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## **Title**

**Anodal tDCS targeting the left temporo-parietal junction disrupts verbal source-monitoring**

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**Running title: tDCS & source-monitoring**

## **Abstract**

Using transcranial direct current stimulation (tDCS) we aimed to investigate the causal role of the left temporo-parietal and prefrontal regions in source-monitoring. Forty-two healthy participants received tDCS while performing a verbal reality-monitoring task (requiring discrimination between heard and said words) and a verbal internal source-monitoring task (requiring discrimination between imagined and said words). In 2 randomized crossover studies, 21 participants received active and sham anodal tDCS applied over the left temporo-parietal junction (TPJ) and 21 participants received active and sham cathodal tDCS applied over the left prefrontal cortex (PFC). The reference electrode was placed over the right occipital region in both experiments. Active tDCS over the left TPJ decreased reality-monitoring performance but did not modulate source-monitoring performance. Participants were more likely to misattribute self-generated events to externally perceived events (externalisation bias). Active tDCS over the left PFC did not modulate performance of participants in both tasks. In summary, anodal tDCS applied over the left TPJ, assumed to enhance cortical excitability, can alter reality-monitoring processes in healthy subjects. Such abnormal reality-monitoring performances have been reported in hallucinating patients with schizophrenia known to display hyperactivity of the left TPJ. Our results highlighted the role of the left TPJ in self/other recognition.

### **Keywords:**

transcranial direct current stimulation (tDCS), self-recognition, temporo-parietal junction, prefrontal cortex, source monitoring

## **INTRODUCTION**

Source-monitoring refers to cognitive processes involved in identifying the origin of remembered information. Information may be internally generated (e.g., thoughts, imagination) or externally derived (e.g., something perceived, heard or seen). Identifying the origins of information consists in recalling its characteristics: perceptual/sensory cues, spatial, temporal and emotional context, semantic details (e.g., the meaning), and cognitive operations that were established when the memory was formed. One of the most striking illustrations of source-monitoring is wondering whether you have performed an action or merely thought about performing it (e.g., Did I lock the door or did I only think about doing it?). It has been proposed that source-monitoring encompasses three classes of cognitive processes (Johnson et al., 1993): 1) external source-monitoring, which refers to the ability of discriminating between different externally derived sources. An example of this would be to determine which one of our friends phoned us yesterday; 2) internal source-monitoring, which refers to the ability of distinguishing between different internally generated sources. For instance, this process is involved when discriminating between our thoughts and our own performed speech (generated in inner or outer space); 3) reality-monitoring, which is usually defined as the ability to discriminate memories of internally generated information from memories of externally derived information (self-other recognition). This process allows us to distinguish memories of thoughts and imaginations from memories of actually perceived events.

Source-monitoring is crucial in everyday life situations to distinguish fantasy from reality. Patients with schizophrenia show impairments in verbal source-monitoring. In particular, they are more likely to misattribute their inner thoughts or speech as coming from an external source during both internal source-monitoring and reality-monitoring processes (Brunelin et al., 2006a; Waters et al., 2012). This impairment, also called an externalization bias, is suggested to contribute to the emergence of auditory verbal hallucinations – AVH (Brunelin et al., 2006a; Waters et al., 2012; Brookwell et al., 2013). One cognitive model suggested that, at a neural level, verbal source-monitoring operates through a corollary discharge system whereby discharges from left frontal regions dampen activity in the auditory regions located in the

temporal lobe to signal that the speech is self-produced (Ford and Mathalon 2005; Frith 1996; Martikainen et al., 2005). This hypothesis is supported by neuroimaging studies reporting that healthy subjects showed an increased activity in auditory cortical regions including the left superior temporal region when listening to speech derived from an external source, whereas inner speech does not elicit this increased activity in auditory cortical regions (Allen et al., 2007; Simons et al., 2010). A large number of fMRI studies report that source-monitoring is associated to increased activity in the left lateral PFC (Mitchell and Johnson 2009). Confusions between imagined and perceived events are associated to reduced activation in the prefrontal cortex (PFC) in healthy subjects and these confusions are similar to those observed in patients with schizophrenia (Simons et al., 2006). Moreover, in healthy volunteers a greater functional connectivity between frontal and temporal regions has been observed when compared self-versus other- monitoring (Wang et al., 2011).

It has been proposed that impairments in verbal source-monitoring observed in patients with schizophrenia and AVH may arise from a failure to deactivate the left superior temporal region during the processing of inner speech (Allen et al., 2007; Simons et al., 2010). Indeed, patients with schizophrenia displayed abnormal hyperactivity of left temporo-parietal areas during AVH (Jardri et al., 2011). Consistent with this finding, reducing the left temporo-parietal junction (TPJ) activity using non-invasive brain stimulation improve source-monitoring performance in patients with schizophrenia and AVH (Brunelin et al., 2006b; Mondino et al., 2015).

Altogether, these results support the hypothesis of the contribution of the left TPJ and the left PFC in verbal source-monitoring. However, the distinction between reality-monitoring and internal source-monitoring processes has not systematically been investigated in neuroimaging studies so that up to now available data do not disentangle the respective role of the left TPJ and the left PFC in these processes.

