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Original Research

Transcranial direct current stimulation accelerates allocentric target detection

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Background: Previous research on hemispatial neglect has provided evidence for dissociable mechanisms for egocentric and allocentric processing. Although a few studies have examined whether tDCS to posterior parietal cortex can be beneficial for attentional processing in neurologically intact individuals, none have examined the potential effect of tDCS on allocentric and/or egocentric processing.
Objective/hypothesis: Our objective was to examine whether transcranial direct current stimulation (tDCS), a noninvasive brain stimulation technique that can increase (anodal) or decrease (cathodal) cortical activity, can affect visuospatial processing in an allocentric and/or egocentric frame of reference.
Methods: We tested healthy individuals on a target detection task in which the target – a circle with a gap – was either to the right or left of the viewer (egocentric), or contained a gap on the right or left side of the circle (allocentric). Individuals performed the task before, during, and after tDCS to the posterior parietal cortex in one of three stimulation conditions – right anodal/left cathodal, right cathodal/left anodal, and sham.
Results: We found an allocentric hemispatial effect both during and after tDCS, such that right anodal/left cathodal tDCS resulted in faster reaction times for detecting stimuli with left-sided gaps compared to right-sided gaps.
Conclusions: Our study suggests that right anodal/left cathodal tDCS has a facilitatory effect on allocentric visuospatial processing, and might be useful as a therapeutic technique for individuals suffering from allocentric neglect.

Introduction

Hemispatial neglect is a syndrome characterized by an impairment in attending or responding to stimuli presented on the contralesional side of space [1]. Some individuals with right hemisphere damage demonstrate egocentric neglect, an impairment relative to a midline projected from the viewer [2–4]. By contrast, a smaller number of individuals demonstrate allocentric neglect – a deficit in which individuals are impaired relative to a midline centered on a stimulus and not the viewer [5–7]. For example, on an Ogden scene copying task [8], individuals with egocentric neglect will fail to copy the left side of the scene, whereas individuals with allocentric neglect will fail to copy the left side of each object. Furthermore, on a gap detection task [9] individuals with egocentric neglect will fail to respond to the left side of the array of gaps, whereas individuals with allocentric neglect will fail to respond correctly to each left-gapped target. This egocentric/allocentric processing distinction is also supported by evidence from neuroimaging [10,11] and behavioral studies [12–14]. Impairment in egocentric processing has been associated with right inferior parietal damage, whereas impairment in allocentric processing has been associated with damage to the posterior aspect of the superior and middle temporal gyri [15–20], whereas neuroimaging studies have implicated posterior parietal regions in both egocentric and allocentric processing [21–23].

Transcranial direct current stimulation (tDCS) is a technique in which a weak direct current runs through the brain between electrodes placed on the scalp [24]. Relatively few studies have examined the effects of tDCS on the posterior parietal cortex, specifically its effects on attentional processing. Sparing and colleagues [25] found that during a perithreshold stimulus detection task, anodal parietal tDCS facilitated contralateral target detection, whereas cathodal parietal tDCS suppressed contralateral target detection. Bolognini and colleagues [26] found that right

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anodal tDCS to the posterior parietal cortex increased reaction times to contralateral targets on a crossmodal audiovisual integration task. Finally, recent studies have shown that tDCS may improve attentional processing in individuals with hemispatial neglect [25,27].

Although prior investigations have explored the effects of posterior parietal tDCS on attentional processing, no studies have examined whether tDCS has an effect on allocentric and/or egocentric processing. To address this, we instructed neurologically intact subjects to detect whether a circle with a gap appeared in an array of four circles with gaps before, during, and after tDCS. The gap could be located either on the left or right side of the circle (allocentric), and the target could appear either to the left or right of fixation (egocentric).

