Gender differences in the neural structures of (non) emotional perspective-taking: A tDCS study

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Abstract

**Background and objective:** The perspective-taking in social cognition is an ability that makes third-person judgments about the intentions, beliefs and thoughts of others. In cognitive neuroscience literature, perspective-taking has been studied under the guise of the Theory of Mind (ToM). The structural and functional brain differences in males and females in ToM, notably in (non) emotional perspective-taking. We aimed to investigate gender differences in the neural structure differences in (non) emotional perspective-taking ability.

**Methods:** Thirty healthy adults (15 females and 15 males) received anodal and sham transcranial direct current stimulation (tDCS) (2 mA, 15 min) over the right temporoparietal junction (rTPJ) and ventromedial prefrontal cortex (vmPFC) with 1 week interval in three separate sessions. Participants underwent a pain visual analogue scale, a visuospatial perspective-taking task (VPT) and a self-referential attribution task during stimulation.

**Results:** Findings revealed significant differences between vmPFC and rTPJ anodal tDCS stimulation in emotional perspective-taking. Primarily the vmPFC increased emotional perception in comparison with the rTPJ cite. This emotional perception pattern was significant only for men, not women. The rTPJ enhanced the males’ non-emotional perspective ability performance compared to their female contributors. The results indicated that both the rTPJ and vmPFC are associated with self-referential processing (SRP). The vmPFC increased Self Emotional bias negatively while rTPJ increased it positively.

**Conclusion:** both the vmPFC and rTPJ play a role in (non) emotional perspective-taking in men. While the vmPFC increased men’s emotional perspective-taking compared to rTPJ, the rTPJ excitatory stimulation enhanced males’ performance compared to females. Moreover, it indicated that the rTPJ posterior cluster activation in men is higher than in women. in addition, vmPFC increased either Self negative or other positive attribution while rTPJ does the opposite way.

**Keywords:** Gender; Emotional perspective-taking; non Emotional Perspective-taking; transcranial direct current stimulation (tDCS); right temporoparietal junction (rTPJ); ventromedial prefrontal cortex (vmPFC); VPT; SRP
Introduction

Visualizing how a scene emerges from a perspective, which varies from one’s have, is a high-functioning cognitive procedure called Visuospatial Perspective-taking (VPT). From The cognitive neuroscience literature, two levels of perspective-taking have emerged. The first level, also called perspective-tracking, calculates what can be seen from the other's perspective or cannot. The Second level (PT) makes a third-person view of physical objects (Surtees et al., 2013). Visuospatial Perspective-taking (VPT) has been studied in relation to how another agent sees an environment in social and spatial domains (Vogeley & Fink, 2003).

The social cognition aspect of perspective-taking is an ability to make third-person judgments about others' beliefs, thoughts, and intentions. Inferring others' mental states. This brings perspective-taking closer to the concept of "theory of mind" or "Mentalizing" (Shamay-Tsoory, 2010). On the other hand, the spatial cognition literature construes perspective-taking as visualizing how a view looks from a location that differs from one’s own viewpoint, representing a style of processing over how another person views a scene. To put it into a nutshell, the theory of mind (ToM) is a crucial ability for a successful social interaction, which contains both social and spatial traits of a phenomenon.

The substantial difference in emotional and spatial skill performance in males and females has been a long interest in the cognitive neuroscience literature. The Baron-Cohen empathizing/systematizing theory (2010), proposed that, on average, females have a more robust nature to empathize—the motivation to recognize others' mental states in preparation for responding tactfully. Conversely, on average, males have a stronger disposition to systemize—the drive to forecast and respond to non-agentive systems by assuming the rules that regulate such structures. In support of this theory, behavioral studies showed that females achieve better results on tasks that contained affective components of social cognition, for instance, social sensitivity (Baron-Cohen et al., 1999), emotion recognition (Hall et al., 2000; McClure, 2000), and emotional intelligence (Brackett & Salovey, 2006). However, meta-analysis indicates that males are more skilled in spatial abilities than women (Halpern et al., 2007; Voyer & Saunders, 2004; Voyer et al., 1995). The scores of men are higher than women in visuospatial tests, which link with mental rotation (Strand et al., 2006; Wach et al., 2015) and spatial perception or visualization (Hyde, 2014; Yuan et al., 2019). Accordingly, neuroimaging studies revealed functional differences among males and females in tasks, including the appraisal of affective scenes (Proverbio et al., 2009), fairness in pain perception (Singer et al., 2006), and mental rotation decoding.

With respect to neural structure, neuroimaging studies also described gender differences in the neural correlates of perspective-taking. In VPT, men show higher levels of activities in the right medial frontal, bilateral inferior parietal cortex, and precentral, while females show higher activation in the medial temporal, left fusiform gyrus, right superior frontal cortex and right inferior (Gizewski et al., 2006). Halari et al. (2006), revealed that both females and males in VPT showed activation in the bilateral middle occipital gyrus and the right superior parietal lobe. However, males showed higher activation in the left middle temporal gyrus and the right angular gyrus, whereas females showed higher activation in the right superior parietal lobe, bilateral middle occipital gyrus, left precuneus, and left precentral gyrus. Kaiser et al. (2008),
argued that although the brain network for males and females on 3rd person perspective (3PP) is similar, men exhibited extra activation in the right inferior frontal gyrus and precuneus compared to women. However, both females and males displayed more activation in the precuneus and right inferior frontal in 3PP compared to 1st person perspective (1PP) difference in men was more remarkable compared to women. The VPT ability contains emotional and cognitive aspects and shares features with empathy (Lamm et al., 2007).