The aim of this study was to investigate the distinct causal roles of the left TPJ (Experiment 1) and the left PFC (Experiment 2) in reality-monitoring and internal source-monitoring. To achieve this, we used transcranial Direct Current Stimulation (tDCS), a noninvasive brain stimulation tool

which can modulate activity of a targeted brain region and its functionally connected network (Keeser et al., 2011). tDCS has been successfully used to determine the causal role of specific brain regions in specific behaviors and cognitive functions (Moseley et al., 2014; Sehm et al., 2013; Civai et al., in press). It has been observed that anodal tDCS enhances cortical excitability and that cathodal tDCS decreases cortical excitability of the targeted brain region (Nitsche et al., 2008). Therefore, anodal tDCS has been used to enhance the contribution of a particular brain region to a process that involves that brain region in order to improve this process (Ladeira et al., 2011) whereas cathodal tDCS has been used to disrupt the contribution of a particular brain region to a process that involves that brain region (Vines et al., 2006). Based on this dual effect, we conducted two double blind crossover experiments comparing the effects of sham and active tDCS on reality-monitoring and internal source-monitoring in 42 healthy subjects. In Experiment 1, anodal-excitatory tDCS was applied over the left TPJ while in Experiment 2, cathodal-inhibitory tDCS was applied over the left PFC to infer their respective contribution to source-monitoring processes. We hypothesized that anodal-tDCS applied over the left TPJ would mimic hyperactivity observed in patients with schizophrenia (Jardri et al., 2011) and lead to misattributions between internally generated and externally derived speech compared with sham tDCS (reality-monitoring). As the left PFC seems to be also involved in source-monitoring processes (Simons et al., 2006, Mitchell and Johnson 2009), we hypothesized that cathodal-tDCS applied over the left PFC would disrupt source-monitoring processes.

## **METHODS**

### **Participants**

Forty-two right-handed subjects were enrolled in the study and allocated to take part in Experiment 1 (anodal left TPJ tDCS,  $n = 21$ ) or Experiment 2 (cathodal left PFC tDCS;  $n = 21$ ).

All participants were healthy subjects, without contraindications to tDCS, without any serious medical conditions and without any personal or familial (first degree) past or current DSM-IV axis I diagnoses. Contraindications to tDCS were assessed using the same criteria used in rTMS studies. This includes questions such as adverse reactions to a previous tDCS treatment, presence of severe or frequent headache, pregnancy, presence of any metal in the head, history

of serious brain injury, seizure, stroke or neurological diseases. All participants had normal or corrected to normal vision and did not display hearing problems. Written informed consent was obtained from all participants after a detailed description of the protocol prior to entering the study. The study was approved by the ethics committee (CPP Sud Est 6, AU1086). Characteristics of subjects are given in table I.

### Procedure

The study was designed as two double-blind randomized sham-controlled crossover experiments. In each experiment, participants received two sessions of 15 minutes of tDCS: one session of active tDCS and one session of sham tDCS on two separate days with at least a one-week interval. To ensure that experimenters and patients were both blind to the tDCS-condition assignment, specific codes corresponding to either active or sham stimulation were selected from the tDCS device manual by an independent researcher not involved in the study. The order in which participants received the two conditions of stimulation (active or sham) was randomized (Table I). During each tDCS session, participants were seated in front of a computer screen and undertook two computerized source-monitoring tasks in a randomized order: (1) an internal source-monitoring task (“Say-Imagine”) and (2) a reality-monitoring task (“Hear-Imagine”). The order between the two source-monitoring tasks during tDCS session was counterbalanced between participants. Adverse effects and blinding integrity of the procedure were assessed after each session.

Table I: Baseline demographical characteristics of the 42 healthy participants.

SD = standard deviation.

	TPJ Group (N = 21)			PFC Group (N = 21)		
	N	Mean	SD	N	Mean	SD
Gender (male/female)	9/12			10/11		
Order sham/active	9			11		
Order active/sham	12			10		
Age (years)		27.2	5.2		27.6	7.1
Education (years)		16.1	3.2		15.3	2.7

## **tDCS**

tDCS was applied using a commercial NeuroConn DC stimulator device (NeuroConn, GmbH) delivering a direct current through two electrodes placed in saline-soaked sponges. In the *Experiment 1*, a 35 cm<sup>2</sup> anode (7x5 cm) was placed midway between the left temporal cortex (T3) and the left parietal cortex (P3) according to the international 10-20 EEG electrodes sites system. A 100 cm<sup>2</sup> reference cathode (10x10 cm) was placed over the right occipital cortex (O2). By increasing the size of the reference electrode, we aimed to obtain a more focal effect of anodal-tDCS over the left TPJ without relevantly shifting excitability by the cathode (Nitsche et al., 2008). In the *Experiment 2*, a 35 cm<sup>2</sup> cathode (7x5 cm) was placed midway between F3 and Fp1 according to the international 10-20 EEG electrodes sites system. A 100 cm<sup>2</sup> anode (10x10 cm) was placed over the right occipital cortex (O2).

In both experiment, stimulation was delivered for 15 minutes and started 5 minutes before the beginning of source monitoring tasks. tDCS was delivered during the entire course of the source monitoring tasks, which lasted 10 min. Active tDCS consisted in a constant 2 mA current (ramp up 30 s, ramp down 30 s). Sham tDCS consisted in delivering 30 s of active stimulation and no current for the rest of the 15-min stimulation period. This procedure allows participants to feel the same itching sensation than during active tDCS when the stimulation begins. The procedure was reported as reliable for blinding subjects with respect to stimulation condition (Gandiga et al., 2006). In addition, using the study mode of the tDCS device with input codes allowed the experimenter to be blinded to the stimulation condition as the readout on the stimulation apparatus was identical for both active and sham stimulation.

## **Source monitoring tasks**

Computerized versions of the two tasks previously described (Brunelin et al., 2006a; 2007) were used to assess reality-monitoring ('Hear-Imagine' task) and internal source-monitoring ('Say-Imagine' task). Test sensitivity is suitable for revealing source-monitoring deficits (see Waters et al., 2012).

A short practice trial acquainted the patients with the task requirements. Each task was divided in a presentation phase and a test phase. During the presentation phase, 16 words were



presented one by one on a computer screen for 3 s, preceded by its respective instruction (i.e., “Imagine yourself hearing the following word” or “Listen to the following word” in the ‘Hear-Imagine’ task; and “imagine yourself saying the following word” or “say the following word aloud” in the ‘Say-Imagine’ task). The test phase began immediately after the end of the presentation phase. During the test phase, 24 words including the 16 words presented in the presentation phase plus 8 new words (distractors) were presented separately on the screen and for each word, patients were required to recognize the source of the word (i.e. “imagined”, “heard” or “new” in the ‘Hear-Imagine’ task; and “imagined”, “said” or “new” in the ‘Say-Imagine’ task). Two different sets of 24 words were used to avoid a learning effect between the first and the second tDCS session and the order of the sets was randomized across subjects. The order of the two tasks was counterbalanced.