We placed the electrodes on homologous locations over posterior parietal cortex in each hemisphere, examining performance with the anode over the left hemisphere and cathode over the right hemisphere, and vice versa. Our choice of dual-hemisphere tDCS was motivated by a desire to maximize current density underneath the electrodes, and has been used in other tDCS studies that examined cognitive function (e.g. Refs. [28–30]). Furthermore, we employed computer modeling of current flow in order to determine the cortical regions that would be subjected to higher current density due to tDCS given our electrode arrangement, as previous studies have demonstrated that the location of both the anode and reference electrode have significant effects on current flow and behavior [31,32]. Given our electrode montage, if tDCS has an effect on allocentric processing, we predicted that right anodal/left cathodal tDCS would improve performance on left-gapped versus right-gapped targets, whereas right cathodal/left anodal tDCS would worsen in performance on left-gapped versus right-gapped targets. A second possibility was that an egocentric effect would be observed as well, such that individuals undergoing right anodal/left cathodal tDCS would improve at detecting targets on the left side of the array compared to the right side of the array, whereas the opposite pattern of performance was predicted in the right cathodal/left anodal condition.

Methods and materials

Participants

Eighteen right-handed individuals (11 females, ages 18–50, mean age 25.2, SD 7.3) participated in the study. All participants had no history of neurological or psychiatric disorders. They all had normal or corrected-to-normal vision and were naïve to the purpose of the experiment. Participants with implanted electrical devices, metal in the head, and/or history of seizures were not allowed to participate in the study. All research was carried out in compliance with institutional guidelines and approved by the Institutional Review Board of the University of Pennsylvania.

Task

The experiment was run using E-Prime (www.pstnet.com) on a computer attached to a 17″ laptop display. Subjects sat with their head and trunk midlines aligned with the center of the monitor. Subjects were instructed to maintain fixation at the center of the screen during the entire experiment. The subject was seated approximately 60 cm from the screen. Visual stimuli for this experiment consisted of a 6° (visual angle) circle (6.8 cm in diameter) with a 100° (out of 360°) gap (see Fig. 1A). The gap was centered on either the top, bottom, left, or right side of the circle. At the beginning of each trial, participants were shown a fixation point for 1000 ms, followed by a target circle for 1000 ms. A second

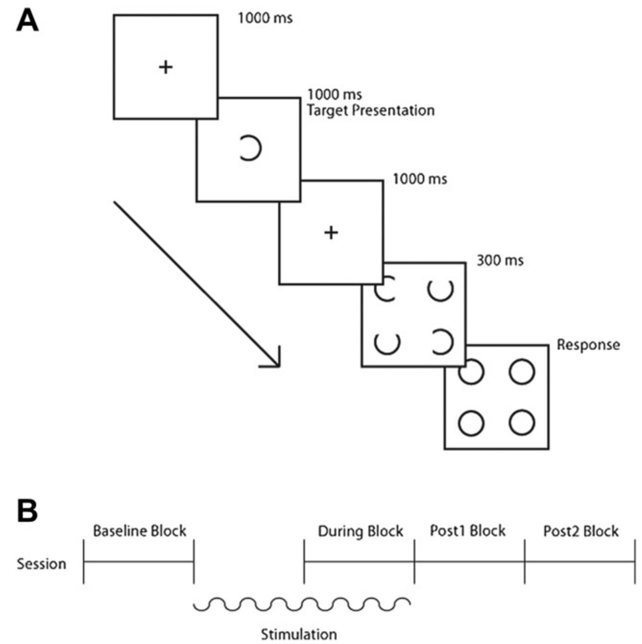

Figure 1. (A) Type and time of stimulus presentation for one typical trial in the experiment. Participants were first presented with a fixation cross for 1000 ms. Next, the target circle was presented, and the participant was instructed to identify if this target circle is in the following array. After presentation of a fixation cross, the array is presented for 300 ms, followed by a mask slide. Participants then responded as to whether the target circle was present (as in the displayed example) or absent in the array. (B) Order of block presentation in a typical session, with time during testing is denoted by a straight line, time during tDCS stimulation is denoted by a wavy line.

