rTPJ causes individuals to take another's beliefs into consideration at a much lower rate, pinpointing the role the rTPJ plays in making decisions, specifically in regards to the actions, values and beliefs of others [83]. The rTPJ is important to social cognition, particularly how it regulates ToM and the ability to process the mental states of others around us during social situations [94]. Bardi et al. [12] asked whether spontaneous ToM follows a similar or different mechanism as explicit ToM based on a false belief. They found that the rTPJ is, in fact, involved in spontaneous ToM and the neural mechanisms of both explicit and spontaneous ToM overlap [95,96].

To make clear distinctions between self and other and attribute identity to individuals as well as oneself, self- and other-face recognition are crucial [30]. Zeugin et al. [97] employed rTMS to observe the rTPJ's role in visual cognition and the processing of faces through the inhibition of the rTPJ of 30 participants. Participants were presented with rotated images of self and others and asked to perform a typical mental rotation task. Self and other comparisons were made before and after either inhibitory TMS or a control condition. It was found that inhibition of rTPJ significantly reduced self-face, but not other-face recognition. This implicates that the rTPJ has a role in self/other distinction beyond correlational.

What happens when rTMS is used to excite the rTPJ? Using theta-burst TMS at 50 Hz, researchers found that higher rTPJ activation inhibits mimicry in a social context [98]. Further, using some interesting manipulations and analyses of self and others, they discovered that the rTPJ (in distinguishing self and other) biases towards self-representations over other representations. In other words, in an excited state, the rTPJ does not imitate others but rather goes into an enhanced 'self' state.

3. tDCS

Transcranial direct current stimulation (tDCS) has also been utilized to observe the involvement of the rTPJ in neural processes regarding social cognition. Through the use of tDCS, cortical excitability is modulated, allowing for the examination of specific brain regions (in this case, the right TPJ) during certain tasks in order to observe its role in self-awareness, self-face recognition, ToM and self-other discrimination, all important processes in social cognition [99].

Payne and Tsakiris [100] investigated self-other discrimination and the right TPJ's responsibility in this crucial neural mechanism while employing anodal, cathodal, and sham tDCS. The participants were asked to complete a video-morphing task before and after brain stimulation. Interestingly, excitatory anodal tDCS over the rTPJ inhibited self-recognition to an extent, finding that participants needed more of their own face shown to be able to recognize themselves and make a clear distinction between self and other. These results also support the findings of Santiesteban et al., [101] the right TPJ affected self-other processing when stimulating the region using tDCS. The inhibition of the representation of the self after tDCS supports the causal role the rTPJ's plays in empathy and mentalizing,

Several brain stimulation studies have found that the right TPJ has been linked to regulating certain emotions, as mentioned before, it is involved in processes like self-other discrimination, ToM, morale and empathy [78], as well as emotional mimicry [102]. Excitatory tDCS findings suggest the right TPJ's important role in social cognition and an individual's ability to represent self and other [101]. The findings of Ye et al. [103] in their tDCS study observing moral judgments confirmed and supported the findings of Young et al. [83]. Participants judged attempted harms and nonharms "as less morally forbidden and more morally permissible" following modulation of the right TPJ's activity using tDCS. This further illustrates the role that the right TPJ is playing in morality and empathy, suppressing it caused a disruption in the participants' abilities to utilize mental states and relate them to certain tasks regarding moral judgment [103]. The right TPJ's involvement in emotional mimicry has also been studied, as it is a process we exhibit frequently in social situations, sometimes without even realizing. Peng et al. [102], were one of the first to explore, through the use of tDCS, the regulation of in-group bias by the right TPJ when it comes to facial emotional mimicry. Interestingly, they found that cortical excitability over the right TPJ resulted in self-other overlap, diminishing the in-group bias regulated by the right TPJ that was observed at first. This modulation caused participants to follow through on both in-group and out-group facial mimicry throughout the study, once again confirming the right TPJ's importance in social cognition, specifically self-other representation.

Hogeveen, Obhi and their colleagues [104] examined excitation of both the Inferior Frontal Cortex (IFC) and the TPJ. Examining these areas with the RH only, it was found that excitation via tDCS caused different effects depending on the area stimulated. Excitation of the IFC leads to improved social performance (via imitation appropriateness). The rTPJ stimulation condition indicated a greater role for self-other distinction in the rTPJ than for socially specific tasks. A similar result was found by Nobusako and colleagues [105]. Here they found that excitation of the rTPJ and the IFC lead to improved perspective-taking and imitation inhibition. Oddly, using a fairly standard indicator of empathy (the Autism-Spectrum Quotient), differences from Sham were not found.

4. Patients and Brain Stimulation

Beyond the scope of this paper is a review of patient data in which the rTPJ is related to disorders of social cognition including Schizophrenia [56,61,106] and Autism Spectrum Disorder [86,107–111]. However, brain stimulation has been employed to treat/disrupt neurological and psychiatric disorders via rTPJ application which provides further evidence for a causal role of the rTPJ in social functioning.

While TMS is now a common treatment for many disorders especially if pilot work is considered, stimulation of the TPJ is often involved in the treatment of Schizophrenia or symptoms related to Schizophrenia [112–116]. While not a recommended replacement for traditional therapies for the disease, it appears that stimulation or the TPJ (both Left and Right) do have an influence on symptoms. While there is some evidence for TPJ as a potential site of treatment (and thus, an area with considerable importance to the disease), a recent study found no effect of TMS when delivered to the cerebellum [117]. In a randomized study, symptoms were not significantly reduced in the cerebelluar treatment group. Unfortunately, other regions were not examined. A similar no-result was found following 10Hz TMS delivered to the frontal cortex [118].

While not used to treat Alzheimer's, the TPJ was implicated in a motor cortex stimulation study [119]. Using both ERP's and TMS, the researchers were able to map out cortical responsiveness following TMS delivered to M1. This proof-of-concept study revealed that TMS combined with ERP may be a method for measuring cognitive decline (or progression) in disorders, such as Alzheimer's.

Based on data collected in non-clinical populations, it has been speculated that modulation of the rTPJ may have an impact on classic socially related patient symptomology. For example, Transcranial direct stimulation (tDCS) delivered to the right TPJ has been shown to improve behavioral issues associated with ASD [120]. Due to the relationship of the TPJ with mental and emotional state attribution, with similar processes associated with autism-relevant traits, tDCS to the TPJ has the ability to influence social-cognitive performance [121]. tDCS to the right TPJ can have negative effects in relation to ASD as it can lower the reaction time to harm as well as decrease the role of beliefs in moral judgment [103]. Despite the negative effects tDCS can have on ASD, it has been proposed as an intervention method to the symptoms of ASD, looking to improve cognitive, motor and social communication abilities [122].

The Salehinejad study, in detail, examined the role of both the vMPFC (ventral Medial Prefrontal Cortex) and the rTPJ implying tDCS [120]. They found a greater clinical role for the vMPFC which indicates that the rTPJ is far from the only site responsible for these complex disorders. With that being said, rTPJ stimulation clearly has an effect in both single-case studies [123], pilot studies [124] and larger studies [121]. In these studies, social deficits are reduced and measured with a reduction of symptomatology.

Brain stimulation has provided us with the confidence to now say that it has been established with experimental rigor that there is a causal relationship between rTPJ functioning and social cognition. We believe that this allows us to reinterpret neuroimaging studies with stronger confidence such that the positive activations observed were likely both real and causal in nature. The right hemisphere's dominance in many social tasks is one of the most fascinating findings in neuroscience.

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