### **Blinding assessment**

Blinding integrity was assessed by asking participants to guess the nature of the received stimulation (active or sham) and to rate the confidence of their guess on a visual analogue scale from 0 (not sure at all) to 100 (completely sure).

### **Adverse effects assessment**

After each tDCS session, adverse effects were collected using a tDCS questionnaire assessing the most common adverse effects related to tDCS such as headache, burning and mood change (Brunoni et al., 2011; 2014). For each adverse effect, participants were asked to rate the severity from 1 (none) to 4 (severe) and the probability that the adverse effect was linked to tDCS, from 1 (none) to 5 (certain).

### **Data analysis**

Experiments 1 and 2 were analysed separately.

According to literature (Brunelin et al., 2006a; Waters et al., 2012), the number of correct responses was measured for each task condition: internally generated events (imagined words,

range 0-8), externally generated events (heard or spoken aloud, range 0-8) and distractors (new words, range 0-8), in each source-monitoring task ('Hear-Imagine' and 'Say-Imagine' tasks).

Statistical analyses were carried out using SPSS version 22 and a significance level of  $p < .05$  (two-tailed) was employed for all analyses. For each experiment, the effects of tDCS on the number of correct responses were assessed using a 2X2X3 repeated-measures analysis of variance with 3 within-subjects factors: stimulation condition (Active and Sham), type of task ('Hear-Imagine' and 'Say-Imagine') and task condition (imagine, hear/say, and new words). We focused on the "Stimulation \* Type of Task \* Task condition" interaction. In case of significance, posthoc tests and Glass's  $\Delta$  posthoc effect sizes were performed.

The presence of outliers was controlled using Cook's distance. The assumption of sphericity was assessed using Mauchly's test. In case of non-sphericity, the analysis of variance was using Huynh-Feldt correction.

In case of an effect of stimulation condition (active versus sham) on the number of correct responses, an exploratory analysis was conducted to investigate the effect of the stimulation condition on two types of misattribution errors: the number of imagined events incorrectly recognized as heard/said (range 0-8) and the number of externally derived events (heard/said) incorrectly recognized as internally generated events (imagined) (range 0-8). These comparisons were done using paired Student t-tests and Glass's  $\Delta$  effect sizes.

In each experiment, Fisher Exact tests were used to explore whether tDCS-blinding guess was beyond chance for participants and to compare confidence rates for tDCS-blinding guess. Paired Student t tests were used to compare adverse affects between conditions (active, sham) in each experiment.

## **RESULTS**

### Experiment 1: Effect of anodal tDCS applied over the left TPJ

No outliers were reported using Cook's distance. Since the sphericity assumption was not met according to Mauchly's test ( $W = 0.710$ ,  $p < .05$ ), the ANOVA was corrected using Huynh-Feldt

correction. The ANOVA revealed a significant interaction between stimulation condition, type of task and task condition ( $F= 3.588$ ;  $p= .04$ ,  $\eta^2 = .15$ ). The ANOVA also revealed a main effect of task condition ( $F= 40.6$ ;  $p< .001$ ,  $\eta^2 = .67$ ). No other main effects or interactions were reported.

*Posthoc comparisons - Between stimulation conditions*

Post-hoc tests highlighted a significant difference between active and sham condition for the correct recognition of imagined words in the “reality-monitoring task” ( $p = .007$ ,  $\Delta = 0.81$ ):  $6.1 \pm 1.5$  correct recognition of imagined words (76%) during sham tDCS *versus*  $4.9 \pm 1.7$  (61%) during active tDCS (figure 1). No significant effects of tDCS condition (active, sham) on the number of correct responses were observed for the “hear” and “new” task conditions in the “reality-monitoring task”. No significant effects of stimulation condition were observed between task conditions in the internal source-monitoring task (figure 2).

*Posthoc comparisons - Between tasks*

A significant difference was reported between reality-monitoring and internal source-monitoring tasks for the “imagine” condition in the active stimulation condition only ( $p= .014$ ,  $\Delta = 1.94$ ). No differences were reported between tasks neither in the active condition for the other task conditions nor in the sham condition.

*Posthoc comparisons - Between task conditions*

Finally, the number of correct recognition for the “new words” condition differed significantly from the number of correct recognition in the “imagine” and “hear”/“say” conditions in both stimulation conditions (active and sham) and in both types of task ( $p < .001$ ).