The functional magnetic resonance imaging (fMRI) studies disclosed different emotional processing brain regions for men and women. Filkowski and colleagues (2017) represented that, in emotion-eliciting conditions, the anterior cingulate cortex, mediodorsal nucleus of the thalamus, frontal pole, and medial prefrontal cortex (mPFC) activation are distinct in men. In contrast, females displayed distinct activation in the hippocampus, regions of the dorsal midbrain: including the locus coeruleus and periaqueductal gray/superior colliculus, and bilateral amygdala. Stevens and Hamann (2012), also indicated that the amygdala reveals valence-dependent gender differences in activation of emotional stimuli, which responded differently in positive and negative emotion processing in males and females. Negative emotional stimulations activated the left amygdala more in women than in men. In contrast, positive emotions increased the left amygdala activation in men compared to women.

Empathy as a social cognition component involves emotional perspective-taking and the matter of self/other distinction. Empathic perception gives us the capability to experience others' negative emotions through painful conditions. The adaptation of Self or other viewpoint triggered Different brain regions' activation. 1PP's painful situation resulted in a bonus motion in the primary somatosensory cerebral cortex. The PFC is activated during the 3PP painful situation (Jackson et al., 2005; Singer et al., 2004). The mid-cingulate cortex activation increased in females who experienced pain, whereas males' evoked signal intensity in the lateral cerebellar cortex increased (Henderson et al., 2008). The authors indicated that the dorsolateral prefrontal cortex (dPFC) activation in men decreased while it did not change significantly in women compared to baseline.

The way we encode information targeting ourselves in the environment is called Self-referential processing (SRP), which indicates in what way individuals encode and process information concerning themselves (Northoff et al., 2006). The SRP is strongly modulated with the activation of cortical midline structures (CMS) and is correlated in all its functional domains, such as spatial, verbal and emotional (Northoff et al., 2006). Kelly and collaborators (2002), showed the role of vmPFC and dorsomedial PFC in SRP by implying an adjective judgment task that compares self- and other- referential. The vmPFC and dmPFC are associated with self-referentiality through emotional processing (Gusnard et al., 2001; Northoff et al., 2006). Northoff and colleagues (2006), indicate that SRP in the spatial domain correlated with tasks considered 1PP and 3PP neural activity, in which 1PP induces the neural activity of vmPFC, dmPFC, medial temporal gyrus, bilateral left inferior, the right anterior insula, and the right postcentral gyrus in comparison with 3PP.

Non-invasive brain stimulation (NIBS) techniques are the safest approaches that permit us to modulate cortical activities in healthy and clinical populations, enabling scientists to experimentally investigate how neural activity causally affects emotional/cognitive functions (Ghanavati et al., 2018; Nitsche et al., 2012; Polanía et al., 2018; Salehinejad et al., 2019; Vicario et al., 2019). In this study, we used transcranial direct current stimulation (tDCS) to examine the excitatory influence on vmPFC and rTPJ in males' and females' (non) emotional VPT and SRP ability. tDCS modulates brain activity by applying a weak electrical current through the scalp. The current flows from a relatively positive voltage (anode electrode) to a relatively negative voltage (cathode electrode) position, engenders an increase or decrease in cortical excitability (Knotkova et al., 2019). The primary function of the anodal electrode is "facilitatory," and the cathodal
electrode is "inhibitory" (Nitsche et al., 2008). Conversely, The anodal tDCS electrode enhances cortical excitability, and the cathodal tDCS electrode decreases it (André R. Brunoni, 2021). Furthermore, neural networks underlying VPT and SRP can be tracked by modulating the cortical activity of the relevant regions, as recommended by recent studies (Mainz et al., 2020; Martin et al., 2019).

Santiesteban, Banissy, et al. (2012) demonstrated that anodal tDCS over the rTPJ modified on-line regulation of self-other perception in VPT performance, but has no effect on Self or others' mental state attribution. On the other hand, inhibition in the rTPJ by tDCS would impair the ability to make inferences about emotional states (Mai et al., 2016). Similarly, Coll et al. (2017), described that inhibitory stimulation over rTPJ reduced the intensity of others' pain perception in comparison with anodal and sham stimulation. Some earlier tDCS studies found gender differences in the neural structure of social and spatial perception. For instance, Martin et al. (2017), showed the role of sex as a mediator in an anodal tDCS stimulation on the dorsomedial prefrontal cortex (dmPFC), which improves the accuracy of females' mental state scores, but impaired men's performance. Similarly, anodal tDCS in mPFC enhances cognitive ToM performance only in females (Adenzato et al., 2017).

Given the sex differences in spatial and emotional perception, female and male preference in order and relevance of cortical correlates, we hypothesized differences in the neural structure of (non) emotional perspective-taking in both genders. We applied anodal tDCS stimulation over the rTPJ and vmPFC to investigate both genders' neural relevance of physical (non-emotional), emotional perspective-taking and self-referential processing.

Methods and materials

Participants

Thirty healthy participants (15 females, mean age 25, SD =3.443 range 18-30, 15 males, mean age 23.53, SD =3.662 range 18-30) informed agreement to participate in this study and were free to leave at any time. To define the required sample size based on a power of 0.95 and α=0.05, We employed G*power (Faul et al., 2007). Inclusion criteria were: (1) age between 18-30 years; (2) no background of neurological disorders; (3) no previous history of substance dependency; (4) no current use of psychotropic medication; (5) no history of brain surgery, intracranial metal implantation, epilepsy, tumor or seizures. All participants were right-handed and had normal vision. This study was approved by a national ethics committee (IR.SBU.REC.1399.069).