fixation point then appeared for 1000 ms, followed by an array of four circles with gaps. The center of each circle was 6° horizontally and 4.62° vertically (visual angle) from fixation. On target present trials, the array consisted of one target, one non-target of a different orientation, and two non-targets of a third orientation. Target absent trials also had three stimulus types in the array (with one stimulus type repeated twice). The array was presented for 300 ms, followed by a mask consisting of four filled black circles in the same position as the stimulus array. Participants were instructed to identify as quickly and accurately as possible whether the target circle presented previously was present (by pressing “z” on the keyboard using the index finger of the left hand) or absent (by pressing “/” on the keyboard using the index finger of the right hand). Subjects were given unlimited time to respond. During the experiment, a researcher monitored the subject using a small video camera mounted above the monitor to ensure that there were no overt eye movements toward the target after array presentation. In pilot testing, we observed that saccades to any targets in the array were observable. During the practice block, subjects were verbally warned if any overt eye movements were noticed. No overt movements were noticed during any of the experimental blocks.

Each session began with a practice block of 60 trials. Next, a *baseline* block was performed before either sham or real tDCS (see Fig. 1B); this and other experimental blocks included 128 trials balanced for presence/absence of target in the array, location of target circle in the array (16 trials at each of the four targets), target circle orientation, and type and location of non-target circles (e.g. the distractor circles that were not the target) in the array. After the baseline block, 20 min of real or sham tDCS started. After 10 min of real/sham tDCS, subjects began the *during* tDCS block, in which they were stimulated while performing the task. Each experimental block lasted approximately 10–11 min, such that the participants received tDCS during the majority of this block. Next, participants were tested on two more blocks (post1 and post2) directly after finishing the during tDCS block. During these blocks there was no brain stimulation.

Individuals participated in three sessions on three separate days, each with a different tDCS manipulation. Real or sham tDCS was presented using a battery-driven, constant current Magstim Eldith device, connected to two 5 $\times$ 5 cm saline-soaked pads. In the right cathodal/left anodal condition, the anode was located over left parietal cortex (CP3 in the International 10/20 system) while the cathode was located over right parietal cortex (CP4). In the right anodal/left cathodal condition, the anode was located over CP4, while the cathode was located over CP3. Pads were kept in place using rubber straps. During the real tDCS conditions, 1.5 mA of current was applied for 20 min, with 10 s of ramp up and ramp down at the beginning and end of stimulation, respectively. In the sham tDCS condition, the pad configuration was the same as in either real tDCS conditions, thereby serving as a control to both active tDCS conditions. To mimic the sensation of tDCS, the current was ramped up for 30 s, and then immediately ramped down for 10 s. Session order was counterbalanced across subjects.

Analysis

Although subjects did not make overt eye movements to specific targets during the experiment, we could not determine whether a subject was covertly focusing on a specific array position. Because we were concerned that subjects might preferentially attend to one target as a task strategy, we first analyzed the mean accuracy by target position for each subject. Three subjects who performed at greater than 90% accuracy at one target location (e.g. top left of the array) while performing at or below chance (50%) on the opposite target location (e.g. bottom right) were discarded before any further analysis.

We analyzed our data using linear mixed models, due to their sensitivity to differences in the overall reaction time of individual subjects, robustness to issues such as unequal sample sizes for individuals and items, and the ability to reduce variance by accounting for trial-by-trial differences in performance (see Ref. [33]). Accuracy and log transformed reaction time data [34] for correct responses on target present trials were analyzed using linear mixed modeling [35] computed in R (2.12.1) using the LMER and languageR packages. For reaction time data, all trials with responses three standard deviations outside of the within subject mean were excluded (1.38% of trials).

For model testing of both reaction time and accuracy data, factors and the interactions between them were entered separately into the model in a stepwise manner. A factor, or the interaction between factors, was included in the final model only if its inclusion resulted in a significant improvement in model fit compared to exclusion of the factor (tested using ANOVAs). After identifying the best model, we then used pvals.fnc (part of the languageR package) to identify which factors in the linear mixed model were significant. Significance was determined using Markov Chain Monte Carlo *P*-values (pMCMC) with 10,000 iterations. Model testing was performed separately for reaction time and accuracy data, with a binomial logit model used for accuracy data.