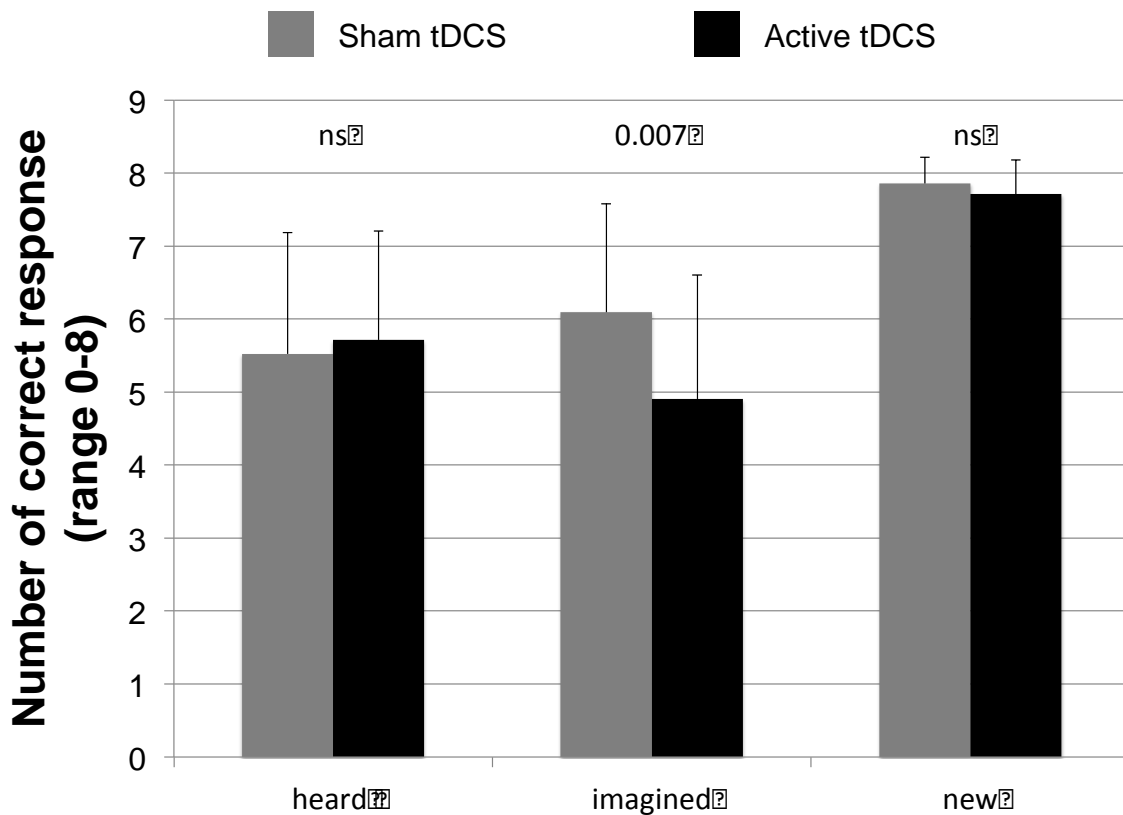
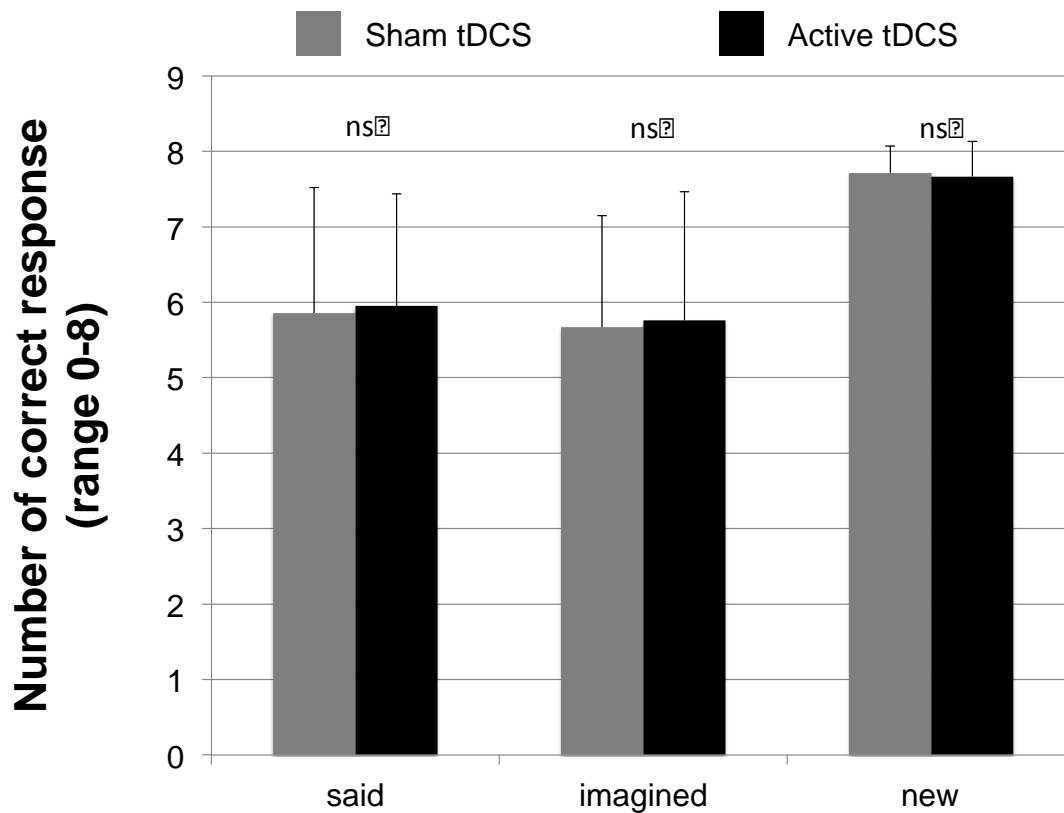


Figure 1: Effects of active and sham anodal tDCS over the left TPJ on reality-monitoring processes assessed by the number of correct responses for heard words, imagined words and new words (range 0-8). Active tDCS decreased the recognition of imagined words ( $p = .007$ ) but had no effect on heard and new words. Results are given as mean  $\pm$  standard deviation.

Regarding the significant difference between active and sham condition for the correct recognition of imagined words in the “reality-monitoring task”, we investigated the direction of misattribution errors. Active anodal tDCS significantly increased the number of occurrences when imagined words have been incorrectly recognized as heard words compared to sham tDCS ( $0.57 \pm 0.67$  during sham *versus*  $1.04 \pm 0.92$  during active tDCS;  $t = 2.351$ ,  $ddl = 20$ ,  $p = .029$ ,  $\Delta = 0.70$ ) whereas no effects of tDCS were reported for the number of time heard words have been

incorrectly recognized as imagined ( $1.57 \pm 1.36$  during sham versus  $1.62 \pm 1.32$  during active tDCS;  $t = 0.113$ ,  $ddl = 20$ ,  $p = .911$ ,  $\Delta = 0.33$ ).



**Figure 2:** Effects of active and sham anodal tDCS over the left TPJ on internal source-monitoring processes assessed by the number of correct responses for said words, imagined words and new words (range 0-8). No effect of tDCS was observed. Results are given as mean  $\pm$  standard deviation.