Instrument

Our study was a sham-controlled, single-blind, randomized design with stimulation conditions (anodal vmPFC, anodal rTPJ, Sham). Participants' stimuli session and the order of the tasks were selected by two separated numbers from two different boxes (red and blue), the red one determined their stimuli session, and the blue one detected the order of the tasks.

Tasks and stimuli

Participants performed three tasks: (a) Visuospatial perspective-taking task (VPT), (b) pain visual analogue scale rating test, and (c) Self -referential attribution task. The first task was supposed to measure cognitive non-emotional perspective-taking, the pain visual analogue scale is regarded as a measurement for the emotional perspective-taking, and the last task was performed to distinguish the self- and other-referential bias.
Visuospatial perspective-taking task (VPT)

The participants accomplished a visuospatial perspective-taking task on a 13-inch-screen laptop. The task consisted of 144 trials in which participants responded by choosing the best view as the avatar's viewpoint from alternatives. For each trial, the screen displayed a reference picture with the exact dimensions depicting a circular table upon which were several geometrical objects differing in color, shape, and size displayed on the upper half of the screen and the alternative perspectives as avatar viewpoints presented on the lower half of the screen (see fig 1). An avatar stands beside the table at different angles and faces the table's center on the reference picture. In their research, Shelton and collaborators (2012), showed that using a human-like model as an alternative for an object has positively influenced subjects' precision in the perspective-taking task. The participants were instructed to suppress their viewpoint, put themselves in the avatar's place, and visualize the scene. They were asked to indicate the correct answer by Pressing its number on the keyboard. The contributors had no time limit. Pressing the wrong number led to the display of the afterward trial. The order of presentation and trials were identical for all participants. The compositions of the visuospatial perspective-taking task were (avatar perspective angles, number of objects, number of choices, and the avatar's gender). In total, our task contained 144 trials. The avatar orbited around the table at fixed angles. By considering the participants' perspective as zero degrees, the avatar orbits 45 degrees counterclockwise for the next spot until it reaches the start point. In that case, we got eight spots for the avatar's viewpoint. The number of objects on the table varied, containing 10, 20, or 30 different geometrical objects. The number of alternatives in which the participants had to select the avatar's viewpoint was 2, 3, or 4. Half of the avatars were females and half were males. The 1PP viewpoint contains the contributors' perspective (0 degrees) with a variation of 45˚ (Jauniaux et al., 2019). Thus the 3PP viewpoint includes 180° ± 45°.

Table 1. Difficulty variation in VPT

| Angle  | 1PP       | 3PP        |
|--------|-----------|------------|
| 0, 45, 315 | 135, 180, 225 |
| N.Chances  | 2, 3 & 4   |            |
| N.Objects  | 10, 20 & 30 |            |

Note 1PP = 1st person perspective; 3PP = 3rd person perspective

Figure 1. An example of a (female) stimulus in the visuospatial perspective-taking (VPT) task. In this case, the angle is 135 degrees (3rd person perspective) and the correct answer is 2.
Pain visual analogue scale

A series of 120 digital color pictures were prepared despite another person's left hand in two situations (painful and painless). The pictures were taken from both the first-person and third-person angle (although the observers did not require to mental rotate on the former angle they needed to mental rotate on the latter perspective angle), as mentioned in previous studies (Gu & Han, 2007; Jackson et al., 2005; Saito et al., 2016). The pictures demonstrated the various type of pain (burning, cutting, smashing, injection, and slashing), and for the painless situation, we used non-painful stimuli (cotton, rubber, makeup brush, lighter without flame, and Play Dough), which commonly are used in everyday life (fig 3). Half of the images represented a painful situation, and the other half represented a painless situation. For half of the situations, we used a young female left hand whose age was in the participants' range (18-30), and the other half used a male left hand. We used the stimulus 3 times on both perspective angles for each condition. By determining these compositions, we reach 120 different situations (angles (2), number of stimuli for each situation (5), painful or painless situations (2), gender (2), and repetition (3), 2×5×2×2×3). We requested the participants to estimate how painful the presented situation would be and rate it with the bar beneath the image from 1 (minimum pain) to 9 (worst unbearable pain). To acknowledge the painfulness and painlessness of the stimulations, we use a preliminary investigation (N= 15; 8 females; mean age = 22.34, SD =3.43). In the preliminary investigation, Contributors were asked to estimate how painful the depicted condition would be by rating them (0: no pain to 9: unbearable pain). We utilized pictures that averaged the severity of felt pain more than 5 and less than 1 for painful and painless conditions.

Figure 2. Samples of the pain evaluation task. (a) Displaying a painful female hand situation from a first-angle perspective. (b) Showing a painless female hand situation from a first-angle perspective. (c) Representing a painful male hand situation from a third-angle perspective. (d) showing a painless male hand situation from a third-person angle perspective. Note 1PP = 1st person perspective; 3PP = 3rd person perspective.
Self-referential attribution task