The following fixed factors were used in model testing: block, stimulation session, horizontal target position in array, vertical target position in array, target orientation (up, down, left, right), and gap eccentricity (whether the gap was oriented toward or away from the fixation point). Furthermore, to reduce variance in the model for the reaction time analyses, we also added other fixed factors that have been found to predict performance on reaction time tasks (see Ref. [33]): session order, reaction time on the preceding trial, and trial number within a block. Finally, subject was included in all models as a random factor.

Note that comparisons within factors with more than two levels (block, stimulation, target orientation) are not fully factorial, and compare changes in performance on one specified level to the remaining levels. As our hypotheses were based on comparisons to no intervention, our model compared performance on the baseline block to subsequent blocks (during, post1, and post2). Performance during the sham tDCS session was compared to performance during either right anodal/left cathodal or right cathodal/left anodal stimulation sessions. Furthermore, we hypothesized that tDCS would most likely have an effect on left-gapped targets, due to the role of the right hemisphere in attentional processing. Therefore, our model compared performance on left-gapped targets to all other target orientations.

Modeling

In order to evaluate the brain regions most likely to be affected by tDCS, induced electrical fields were modeled (for details, see Ref. [36]) on the brain of an adult male, created from a high resolution magnetic resonance imaging scan. From this scan, the head model was segmented into separate compartments representing the brain (gray matter and white matter separately), skull, scalp, eye region, muscle, cerebrospinal fluid (CSF), blood vessels, and air compartments (Custom Segmentation, Soterix Medical, New York, NY). Square 5 $\times$ 5 cm pads were imported as CAD models and placed on the head model. In order to account for tissue clipped by the MRI acquisition volume, a synthetic region was added to complete the model. For computation of electric fields (EF), the finite element mesh was generated from the segmentation data and exported to COMSOL Multiphysics 3.5a (Burlington, MA). The following isotropic electrical conductivities (in S/m) were assigned: gray matter: 0.276; white matter: 0.126; CSF: 1.65; skull: 0.01; scalp: 0.465; eye region: 0.4; muscle: 0.334; air: 1e-15; synthetic region: 0.17; sponge: 1.4; electrode: 5.8 $\times$ 10^7. Finally, the Laplace equation was solved for our total current and pad configuration, and maps plotting the magnitude of EF were determined. The model displayed was for right anodal and left cathodal tDCS under the parameters of stimulation in our experiment (Fig. 2). Modeling identified areas of increased current directionality in right posterior parietal cortex (see Fig. 2, right panel). Furthermore, this increased current directionality extended into right superior parietal cortex, posterior superior and middle temporal gyrus. A similar pattern of decreased current directionality was modeled for homologous regions in the left hemisphere. Note that the opposite polarity (right cathodal/left anodal) would result in the inverse of the displayed model in Fig. 2.

Results

For reaction time with the target present, the best regression model included the fixed factors block, stimulation session, gap eccentricity, horizontal target position, vertical target position, target orientation, session order, preceding RT, and trial number; full three-way interactions of block $\times$ stimulation $\times$ horizontal target position and block $\times$ stimulation $\times$ target orientation; and a random effect of subject (see Supplementary Table 1). We found significant simple effects of various factors, including session order subjects were faster on later sessions, gap eccentricity subjects were faster when the target faced the fixation point, target orientation subjects were faster on right-facing gaps compared to other orientations, and vertical target position (faster above versus below fixation). Furthermore, there were significant effects of preceding