#### Experiment 2: Effect of cathodal tDCS applied over the left PFC

No outliers were reported using Cook's distance. The ANOVA revealed no significant interaction between stimulation condition, type of task and task condition ( $F = .98$ ;  $p = .39$ ,  $\eta^2 = .093$ ). The ANOVA only revealed a main effect of task condition ( $F = 69.2$ ;  $p < .001$ ,  $\eta^2 = .78$ ). No other main

effects or interactions were observed. Thus, no significant differences between active and sham cathodal tDCS applied over the left PFC were observed for reality-monitoring performance (figure 3) and for internal source-monitoring performance (figure 4).

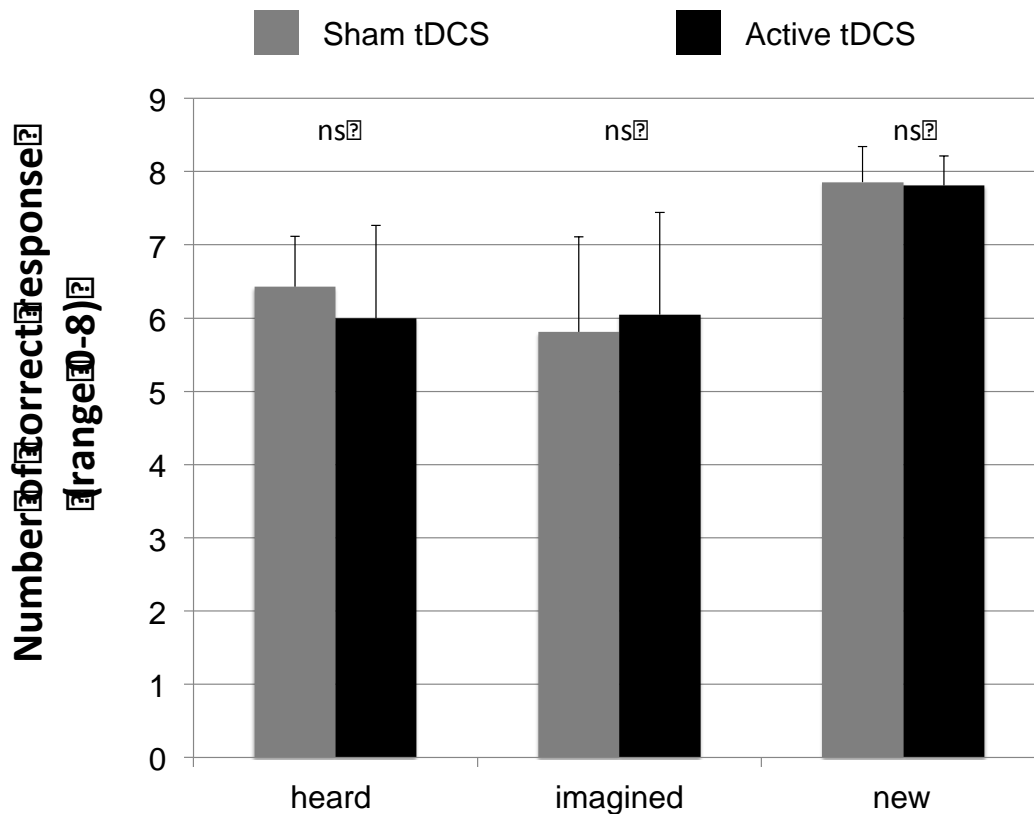
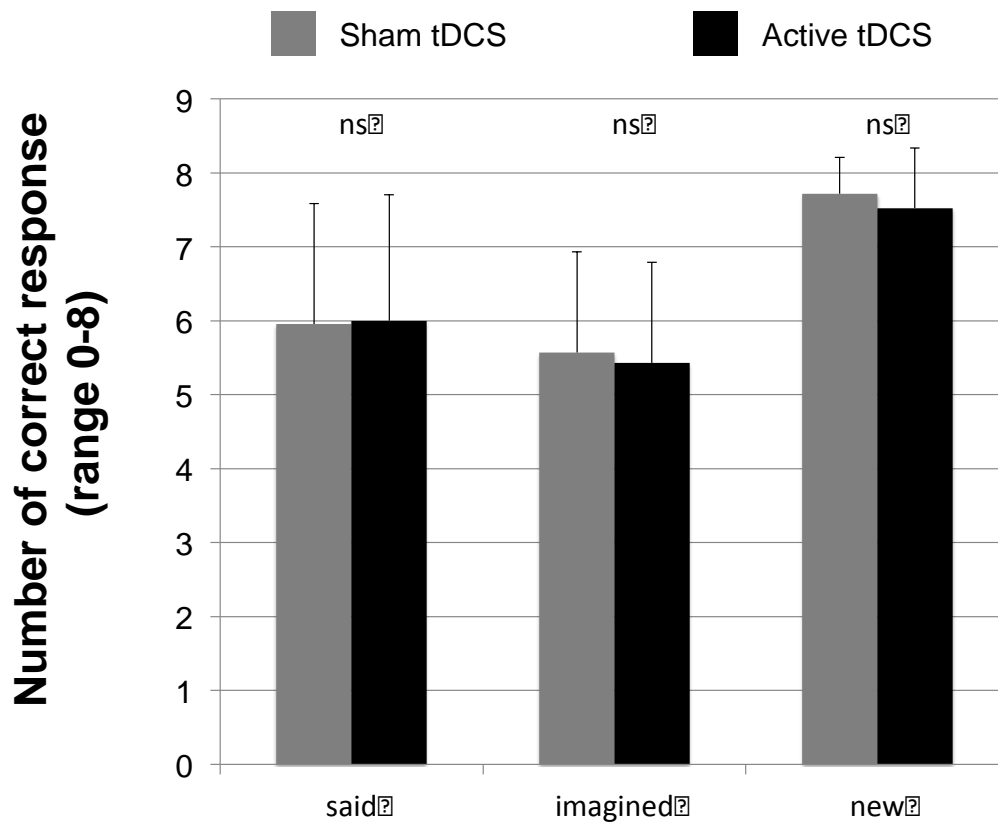


Figure 3: Effects of active and sham cathodal tDCS over the left PFC on reality-monitoring processes assessed by the number of correct responses for heard words, imagined words and new words (range 0-8). No effect of tDCS was observed. Results are given as mean  $\pm$  standard deviation.