The Stroop concept is an experimental paradigm for exploring selective attention (Roelofs et al., 2002). Utilizing this paradigm, we designed a computerized task that evaluated the participants’ self- and other-referential judgments over positive and negative statements. In the self condition trials, contributors were asked whether (positive or negative) Trait adjectives presented describe them (“I am” or “I am not”). In the other condition trials, we utilized the term “the president” as the well-known person and participants were asked whether the (positive or negative) Trait adjectives describe the president or not (“he is” or “he is not”). The conditions of the task designed based on the task were represented by previous studies (Dinulescu et al., 2021; Harvey et al., 2011; Salehinejad et al., 2020). The total trials were 100, of which half were described self conditions, the other half depicted other conditions, in the manner in which both of the Self and other conditions included positive and negative trait adjectives. Output was RT to the self- and other-related statement. The trials were displayed with 2500 ms fixation time, in the manner, the times finished, the subsequent trial shows automatically. In order to avoid the miss clicking, the answers were counted 200 ms after display. The order of trials presentation was identical across participants. The bias measures are defined in 3 separate concepts. 1) The self-bias (Sb) is defined as the difference between the average RT of the self-related statements and other-related statements, 2) the Emotional-bias (Eb), the difference between the average RT of the negative conditions and positive ones, Regardless of Self and other, 3) The self-Emotional bias (SEb) is defined as the difference between the average RT of self- and other-related statements after the determination of Emotional-bias for each condition separately.

tDCS protocol.

The non-invasive tDCS stimulator was an "ActivaDose II Iontophoresis" manufactured by Activa Tek, with a 9 voltage battery as the power source. The direct electrical current was applied through a pair of saline-soaked sponge electrodes with a size of 25 cm² (5x5). The current intensity was 2 mA for 15 min with a 15 s ramp up, and a 15 s ramp down. In the present study, we induced three tDCS conditions according to the 10–20 EEG international system: a) anodal electrode over the vmPFC (Fpz)/cathodal over the right shoulder, b) anodal electrode over the rTPJ (Cp6)/cathodal over the right shoulder, and (c) sham one electrode over the left TPJ and the other one over the shoulder. The electrode positions were used in former studies for stimulating the respective cortical regions (Coll et al., 2017). For the sham condition, the electrical current ramped up for 15 seconds to induce the same sensation as the stimulation conditions in the participants and afterward turned it off without their knowledge (Palm et al., 2013). After each tDCS session, a side-effect checklist was completed.

Figure 3. The tDCS procedure. The stimulation and task order was random for each participant
Figure 4. Electrode placements over candidate regions of the study. The blue color shows the cathodal electrode placements, the red color shows the anodal electrode placement, and the gray color shows the sham stimulation. 1: anodal vmPFC/extracranial return electrode, 2: anodal rTPJ/extracranial return electrode, 3: sham stimulation conditions.

Statistical analysis.

To perform our data analysis, we used SPSS software version 28 (IBM, SPSS, Inc., Chicago, IL). For each task, the normality and homogeneity of variance of the data were confirmed using Shapiro-Wilk and Levin test, respectively. To investigate the effect of tDCS stimulation on each task for both male and female participants, a mixed-design analysis of variance (ANOVA) has carried out with the tDCS conditions (anodal rTPJ, anodal vmPFC, and Sham) and the viewpoint (1PP and 3PP) as within-subject factors and Gender (male and female) considered as the between-subject factor. The numerical values of every task are considered as the dependent variable. Mauchly's test was applied To evaluate the sphericity. In cases the violation of sphericity appears, the degrees of freedom were modified utilizing the Greenhouse-Geisser Correction test. Values were pair-wise compared by the Šidák post hoc test. Values of each active tDCS and sham condition side effect report were analyzed with ANOVA. A significance level of P < 0.05 was used for all statistical comparisons.

Results

Side effect

All the contributors tolerated the tDCS stimulations. After stimulation, no adverse effects were reported except for pain, burning and tingling sensations under the anodal electrode during the first minute in each condition. The indicant of side effects is summarized in table 1. The repeated measure ANOVAs represented no differences between stimulations in vertigo ($F_{2,58} = 1.955, P = 0.151$), drowsiness ($F_{2,58} = 0.021, P = 0.979$), confusing ($F_{2,58} = 1.67, P = 0.197$). the ANOVA showed a significant result for side effects were significantly different for items "Pain" and "Itching sensation," which was rated relatively higher for anodal vmPFC tDCS ($P = 0.02$) and ($P < 0.001$). The "Trouble concentrating" side effect was rated higher for anodal rTPJ tDCS ($P = 0.02$) compared to the sham condition.
Table 2. Reported side effects during tDCS stimulation. The mean severities of reported side effects are presented, with standard deviations in parentheses.

| Measures  | Conditiones, Mean(SD) | Statistics |
|-----------|-----------------------|------------|
|           | rTPJ                  | vmPFC      | Sham       | df | F     | P      | ηp² |          |
| pain      | .43(0.73)             | .8(1.13)   | .27(0.64)  | 2.58 | 3.941 | .025   | .12 |          |
| vertigo   | .3(0.60)              | .3(0.71)   | .1(0.31)   | 2.58 | 1.955 | .151   | .063|          |
| drowsiness| .37(0.81)             | .4(0.82)   | .4(0.73)   | 2.58 | 0.021 | .979   | .001|          |
| confusing | .4(0.62)              | .5(1.05)   | .23(0.68)  | 2.58 | 1.67  | .197   | .054|          |
| burning   | .97(1.10)             | 1.67(1.3)  | .57(0.78)  | 2.58 | 10.919| <.001  | .274|          |
| tingling  | .9(1.40)              | .3(0.66)   | .27(0.45)  | 2.58 | 5.216 | .008   | .152|          |

tDCS = Transcranial direct current stimulation; rTPJ = right temporoparietal junction; vmPFC = ventromedial prefrontal cortex; significant results (p < 0.05) are reported in italic and bold.