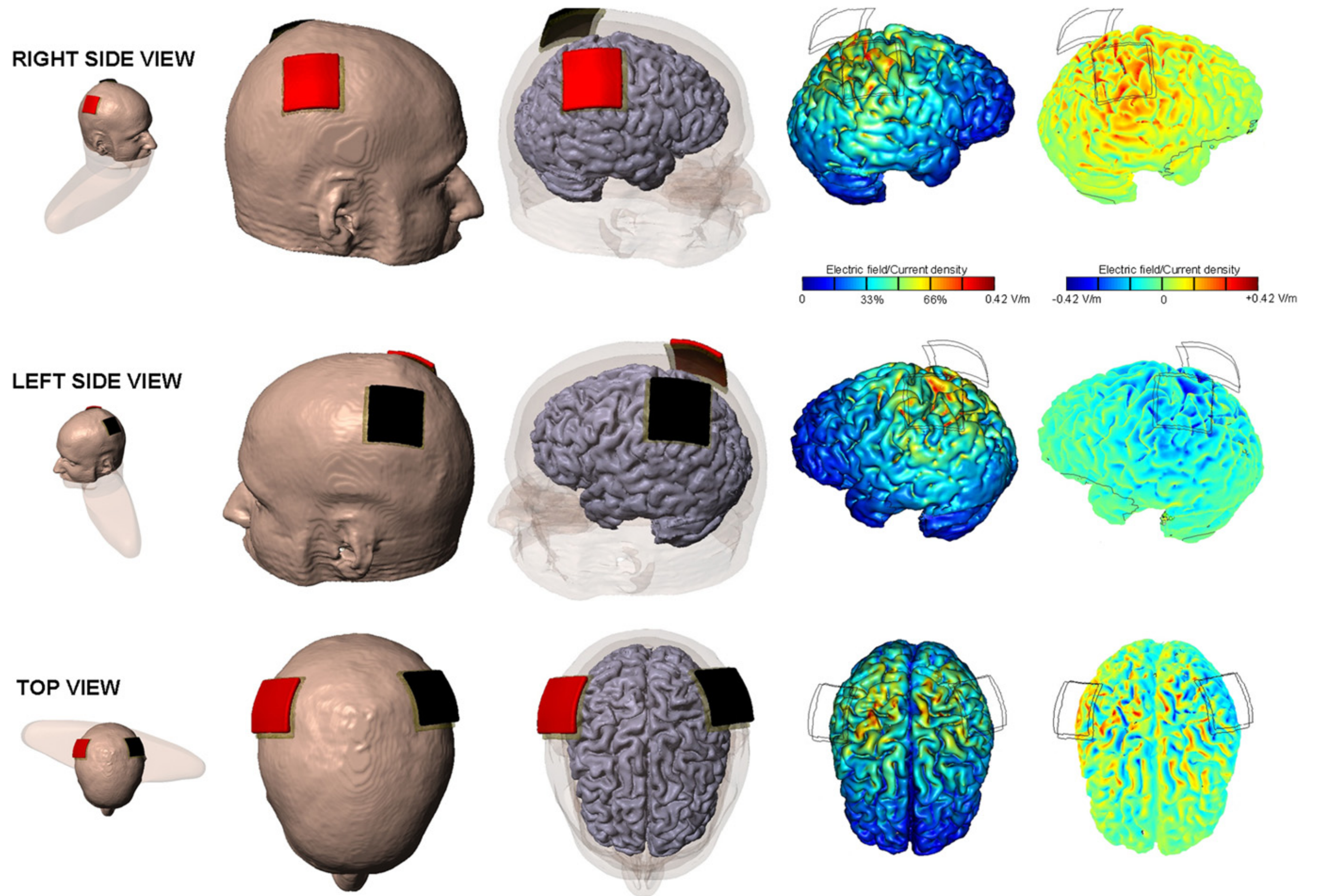

Figure 2. Electrical field modeling induced by tDCS, with placement of the anode (red) on the right hemisphere, and cathode (left) on the left hemisphere. The fourth column shows the magnitude of the induced electric field without respect to current directionality. The fifth rightmost column shows the directional electric fields, with positive changes in current density shown in red (depolarization) and negative changes in blue (hyperpolarization). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

reaction time and trial number, as observed in other analyses of reaction time data [33].