**Figure 4:** Effects of active and sham cathodal tDCS over the left PFC on internal source-monitoring processes assessed by the number of correct responses for said words, imagined words and new words (range 0-8). No effect of tDCS was observed. Results are given as mean  $\pm$  standard deviation.

**Blinding integrity**

Neither the 21 participants receiving anodal left TPJ tDCS ( $p = .53$ ) nor the 21 participants receiving cathodal left PFC tDCS ( $p = .53$ ) guessed beyond chance the tDCS conditions (active or sham) they received. (Table II). Confidence rates were not significantly different for active and sham condition in both experiments ( $p = .52$  in experiment 1 and  $p = .28$  in experiment 2).

Table II. Distribution of guessing among participants in each experiment

Anodal TPJ tDCS				Cathodal PFC tDCS			
Correct group				Correct group			
Gessed group	<i>Active</i>	<i>Sham</i>	p	Gessed group	<i>Active</i>	<i>Sham</i>	p
<i>Active</i>	11	8		<i>Active</i>	14	11	
<i>Sham</i>	10	13	0.53	<i>Sham</i>	7	10	0.53

% confidence				% confidence			
Correct group				Correct group			
Gessed group	<i>Active</i>	<i>Sham</i>	p	Gessed group	<i>Active</i>	<i>Sham</i>	p
<i>Active</i>	32.2	48.7		<i>Active</i>	59.9	48.7	
<i>Sham</i>	28.8	56.4	0.52	<i>Sham</i>	53.8	59.8	0.28

In the upper tables, each cell represents the absolute number of healthy subjects according to the cross-tabulation guessing vs. correct group. Confidence rates were expressed as percentages.

For each distribution the Fisher's exact test was calculated ( $p$  values are shown). No statistical differences were reported. In the lower tables, each cells represents the confidence rates of patients according to the cross-tabulation guessing vs correct group.

### Safety assessment

In the two experiments, no significant differences were reported for adverse effects between tDCS conditions (active or sham; see Table III). However, a trend towards a significant effect was reported for the number of reported adverse effects between active and sham conditions in the anodal TPJ tDCS group ( $p = .08$ ).



Table III. Number of reported adverse effects in each Experiment and each tDCS condition (active and sham)

For each experiment the paired Student t test was calculated to compare the number of adverse effects in active vs sham tDCS conditions ( $p$  values are shown).

	Anodal TPJ tDCS			Cathodal PFC tDCS		
	Active	Sham	$p$	Active	Sham	$p$
Headache	3	1		0	5	
Neck pain	2	0		2	1	
Convulsions	0	0		0	0	
Burning	5	7		5	4	
Auditory difficulties	0	0		3	1	
Cognitive difficulties	3	1		3	1	
Attention difficulties	5	1		6	4	
Acute mood changes	0	0		0	0	
Itching	3	0		4	1	
	21	10	0.08	23	17	0.42

## DISCUSSION

This study sought to examine the involvement of the left TPJ and the left PFC in source-monitoring processes, specifically reality-monitoring and internal source-monitoring of speech. Anodal tDCS applied over the left TPJ significantly impaired reality-monitoring of speech in healthy subjects. Participants were more likely to misattribute internally generated speech to externally perceived speech but not the other way around (i.e., to misattribute externally perceived speech to internally generated speech). No effect of tDCS was found on internal source-monitoring of speech. These findings suggest a key role of the left TPJ in the recognition of self-generated from perceived speech. In contrast, the left TPJ does not seem to be involved in the distinction between the self-generated speech produced in inner space and the self-

generated speech produced in outer space. We also reported that cathodal tDCS applied over the left PFC did not modulate source-monitoring of speech, neither internal source-monitoring nor reality-monitoring. We also observed a main effect of task condition in both experiments that may be explained by the fact that the number of correct recognition in the “new words” condition differed from the number of correct recognition in the “imagine” and “hear”/“say” conditions whatever the type of task (hear or say), the stimulation condition (active or sham) and the experiment (1 or 2). These results highlighted that the recognition of new words was easier than recognition of heard/said and imagined words. Indeed, new words were introduced in source-monitoring tasks as distractors to eliminate a possible confounding effect of memory capacities on performances (Brunelin et al., 2006a).

Our findings indicate that the left TPJ plays a major role in reality-monitoring processes in healthy subjects. In particular, tDCS-induced hyperactivity of the left TPJ during an imagination task led to misattribution describing this word as heard instead of imagined. Anodal tDCS applied on the left TPJ was thus able to impair verbal reality-monitoring. The effect of tDCS was specific to reality-monitoring process. A possible interfering effect with an early cognitive process involved in the imagination of a word can be ruled out. Indeed, the ‘imagined condition’ was modified by stimulation only in the reality monitoring task and not in the internal source-monitoring task whereas ‘imagined’ conditions’ are very close in both tasks. These findings are in line with brain imaging studies reporting that temporal areas are more active when processing other-generated relative speech compared to self-generated speech in healthy controls but not in hallucinating patients with schizophrenia, suggesting a hyperactivity within temporal areas during self-generated speech in patients with schizophrenia (Allen et al., 2007). The TPJ hyperactivity observed during the occurrence of AVH in schizophrenia (Jardri et al., 2011) may thus also in part explain why patients with AVH displayed reality-monitoring errors, particularly misattribution of inner speech as externally-generated (Waters et al., 2012). Furthermore, it was reported that AVH proneness was positively correlated to activity in the temporal areas (superior temporal gyrus) for imagined words that subsequently participants incorrectly recognized as heard words (Sugimori et al., 2014). Moreover, our findings indicating

that a hyperactivity of the left TPJ may underlie the externalization bias are consistent with recent neuroimaging studies reporting that the left TPJ is crucial in spatial localization of speech. Indeed, a higher activity in the planum temporale was reported in patients with AVH when the AVH were experienced as located in the external environment than when AVH were experienced in the inner space (Looijestijn et al., 2013).