Pain visual analogue scale

We considered painful and painless conditions as within-subject factors and the rates as the dependent variable in this task. the ANOVA results showed a significant main effect of overall tDCS stimulation (F_{2,56} = 3.668, P = 0.032, ηp² = 0.116) implying a significant overall implementation difference between vmPFC (3.051 ± 0.435), rTPJ (2.793 ± 0.451), and sham stimulation conditions (2.808 ± 0.470) see table 2. Šidák post hoc test indicate that the vmPFC anodal tDCS stimulation increased pain rate compared to anodal stimulation over rTPJ significantly (mean difference (MD) = 0.258, p = .042), while its difference with the sham condition was non-significant (MD = 0.243, p = 0.073) and the pain rate between rTPj tDCS stimulation and sham condition was nonsignificant (MD = 0.015, p = 0.999) (see Fig 5). the ANOVA revealed significant main effect of viewpoint (F_{1,28} = 4.262, P = 0.048, ηp² = 0.132) and pain (F_{1,28} = 126.31, P < 0.001, ηp² = 0.819). although the result showed a non-significant main effect of Gender (F_{1,28} = 0.212, P = 0.649, ηp² = 0.008). The interaction between tDCS condition*gender performed a significant result (F_{2,56} = 3.322, P = 0.043, ηp² = 0.106), indicating that stimulation conditions have variate effects on men and women. Follow-up Šidák post hoc correction revealed that anodal vmPFC stimulation significantly increases the males' pain perception rate in comparison only with anodal rTPJ (MD = 0.532, p = 0.002) not sham conditions (MD = 0.354, p = 0.063). the tDCS stimulation did not significantly affect females’ pain rate (see Fig 6). The ANOVA results elicited significant interaction effects of tDCS condition*gender*pain (F_{2,56} = 7.159,P = 0.002, ηp² = 0.204), implying that both PF/PL and the tDCS stimulation conditions significantly affect male and females’ pain rates. Šidák's post hoc analysis revealed that in PL conditions, the female participants' pain rates at rTPJ stimulation were significantly lower than their male contributors (MD = -0.369 p = 0.073). Regarding In PF situations, the active tDCS stimulation conditions did not increase females' pain rates significantly compared to the sham condition, the vmPFC anodal tDCS increased pain rate significantly compared to rTPJ anodal tDCS in males contestants (MD = 0.970 p = 0.002) (see Fig 7). The results prompted non-significant interaction effect of tDCS condition*gender*pain* viewpoint (F_{2,56} = 1.394,P = 0.256, ηp² = 0.047). Results are shown in Table 3.
Figure 5. Presented are the effects of tDCS stimulation in pain visual analogue scale rating. Note tDCS = Transcranial direct current stimulation; rTPJ = right temporoparietal junction; vmPFC = ventromedial prefrontal cortex; ns= non-significant; * = mentions significant pairwise comparisons between tDCS conditions base on the result of the Šidák post-hoc correction ($P < 0.05$) n = 15 for each gender; all the error bars show Standard Error of Mean (SEM).
Figure 6. Presented are the effects of tDCS stimulation on gender in pain visual analogue scale rating. Note tDCS = Transcranial direct current stimulation; rTPJ = right temporoparietal junction; vmPFC = ventromedial prefrontal cortex; ns = non-significant; * = mentions significant pairwise comparisons between tDCS conditions based on the result of the Šidák post-hoc correction ($P < 0.05$) n = 15 for each gender; all the error bars show Standard Error of Mean (SEM).

Figure 7. Presented are the effects of interactions of tDCS condition*gender*pain in pain visual analogue scale rating. Note tDCS = Transcranial direct current stimulation; rTPJ = right temporoparietal junction; vmPFC = ventromedial prefrontal cortex; PF = painfull; PL = painless * = mentions significant pairwise comparisons based on the results of the Šidák post-hoc correction ($P< 0.05$) n = 15 for each gender; all the error bars show Standard Error of Mean (SEM).
Visual Perspective-Taking task (VPT)

The reaction time (RT) and accuracy (AC) as dependent variables. In this task. All the ANOVA results of AC measurement were non-significant (\( P > 0.05 \)). Mixed ANOVA results of RT exhibited a non-significant effect of overall tDCS condition (\( F_{2,56} = 0.105, P = 0.9, \eta^2_p = 0.004 \)), gender (\( F_{1,28} = 3.324, p = 0.079, \eta^2_p = 0.106 \)) and the interaction between stimulation condition*gender (\( F_{2,56} = 1.691, p = 0.194, \eta^2_p = 0.057 \)). The interaction results indicate that the tDCS conditions did not manipulate the RT of males and females in a significant way. The ANOVA showed a significant result of the viewpoint in RT (\( F_{1,28} = 65.692, P < 0.001, \eta^2_p = 0.701 \) ) (see Fig 8), and the interaction effect of stimulation condition*viewpoint (\( F_{2,56} = 3.244, p = 0.046, \eta^2_p = 0.104 \) ) see table 2. The RT in the 3PP viewpoint is significantly higher than 1PP in all the tDCS stimulation conditions (MD ≥ 0.660, \( P \leq 0.001 \)). The interaction effect of stimulation condition*gender*viewpoint was significant (\( F_{2,56} = 3.501, p = 0.037, \eta^2_p = 0.111 \)). Carrying out post hoc comparisons using Šidák modification indicated that the RT between viewpoints in all three stimulation conditions for each gender was significant (MD ≥ 0.575, \( P \leq 0.008 \)). In addition, in anodal rTPJ the female participants were slower on both 1PP and 3PP trials in comparison with their male contributors (1PP: MD = 1.405, \( p = 0.018 \); 3PP: MD = 2.089, \( p = 0.013 \) ) (see Fig 9). Results are shown in Table 3.