In order to observe whether tDCS had an effect on overall reaction times, we first compared performance in the baseline block to performance in the during- and post-tDCS blocks. We found significant simple interactions between block and stimulation session. Comparing performance to the baseline block, subjects responded more quickly either during (baseline:during, $t = -1.92$, $P = .055$) or after right anodal/left cathodal tDCS (baseline:post1, $t = -3.28$, $P = .001$; baseline:post2, $t = -3.10$, $P = .002$) compared to sham tDCS, indicating that right anodal/left cathodal tDCS speeds overall performance. There were no significant blocks by stimulation session interactions when comparing sham to right cathodal/left anodal tDCS. Second, we found a significant tDCS stimulation session by target interaction, as subjects were significantly faster in the right anodal/left cathodal stimulation versus the sham stimulation on right targets compared to left targets overall. However, this comparison collapses over all four blocks, including the baseline block where no tDCS was presented. Importantly, we hypothesized that if tDCS has a lateralized effect on target detection, there would be a three-way interaction between block, stimulation session, and horizontal target position (egocentric processing) and/or target orientation (allocentric processing). Therefore, we compared the change in performance from the baseline block to the during or post-tDCS blocks across tDCS stimulation sessions (sham versus right cathodal/left anodal, sham versus right anodal/left cathodal, see Supplemental Table 2). Examining allocentric processing, we found interactions between target orientation (left-sided versus right-sided targets), tDCS stimulation session (sham versus right anodal/left cathodal) and all three block comparisons (baseline:during, $t = 1.82$, $P = .069$; baseline:post1, $t = 2.66$, $P = .008$; baseline:post2, $t = 2.01$, $P = .045$). Due to right anodal/left cathodal tDCS, participants responded significantly faster on left-gapped targets versus right-gapped targets (see Fig. 3, upper panel).

This significant interaction could be caused by either faster reaction times toward left-gapped targets, slower reaction times to right-gapped targets, or a combination of both. For example, left cathodal tDCS could be disrupting left-lateralized letter identification processing [37,38], as the right-gapped circle resembles the letter "C". To test the effects of tDCS separately on left- or right-gapped circles, we ran separate regression analyses (fixed factors, block and stimulation session; random factor, subject) on performance on left-gapped circles only, or right-gapped circles only. For left-gapped circles only, participants were significantly faster after right anodal/left cathodal tDCS compared to sham tDCS over all three comparisons to baseline performance (baseline:during, $t = -1.95$, $P = .051$; baseline:post1, $t = -2.70$, $P = .007$; baseline:post2, $t = -3.11$, $P = .002$). For right-gapped circles ("C"), there were no significant differences between right anodal/left cathodal tDCS compared to sham (all ps > 0.46).

Regarding egocentric processing, we found a marginally significant three-way interaction between block (baseline versus during