The contribution of the left TPJ in false recognition of an imagined word as a perceived one is also consistent with neuroimaging studies reporting that the left temporal regions are active when a voice is falsely detected in white noise (Barkus et al., 2007), a misattribution more frequently observed in people with AVH (Brookwell et al., 2013). A recent study using tDCS also supported the role of the left TPJ in false recognition of speech (Moseley et al., 2014). The authors investigated the effects of tDCS applied over the left superior temporal gyrus, including part of the left TPJ, on the performances during an auditory signal detection task in which participants were required to detect speech in white noise (Moseley et al., 2014). They reported that compared to sham, anodal tDCS led to a higher rate of false detections of speech in white noise while cathodal tDCS was associated with a decrease of this rate. The authors suggested that higher levels of activity in the left TPJ may lead to false detections of speech in white noise by reducing the signal-to-noise ratio and making it difficult to disentangle internally from externally derived perceptions.

Finally, the left TPJ has been constantly related to self-agency processes. Namely, the TPJ has been associated with less sense of self and other-generated attribution (Sperduti et al., 2011).

Altogether, these findings indicate that hyperactivity within the left TPJ may disturb the disambiguation between internal speech/thoughts and externally perceived events leading to label inner speech as externally perceived and less self-generated. No effect of anodal tDCS applied over the left TPJ was reported on internal source monitoring performances, suggesting a specific linkage between the left TPJ and reality-monitoring processes. Indeed, internal source-monitoring processes, i.e. deciding whether a self-generated item was imagined or performed, does not involve self/other recognition and thus may be underpinned by other neural processes.

Our results did not account for a contribution of the dorsal part of the left PFC in source-monitoring processes. Indeed, cathodal stimulation applied over the left PFC had no influence on reality-monitoring and internal source-monitoring in healthy subjects. One can hypothesize that impaired functioning of this region may not be sufficient to disturb source-monitoring processes but should be combined with impaired functioning of other brain areas such as the left TPJ. For instance, more activity in the left inferior frontal gyrus during imagining another person's voice led healthy people to later judge imagined items as heard (Sugimori et al., 2014). It would be interesting to evaluate the effects of tDCS applied over this region, known to be also involved in auditory hallucinations (Jardri et al., 2011). Some neuroimaging studies have also reported that low activation of the PFC, particularly its medial part (mPFC), is associated with poor performance during reality-monitoring tasks in patients with schizophrenia (Simons et al., 2006; Subramaniam et al., 2012). Another explanation for the lack of effect of cathodal-tDCS applied over the left PFC may be related to the imprecision of the electrode placement between F3 and Fp1 based on EEG system that could not allow the modulation of mPFC activity. Further noninvasive brain stimulation studies are needed to highlight the causal role of the mPFC region in self, reality and source-monitoring processes (e.g., Civai et al., in press). Moreover, it has been previously shown that anodal stimulation is more effective than cathodal to induce modification in cognitive tasks (Jacobson et al., 2012), one can argue that cathodal stimulation applied over the PFC was not enough effective to modulate source monitoring performance in the current study. Finally, the contribution of the left PFC in source-monitoring processes cannot completely be excluded since the study is limited by the absence of direct neuronal measures.

Our study have limitations, in particular due to the size of the electrode (35cm<sup>2</sup>) and the technique itself that does discriminate the respective contribution of the various structures comprised within the TPJ and PFC. For instance, the TPJ encompasses at least part of the STG including secondary auditory cortices such as Wernicke's area, the planum temporale, the supramarginal gyrus and the inferior parietal lobe. It is known that tDCS is able to modulate a large cortical network of interconnected brain regions and not only a single targeted brain

region (Keeser et al., 2011). Thus, the left TPJ stimulation may modulate a large network implicated in language processing and in self/other recognition. Further studies combining tDCS with neuroimaging investigations are needed to determine the brain changes associated with the observed behavioral effect. In addition, the present study does not provide evidence as to whether targeting the left TPJ with tDCS affects encoding or recall of source information since the stimulation was delivered during both phases. Future studies should differentially deliver tDCS during the encoding or the recall phase to provide a better understanding of source-monitoring mechanisms. Finally, the sample size is limited and results should be taken with caution.

Despite these limitations, our findings are showing that tDCS can safely modulate cognitive functions in healthy subjects since no serious adverse effects were reported during the several conditions of our experiment. Most common reported adverse effects were burning sensation and trouble concentrating but no differences were observed between active and sham conditions. We also confirmed that tDCS was a valuable method for double blind crossover studies since participants were not able to know whether they had received active or sham tDCS.

In sum, this study shows that targeting the left TPJ with anodal tDCS disturbs reality-monitoring processes in healthy participants, leading to a similar externalization bias mimicking to some extent what is seen in patients with schizophrenia and auditory hallucinations.