![Figure 8](image_url)

Figure 8. Shown are the effects of the interaction effect of viewpoint/avatar sex in reaction time. Note ns = non-significant; *** = mentions significant pairwise comparisons on the result of the Šidák post-hoc correction (\( p < 0.001 \)) \( n = 15 \) for each gender; all the error bars show Standard Error of Mean (SEM).
Self-referential attribution task

Self-bias (Sb), Emotional-bias (Eb) and Self-Emotional bias (SEb) are considered as the dependent variables. The mixed ANOVA results showed a significant main effect for self-Emotional bias of tDCS stimulation ($F_{1,28} = 3.902$, $p = 0.026, \eta_p^2 = 0.122$) see table 2. With respect to the post hoc test, the negative point in SEb indicates either higher self-negative or higher other-positive SRP attribution, and the positive point in SEb elicited either higher self-positive or higher other-negative SRP attribution. Šidák modification revealed significant variation between the anodal vmPFC and rTPJ ($MD = 0.225, P = 0.020$), in which SEb was negative and positive, respectively (see Fig10). Results are shown in Table 3. In addition, the mixed ANOVA results revealed a non-significant effect of gender ($F_{1,28} = 0.886, p = 0.355, \eta_p^2 = 0.031$) and the interaction of tDCS stimulation*gender ($F_{1,28} = 0.502, p = 0.608, \eta_p^2 = 0.018$). The ANOVA showed a non-significant result of the main tDCS effect in Sb ($F_{1,28} = 0.421, p = 0.658, \eta_p^2 = 0.015$) and Eb ($F_{1,28} = 1.110, p = 0.337, \eta_p^2 = 0.038$), gender effect in Sb ($F_{1,28} = 0.744, p = 0.396, \eta_p^2 = 0.026$) and Eb ($F_{1,28} = 0.021, p = 0.885, \eta_p^2 = 0.001$) and the interaction effect of tDCS stimulation*gender in Sb ($F_{1,28} = 1.767, p = 0.180, \eta_p^2 = 0.059$) and Eb ($F_{1,28} = 0.528, p = 0.593, \eta_p^2 = 0.019$).
Figure 10. Shown is the interaction effect of stimulation condition in Self-Emotional bias. Note: * = mentions significant pairwise comparisons on the result of the Šidák post-hoc correction (p < 0.05) n = 15 for each gender; all the error bars show Standard Error of Mean (SEM).

Table 3. Results of mixed ANOVA for effects of tDCS conditions (anodal vmPFC, anodal rTPJ, Sham) on pain rating and Visual Perspective-Taking task (VPT) and self-referential attribution task (SRA).

| measures                        | Task          | df  | Mean Square | F       | P       | $\eta_p^2$ |
|---------------------------------|---------------|-----|-------------|---------|---------|------------|
| Pain visual analogue scale      | tDCS          | 2.56| 2.515       | 3.668   | 0.032   | 0.116      |
|                                 | Gender        | 1.28| 3.434       | 0.212   | 0.649   | 0.008      |
|                                 | ViewPoint     | 1.28| 0.087       | 4.262   | 0.048   | 0.132      |
|                                 | Pain          | 1.28| 2109.401    | 126.31  | <0.001  | 0.819      |
|                                 | tDCS*Gender   | 2.56| 2.278       | 3.322   | 0.043   | 0.106      |
|                                 | tDCS*ViewPoint| 2.56| 0.017       | 0.637   | 0.533   | 0.022      |
|                                 | Gender*ViewPoint| 1.28| 0.014      | 0.693   | 0.412   | 0.024      |
|                                 | tDCS*Pain     | 2.56| 0.554       | 0.968   | 0.386   | 0.033      |
|                                 | Gender*Pain   | 1.28| 18.153      | 1.087   | 0.306   | 0.037      |
|                                 | ViewPoint*Pain| 1.28| 0.099       | 4.232   | 0.049   | 0.131      |
|                                 | tDCS*Gender*ViewPoint | 2.56| 0.027   | 1.036   | 0.362   | 0.036      |
|                                 | tDCS*Gender*Pain| 2.56| 4.093      | 7.159   | 0.002   | 0.204      |
|                                 | tDCS*ViewPoint*Pain| 2.56| 0.018   | 0.694   | 0.504   | 0.024      |
|                                 | Gender*ViewPoint*Pain| 1.28| 0.002      | 0.073   | 0.788   | 0.003      |
|                                 | tDCS*Gender*ViewPoint*Pain| 2.56| 0.037   | 1.394   | 0.256   | 0.047      |
| VPT (RT)                        | tDCS          | 2.56| 0.563       | 0.105   | 0.9     | 0.004      |
tDCS = Transcranial direct current stimulation; rTPJ = right temporoparietal junction; vmPFC = ventromedial prefrontal cortex; VPT = Visuospatial Perspective-Taking task; RT = reaction time; AC = accuracy; SRA = Self-referential attribution task; Sb = Self-bias; Eb = Emotional-bias; SEb = Self-Emotional bias; Viewpoint = 1st person perspective and 3rd person perspective; $\eta^2_p$ = partial eta squared; significant results ($P < 0.05$) are reported in italic and bold.