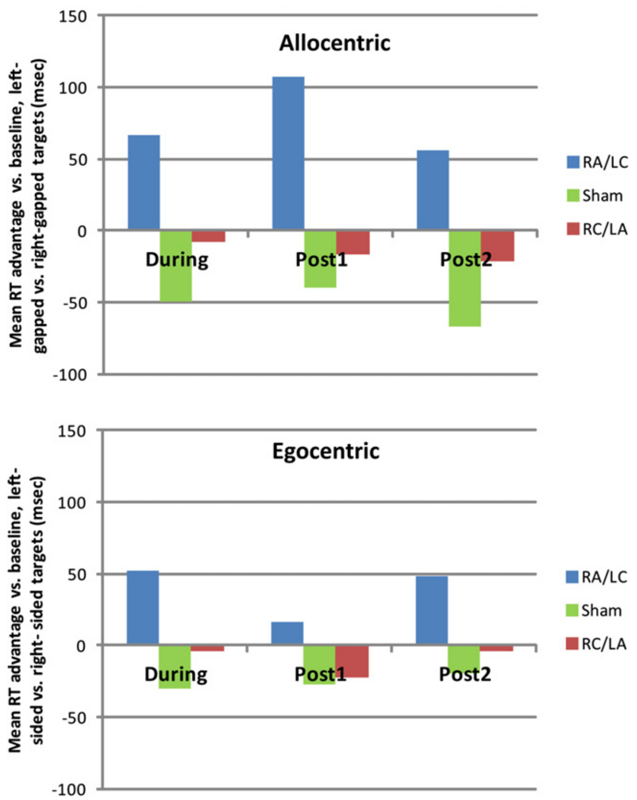

Figure 3. Grand mean reaction time advantage for left versus right targets on target present trials, comparing baseline block performance to performance during and in the two blocks after tDCS (post1, post2). Faster RTs on left targets shown as positive. Upper panel – left-gapped versus right-gapped targets (allocentric). Lower panel – left-sided versus right-sided targets (egocentric). RA/LC – right anodal/left cathodal; RC/LA – right cathodal/left anodal.

tDCS), stimulation session (sham versus right anodal/left cathodal tDCS), and horizontal target position ($P = .059$), such that participants were faster for targets on the left compared to the right due to right anodal/left cathodal tDCS (see Fig. 3, lower panel). Although there was a similar trend, there were no significant interactions for the two post-tDCS blocks (baseline:post1, $t = 1.68$, $P = .094$; baseline:post2, $t = 1.39$, $t = 0.166$). Finally, there were no significant three-way interactions between block, stimulation session, and either target position or target orientation comparing sham to right cathodal/left anodal tDCS stimulation.

For accuracy on target present trials, there were significant effects of block (baseline (68.2%) versus post2 (70.5%), $z = 2.352$, $P = .011$; subjects performed most accurately on the final block), target (better on right- (83.1%) versus left-gapped (68.1%) targets; $z = 3.72$, $P > 0.001$; session order ($z = 2.69$, $P = .007$, more accurate on sessions 2 (71.2%) and 3 (70.4%) compared to session 1 (67.8%)), gap eccentricity ($z = 18.77$, $P < .001$, better on inward-facing (77.2%) versus outward-facing (62.3%) targets), and vertical target position ($z = 3.12$, $P = .001$; better on upper (70.8%) versus lower (68.8%) targets). However, there were no significant main effects or interactions of either right cathodal/left anodal or right anodal/left cathodal tDCS, compared to sham tDCS.

Discussion

We found that right anodal/left cathodal tDCS has multiple effects on reaction time in a target detection task. Most importantly, we found that right anodal/left cathodal tDCS speeds reaction times for allocentric processing, resulting in participants being faster when responding to left-gapped targets compared to right-gapped targets. This effect was present both during and approximately 20 min after tDCS stimulation.

As previously noted, allocentric neglect has been primarily associated with damage to right superior temporal and middle temporal structures. In this experiment, the electrodes were located directly over posterior parietal cortex and the superior tip of the posterior superior temporal gyrus. The typical assumption is that current density and polarization are strongest directly underneath the electrode – in this case, over posterior parietal cortex. As the electrodes were not located directly above posterior temporal regions, one might predict that right anodal tDCS would have a limited effect on allocentric processing. However, electric field modeling (see Fig. 2, rightmost panel) showed that the regions of strongest current directionality are both in posterior parietal cortex, superior parietal cortex, and inferior to the electrode in posterior superior and middle temporal gyrus. Therefore, one possibility is that the observed effect of right anodal/left cathodal tDCS on allocentric processing is related to increased current directionality in these posterior temporal regions. However, imaging studies have also implicated the posterior parietal cortex in allocentric processing, which would also be consistent with the current findings [21,23,39]. Overall, our results do not adjudicate between different hypotheses regarding the neural correlates of allocentric processing, as the areas affected by tDCS (both PPC and STG/MTG) have both been implicated in allocentric processing.