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## References

- Allen P, Amaro E, Fu CHY, Williams SCR, Brammer MJ, Johns LC, McGuire PK. 2007. Neural correlates of the misattribution of speech in schizophrenia. *Br J Psychiatry* 190:162–169.
- Barkus E, Stirling J, Hopkins R, McKie S, Lewis S. 2007. Cognitive and neural processes in non-clinical auditory hallucinations. *Br J Psychiatry* 51:s76–81.
- Brookwell ML, Bentall RP, Varese F. 2013. Externalizing biases and hallucinations in source-monitoring, self-monitoring and signal detection studies: a meta-analytic review. *Psychol Med.* 43:2465–2475.
- Brunelin J, Combris M, Poulet E, Kallel L, D’Amato T, Dalery J, Saoud M. 2006a. Source monitoring deficits in hallucinating compared to non-hallucinating patients with schizophrenia. *Eur Psychiatry* 21:259–261.
- Brunelin J, Poulet E, Bediou B, Kallel L, Dalery J, D’amato T, Saoud M. 2006b. Low frequency repetitive transcranial magnetic stimulation improves source monitoring deficit in hallucinating patients with schizophrenia. *Schizophr Res.* 81:41–45.
- Brunelin J, d’ Amato T, Brun P, Bediou B, Kallel L, Senn M, Poulet E, Saoud M. 2007. Impaired verbal source monitoring in schizophrenia: An intermediate trait vulnerability marker? *Schizophr Res.* 89:287–292.
- Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. 2011. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *Int J Neuropsychopharmacol.* 14:1133–1145.
- Brunoni AR, Schestatsky P, Lotufo PA, Benseñor IM, Fregni F. 2014. Comparison of blinding effectiveness between sham tDCS and placebo sertraline in a 6-week major depression randomized clinical trial. *Clin Neurophysiol.* 125:298–305.
- Civai C, Miniussi C, Rumiati RI. In press. Medial prefrontal cortex reacts to unfairness if this damages the self: a tDCS study. *Soc Cogn Affect Neurosci.* 2014 Dec 30. pii: nsu154. [Epub ahead of print]
- Ford JM, Mathalon DH. 2005. Corollary discharge dysfunction in schizophrenia: Can it explain auditory hallucinations? *Int J Psychophysiol.* 58:179–189.
- Frith C. 1996. Neuropsychology of schizophrenia: What are the implications of intellectual and experimental abnormalities for the neurobiology of schizophrenia? *Br Med Bull.* 52:618–626.
- Gandiga PC, Hummel FC, Cohen LG. 2006. Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clin Neurophysiol.* 117:845–850.
- Jacobson L, Koslowsky M, Lavidor M. 2012. tDCS polarity effects in motor and cognitive domains: a meta-analytical review. *Exp Brain Res.* 216(1):1-10.
- Jardri R, Pouchet A, Pins D, Thomas P. 2011. Cortical activations during auditory verbal hallucinations in schizophrenia: a coordinate-based meta-analysis. *Am J Psychiatry* 168:73–81.
- Johnson MK, Hashtroudi S, Lindsay DS. 1993. Source monitoring. *Psychol Bull.* 114:3–28.
- Keeser D, Meindl T, Bor J, Palm U, Pogarell O, Mulert C, Brunelin J, Moller HJ, Reiser M, Padberg F. 2011. Prefrontal Transcranial Direct Current Stimulation Changes Connectivity of Resting-State Networks during fMRI. *J Neurosci.* 31:15284–15293.
- Looijestijn J, Diederens KMJ, Goekoop R, Sommer IEC, Daalman K, Kahn RS, Hoek HW, Blom JD. 2013. The auditory dorsal stream plays a crucial role in projecting hallucinated voices into external space. *Schizophr Res.* 146:314–319.

- Martikainen MH, Kaneko K, Hari R. 2005. Suppressed responses to self-triggered sounds in the human auditory cortex. *Cereb Cortex* 15:299–302.
- Mitchell KJ, Johnson MK. 2009. Source monitoring 15 years later: what have we learned from fMRI about the neural mechanisms of source memory? *Psychol Bull.* 135:638–677.
- Mondino M, Haesebaert F, Poulet E, Suaud-Chagny MF, Brunelin J. 2015. Fronto-temporal transcranial Direct Current Stimulation (tDCS) reduces source-monitoring deficits and auditory hallucinations in patients with schizophrenia. *Schizophr Res.* 161:515–516.
- Moseley P, Fernyhough C, Ellison A. 2013. Auditory verbal hallucinations as atypical inner speech monitoring, and the potential of neurostimulation as a treatment option. *Neurosci Biobehav Rev.* 37:2794–2805.
- Moseley P, Fernyhough C, Ellison A. 2014. The role of the superior temporal lobe in auditory false perceptions: A transcranial direct current stimulation study. *Neuropsychologia* 62:202–208.
- Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, Antal A, Paulus W, Hummel F, Boggio PS, Fregni F, et al., 2008. Transcranial direct current stimulation: State of the art 2008. *Brain Stimul.* 1 :206–223.
- Sehm B, Schnitzler T, Obleser J, Groba A, Ragert P, Villringer A, Obrig H. 2013. Facilitation of inferior frontal cortex by transcranial direct current stimulation induces perceptual learning of severely degraded speech. *J Neurosci.* 33:15868–15878.
- Simons CJP, Tracy DK, Sanghera KK, O'Daly O, Gilleen J, Dominguez MG, Krabbendam L, Shergill SS. 2010. Functional Magnetic Resonance Imaging of Inner Speech in Schizophrenia. *Biol Psychiatry* 67:232–237.
- Simons JS, Davis SW, Gilbert SJ, Frith CD, Burgess PW. 2006. Discriminating imagined from perceived information engages brain areas implicated in schizophrenia. *NeuroImage* 32:696–703.
- Sperduti M, Delaveau P, Fossati P, Nadel J. 2011. Different brain structures related to self- and external-agency attribution: a brief review and meta-analysis. *Brain Struct Funct.* 216: 151–157.
- Sugimori E, Mitchell KJ, Raye CL, Greene EJ, Johnson MK. 2014. Brain mechanisms underlying reality monitoring for heard and imagined words. *Psychol Sci.* 25:403–413.
- Vines BW, Schnider NM, Schlaug G. 2006. Testing for causality with transcranial direct current stimulation: pitch memory and the left supramarginal gyrus. *Neuroreport.* 17:1047–1050.
- Wang L, Metzak PD, Woodward TS. 2011. Aberrant connectivity during self-other source monitoring in schizophrenia. *Schizophr Res.* 125(2-3): 136–142.
- Waters F, Woodward T, Allen P, Aleman A, Sommer I. 2012. Self-recognition deficits in schizophrenia patients with auditory hallucinations: a meta-analysis of the literature. *Schizophr Bull.* 38:741–750.