Table 4. Descriptive statistics mean (standard deviation) for the effect of tDCS conditions (anodal vmPFC, anodal rTPj, Sham) on pain rating, Visual Perspective-Taking task (VPT) and self-referential attribution task (SRA).

| Measures                  | tDCS conditions | rTPJ | vmPFC | Sham |
|---------------------------|-----------------|------|-------|------|
|                           | M (SD)          | M (SD) | M (SD) |
| Females                   |                 |      |       |      |
| PF                        |                 |      |       |      |
| Male                      |                 |      |       |      |
| Pain visual               |                 |      |       |      |
| analogue scale            |                 |      |       |      |
| Pain visual               |                 |      |       |      |
| analogue scale            |                 |      |       |      |
| Females                   |                 |      |       |      |
| 1PP                       | 5.81(2.6)       | 5.59(2.49) | 5.43(2.42) |
| 3PP                       | 5.96(2.61)      | 5.58(2.45) | 5.43(2.48) |
| Male                      |                 |      |       |      |
| 1PP                       | 4.51(2.3)       | 5.43(1.83) | 4.9(2.24) |
| 3PP                       | 4.57(2.3)       | 5.59(1.81) | 4.92(2.56) |
| Total                     |                 |      |       |      |
| 1PP                       | 5.16(2.5)       | 5.51(2.15) | 5.16(2.39) |
| 3PP                       | 5.26(2.52)      | 5.59(2.12) | 5.18(2.49) |
| PL                        |                 |      |       |      |
| Females                   |                 |      |       |      |
| 1PP                       | 0.21(0.22)      | 0.46(0.71) | 0.37(0.55) |
| 3PP                       | 0.19(0.19)      | 0.48(0.72) | 0.35(0.54) |
|                  | Male       |            |            |            |
|------------------|------------|------------|------------|------------|
|                  | 1PP        | 3PP        | 1PP        | 3PP        |
| VPT (RT)         |            |            |            |            |
| Females          | 0.57 (0.64)| 0.56 (0.62)| 0.39 (0.5) | 0.38 (0.49)|
| Males            | 0.65 (0.6) | 0.67 (0.64)| 0.56 (0.65)| 0.57 (0.67)|
| Total            | 0.55 (0.65)| 0.56 (0.63)| 0.46 (0.6) | 0.45 (0.59)|
| VPT (AC)         |            |            |            |            |
| Females          | 4.56 (1.84)| 4.88 (1.34)| 4.29 (2.01)|
| Males            | 3.15 (1.16)| 3.57 (1.91)| 3.63 (1.80)|
| Total            | 3.86 (1.67)| 3.73 (1.63)| 3.96 (1.90)|
| SRA Self-Bias    |            |            |            |            |
| Females          | 0.56 (0.47)| 0.32 (0.47)| 0.34 (0.45)|
| Males            | 0.22 (0.44)| 0.27 (0.59)| 0.38 (0.53)|
| Total            | 0.39 (0.48)| 0.30 (0.52)| 0.36 (0.49)|
| SRA Emotion-Bias |            |            |            |            |
| Females          | 0.43 (0.40)| 0.34 (0.48)| 0.16 (0.56)|
| Males            | 0.37 (0.37)| 0.30 (0.35)| 0.31 (0.37)|
| Total            | 0.40 (0.38)| 0.32 (0.41)| 0.23 (0.47)|
| SRA Self-Emotion Bias | -0.13 (0.41) | 0.07 (0.36) | 0.06 (0.47) | 0.07 (0.41) |

**tDCS** = Transcranial direct current stimulation; **rTPJ** = right temporoparietal junction; **vmPFC** = ventromedial prefrontal cortex; **1PP** = 1st person perspective; **3PP** = 3rd person perspective; **VPT** = Visuospatial Perspective-Taking task; **RT** = reaction time; **AC** = accuracy; **SRA** = Self-referential attribution.

**Discussion**

This paper demonstrated gender brain differences in (non) emotional perspective-taking ability by applying a tDCS paradigm. The total effect of vmPFC anodal tDCS stimulation increased pain rates significantly compared to rTPJ anodal tDCS stimulation, not Sham condition. Pointing that vmPFC increased the emotional pain perception versus rTPJ. The ventromedial region of the prefrontal cortex is theorized to participate a crucial role in negative emotion regulation (Hiser & Koenigs, 2018; Marković et al., 2021), as well as the arousal aspect of emotion (Nejati et al., 2021). The previous studies elicited anterior/perigenual and posterior/subgenual regions based on valence, in which the former region was linked with positive valence (e.g., reward) and the latter region linked with negative valence (e.g., fear, threat) (Myers-Schulz & Koenigs, 2012; Roy et al., 2012). The meta-analysis was done by Hiser and Koenigs (2018), indicating that the anterior/perigenual vmPFC region and the ventral striatum are associated with decision making, the anterior/pregenual vmPFC region, the dorsomedial PFC, precuneus, and temporoparietal cortex are associated with social cognition, and the posterior/subgenual vmPFC region and the amygdala are associated with emotion. In an fMRI study, Phan and collaborators (2003), revealed...
the activation of the medial prefrontal cortex and the amygdala through arousal ratings. The vmPFC and amygdala respond correspondingly to high-arousal words and pictures (Kensinger & Schacter, 2006). The vmPFC regulates the activity of the amygdala in a top-down manner in high arousal situations (Milad et al., 2007; Motzkin et al., 2015). On the other hand, the tDCS activation of vmPFC enhanced the ToM precursors such as emotion recognition and perception (Salehinejad et al., 2021). Our result showed that the vmPFC anodal tDCS increased the pain rate in comparison with rTPJ tDCS conditions only in men. The fMRI studies indicated respective brain regions for men and women in emotional conditions. Filkowski and colleagues (2017), in their meta-analysis of the emotional perception, mentioned higher activity over mPFC for men, in which the ventral site of mPFC is associated with the rapid judgment of emotional substance, persistent affective states, and autonomous response regulation (Phan et al., 2002; Phillips et al., 2003).