Although we found significantly faster reaction times for allocentric processing due to right anodal/left cathodal tDCS, we did not find significantly *slower* reaction times due to right cathodal/left anodal tDCS. Inverting the polarity of stimulation is expected to reverse the polarization of underlying neurons [40], such that previously depolarized structures are hyperpolarized and vice versa. Based simply on neuron polarization, inverting tDCS polarity would be theoretically expected to invert the effects of tDCS. Although not predicted, previous studies of both somatosensory [41], motor [42,43], and visual [44] processing have also demonstrated significant effects only in one polarity. One explanation for this is that active networks may make unidirectional the effects of applied fields on ongoing activity (oscillations), thus reducing sensitivity to one polarity [45]. The neural mechanisms underlying observed distinctions in behavioral effects associated with anodal and cathodal stimulation are incompletely understood and remain an area of active investigation.

Finally, we also found that right anodal/left cathodal tDCS had a more general effect on performance, resulting in faster reaction times when detecting a target as compared to the sham condition. One possibility is that right anodal tDCS increased attention over the entire array, consistent with accounts of attentional processing that postulate that the right hemisphere is involved in attending to the entire visual field [46].

Although our task also has an egocentric component, we found no significant effect of tDCS on this type of processing. One explanation is that tDCS had a similar effect on egocentric and allocentric mechanisms, but differences in task demands on these types of processing resulted in a difference in performance. Individuals with hemispatial neglect demonstrate a gradient deficit, such that they are more likely to fail to respond to stimuli the farther they are located in contralesional space [47–49]. This eccentricity effect suggests that both hemispheres are likely to be involved in attending to or representing stimuli near the midline, with the relative contributions of the right hemisphere increasing as stimuli are farther to the left in an egocentric representation. In our experiment, stimuli were presented somewhat near the center of the visual field, with only 12° of visual angle separating the two targets. Even if right anodal/left cathodal tDCS was enhancing egocentric processing on the left side, it is possible that the relative proximity of the two stimuli resulted in a limited difference in the contribution of right-hemisphere mechanisms to identifying left- versus right-sided targets. This is consistent with our mild (though not significant) effects of right anodal/left cathodal tDCS on egocentric processing. Importantly, this contrasts the relative position of left- versus right-sided gaps in an allocentric frame of reference. Relative to the boundaries of the actual object, the left- and right-sided gaps are on the farthest extent of the stimulus. The contrast between processing a left-sided gap versus a right-sided gap would be maximal in an allocentric representation, and presumably would result in the greatest possible difference in allocentric processing; making it easier to observe the effects of tDCS on allocentric versus egocentric mechanisms. Furthermore, the task involves searching for a target defined by its allocentric components. Participants may be using allocentric mechanisms more than egocentric mechanisms, making the effects of allocentric processing more salient in the task. A second possibility, not exclusive from the first two, is that based on our electrode placement, right anodal/left cathodal tDCS has a greater effect on allocentric processing and a weaker effect on egocentric processing, as evidenced by our marginally significant effect on egocentric processing during right anodal/left cathodal tDCS.

Our results, demonstrating beneficial effects of right anodal/left cathodal tDCS on a target detection task, set the stage to use similar neurostimulation strategies in the field of visuospatial attentional disorders, including neglect. Although the technique is promising, there are two important factors to consider before using this specific montage in rehabilitation. While our results are novel in that they demonstrated that the effects of tDCS on target detection last at least 20 min after stimulation, there has been no work to see if tDCS of posterior parietal and superior temporal areas can have long lasting effects after stroke. Second, our current density model is based on current flow in a normal, intact brain. In the case of a subject with brain damage, it is likely that current density will differ substantially depending on both lesion and electrode location [50]. Therefore, it may be helpful to model current density on lesioned brains, with the goal of identifying the configuration of electrodes that will result in optimal stimulation of perilesional regions of the right hemisphere, or possibly contralesional areas in the left hemisphere.

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Appendix A. Supplementary data

Supplementary data related to this article can be found, in the online version, at doi:10.1016/j.brs.2012.05.008.

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