rTPJ partakes a vital role in the self-other distinction aspects relevant to VPT, including decoding self-other incongruences and preventing non-relevant representation effect through orienting attention (Bahnemann et al., 2010; Decety & Lamm, 2007; Lamm et al., 2016; Quesque & Brass, 2019). Our results showed that the VPT performance was manipulated by gender over rTPJ anodal stimulation in the 3PP viewpoint. Previous studies support the effect of rTPJ anodal tDCS in the 3PP VPT (Martin et al., 2019; Santiesteban, White, et al., 2012). Our results indicated that male participants accomplished the 3PP VPT in a quicker time than their female contributors with the same accuracy rate. The rTPJ is functionally and microstructurally divided into two individual anterior and posterior clusters (Bzdok et al., 2013). The arTPJ has strong functional connectivity with the medial cingulate cortex (MCC), insular cortex and inferior frontal gyrus (IFG) (Bzdok et al., 2013; Mars et al., 2012), regions commonly correlated with affect regulation (Shackman et al., 2011; Vogt, 2005) and emotion sharing (Lamm et al., 2011). The across connectivity of the arTPJ cluster with subdivisions is referred to as "arTPJ network." Functional outlining of the arTPJ network exhibited the association with pain assessment (Bzdok et al., 2013). In contrast, The prTPJ, which is associated with social cognition and theory of mind (Brass et al., 2009; Mar, 2011), and is centered on the angular gyrus, has intense connectivity with regions such as the precuneus, medial prefrontal cortex, bilateral inferior parietal cortex and right middle temporal gyrus (Bzdok et al., 2013; Caspers et al., 2008; Caspers et al., 2006; Silani et al., 2013). The precuneus is associated with perspective-taking through a role in mental imagery (Aichhorn et al., 2009; Döhnel et al., 2012; Sommer et al., 2007). Our results indicated that the prTPJ network is dominant in males compared to women. This conclusion is in line with the Kaiser et al. (2008) findings which argued that while the 3PP decoding network is comparable for both men and women, the precuneus activation is more remarkable in males than females.

Our result in the manner of the variation of emotional rates between viewpoints over rTPJ anodal tDCS in females indicates that both anterior and posterior rTPJ networks activate by tDCS stimulation. In males, the decline of emotional rates compared to other stimulations exhibit that the prTPJ network is dominantly activated. In addition, male participants' performance was better than their female contributors in the 3PP viewpoint on the VPT task over rTPJ stimulation, which supports the dominance of the prTPJ network in men.

The other possible reason for the gender-specific reaction to region stimulation could be discovered in gender-related variations in brain modulation on the application of non-invasive stimulations (Chaieb et al., 2008). Variate studies using different stimulation on separated regions, investigating a variety of cognitive abilities revealed diverse outcomes such as the females' improvement in ToM with anodal tDCS stimulation over medial PFC (Adenzato et al., 2017; Martin et al., 2017), drop and rise of females utilitarian response with cathodal and anodal tDCS over ventral PFC (Fumagalli et al., 2010). In addition, lateralized gender differences in working memory in a way that the right dlPFC enhanced females' performance whereas the
left dIPFC improved males (Meiron & Lavidor, 2013), men's total errors in attention task declined under anodal activation of the left parietal cortex (De Tommaso et al., 2014) and better performance on facial recognition in females over the tDCS modulation of the temporal cortex (Boggio et al., 2008).

In the third experiment, we study the rTPJ and vmPFC tDCS effect over SRP with the SRA task. The result showed that the SRP increased under anodal vmPFC tDCS stimulation, which is in line with the previous tDCS study (Salehinejad et al., 2020). The involvement of mPFC, particularly vmPFC in SRP, has been indicated by previous fMRI studies (Kelley et al., 2002; Northoff & Bermpohl, 2004; Northoff et al., 2006). One possible explanation for the rise of SEb could be the increase in self-esteem and the inhibition of attenuating negative self-referential thoughts (De Raedt et al., 2017; Salehinejad et al., 2020).

Neuroimaging review studies proposed the association between the SRP and default mode network (DMN) and its sub-regions (Bao et al., 2021). The DMN activity in MPFC, PCC and ventral precuneus mediates the verbal SRP (V-SRP) (Araujo et al., 2015; Davey et al., 2016), as well as vmPFC and dIPFC, which mediate self-evaluation (Fingelkurts et al., 2020). In V_SRP, mPFC plays a critical role in the affective evaluation of emotional SRP (Bao et al., 2021). The mPFC has a vital role in self-specific encoding (Qin & Northoff, 2011). This statement is supported by transcranial magnetic stimulation (TMS) studies (Kwan et al., 2007; Luber et al., 2012). In their study, Mainz et al. (2020), were unsuccessful in finding an anodal tDCS effect over mPFC in emotional SRP. Another study by Schäfer and Frings (2019), elicited no effect of anodal tDCS over VMPFC with cathodal tDCS over DLPFC tDCS on neutral SRP. One reason for not finding an effect of vmPFC on SRP could be the low current of the stimulation (0.5 mA).

Limits

Some limitations of this study should be taken into account. In the current research, as usual in studies of emotional measurements, we explicitly asked the contributors to rate the pictures based on a self-assessment manikin. At least for arousal, which is to a relevant grade processed implicitly, it would have been beneficial to add electrophysiological recordings, which take this into account. Thus, we suggest that future studies record somatic indicators such as heart rate, galvanic skin response, or pupil diameter to calculate arousal.
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