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Transcranial direct current stimulation modulates shifts in global/local attention

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TRANSCRANIAL DIRECT CURRENT STIMULATION MODULATES SHIFTS IN GLOBAL/ LOCAL ATTENTION

BY

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B.S., Psychology, The University of New Mexico, 2000
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THESIS

Submitted in Partial Fulfillment of the
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ABSTRACT

The effects of transcranial direct current stimulation (tDCS) on global and local feature processing and cued attentional switch were tested. Anodal and cathodal tDCS were applied to the left posterior parietal cortex while subjects completed a global/local compound feature task. The task required subjects to attend to either the global or local features of compound stimuli while ignoring the features of the irrelevant level. Subjects were cued to frequently shift attention between the global and local features. The processing of global and local features was unaffected by parietal tDCS but attentional shifts were compromised. Anodal tDCS degraded the ability of subjects to shift attention from local to global features, and cathodal stimulation degraded performance on all cued global/local shifts. Electrophysiological activity was monitored while subjects performed the global/local task. Event-related and oscillatory changes were observed immediately following cathodal stimulation. Cathodal stimulation increased early-latency (P1) responses to global/local switch cues. Cathodal tDCS also reversed the pattern of late-

latency (P3) responses to global and local cues. P3 responses to global cues were greater than local cue responses when compared to a sham condition. These changes were accompanied by altered 30 to 50 Hz (beta) oscillatory activity over the left parietal cortical stimulation site. Cathodal stimulation decreased left hemisphere beta activity in response to global cues, and differences in beta activity between global and local responses were greater and in the opposite direction than responses following sham. No significant electrophysiological changes were detected following anodal stimulation. These results support the role of left parietal cortex in cued global/local attentional shifts and represent the first successful modulation of global/local switching using exogenous brain stimulation. Changes in event-related and oscillatory activity reveal possible electrophysiological mechanisms mediating the behavioral effects of tDCS on attentional switch.

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INTRODUCTION

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation procedure where direct electrical current is passed through an electrode on the scalp and temporarily modulates the activity of underlying cortical tissue. Depending on the orientation of the applied current, tDCS can either increase or decrease cortical excitability: an anodal electrode that is placed on the scalp increases excitability, whereas a cathodal electrode produces the opposite effect [1, 2].

TDCS has been used to examine the functionality of numerous cortical areas involved in cognitive tasks, such as the role of dorsolateral prefrontal cortex in working memory [3], the supramarginal gyrus in pitch memory [4], and primary motor cortex in motor learning [5]. In this study, anodal and cathodal tDCS was applied to the left posterior parietal cortex (PPC) to assess the functionality of this area in global and local feature processing and shifts of attention between these features.

The ability to perceive the global features of a visual scene while ignoring the local constituent features or vice versa has been studied extensively, as has the ability to shift attention between global and local features [see ref. 6 for an early review]. Neuroimaging techniques such as function magnetic resonance imaging (fMRI), electroencephalography (EEG), and transcranial magnetic stimulation (TMS) have elucidated the cortical areas and brain dynamics involved in global/local processing and attentional shift. These investigations indicate parietal involvement in both feature processing and attentional switch; however, the extent of parietal involvement in both processes remains unclear. For example, fMRI has revealed activations in the left parietal cortex in response to global/local switches while temporal areas were activated during

global/local feature processing [7]. Alternatively, an EEG study of current source density showed maximal sources in right temporal-parietal and left posterior temporal areas in response to global/local switches [8]. In another study, repetitive TMS (rTMS) of left PPC was successful in modulating global/local feature discrimination, but was unsuccessful in modulating global/local attentional shift [9]. Based on these previous reports, one hypothesis of the present study is that anodal or cathodal tDCS applied to the left PPC will affect global/local feature discrimination, cued attentional shift, or both.

A global/local task was used that required orienting of attention to different and sometimes conflicting levels of compound letter stimuli [10]. Subjects were asked to attend to either the local or global features of the stimuli while ignoring features at the non-relevant level. A target cue preceded some compound stimuli and indicated a global-to-local or local-to-global switch in attended features. The remaining stimuli were not preceded by a target cue. This design permitted the dissociation of effects of tDCS on cued attentional switching from global/local feature processing.

Electrophysiological measures (EEG) were taken before and after DC stimulation to assess underlying changes in brain dynamics that accompany anodal and cathodal stimulation. Event-related potential (ERP) changes and oscillatory activities were measured while subjects performed the global/local task.

Several studies have combined tDCS with EEG recording to examine how tDCS affects neural electrophysiology. These studies suggest that sensory and motor evoked responses are modulated by tDCS. Cathodal DC stimulation has been shown to attenuate components of somatosensory and motor ERPs and increase certain components of visual evoked potentials, while anodal stimulation appears to have an opposite effect [11 -14].

Additionally, several studies have reported changes in the power of oscillatory brain activity as a result of TDCS stimulation. Antal, Varga, and Kincses *et al*. found that cathodal stimulation of the visual cortex can significantly decrease the power of beta and gamma frequencies [12], and Marshall *et al*. found that acute anodal stimulation increased frontal slow oscillatory activity when applied during sleep [15].

While there have been a number of studies that have demonstrated the effects of tDCS on behavioral performance and brain activity, no study has yet monitored ongoing brain activity while concurrently assessing task performances that are altered by DC stimulation. Such an investigation can specifically assess how DC induced changes in brain dynamics may result in altered behavioral performance. The current study attempts to address this issue by combining behavioral and electrophysiological assessments of the effects of tDCS on global/local attention. It is hypothesized that any significant behavioral modulations observed will be accompanied by observable alterations in electrophysiological activity following DC stimulation.

METHODS

Participants

Twenty healthy, right-handed adults (6 women) participated in this study.

Global/Local Task

Visual stimuli were four compound letters and two target cues (Fig. 1). The compound letters were “global” letters ("H" or "S") composed of smaller, “local” letters ("H" or "S"). Compound letter stimuli were either “congruent” (identical global and local letters) or “incongruent” (the global letter and the local letters differed). Target cues appeared every four to eight compound letter presentations and indicated that subjects should respond to either the global feature (a capital "G") or the local features (a capital "L") of the following compound letter stimuli. All stimuli were presented on a computer monitor located at a distance of 150 cm. The global letters (3.6º x 2.1º visual angle), the local letters (0.46º x 0.27º), and target cues (1.5º x 1.1º) were white figures on a black background.

The task began with a target cue presentation (“G” or “L”) for 80 ms. After a 1000 to 2000 ms interval, a sequence of between four and eight compound letters were presented for 80 ms each at interstimulus intervals ranging from 1200 to 1800 ms. Subjects responded to the global or local feature (“H” or “S”) of each of these stimuli (as instructed by the target cue) by pressing one of two buttons on a response device with their right index or middle finger. One finger was assigned the “H” response while the other was assigned the “S” response. Button assignment was counter-balanced across subjects. After this sequence, another target cue (“G” or “L”) was presented that indicated a response switch from local-to-global or global-to-local features, followed by

another sequence of four to eight compound letters. Target cues only preceded switch trials. Approximately 30 target cues and 150 compound stimuli were presented. Task duration was approximately five minutes.

DC Stimulation

Direct current electrical stimulation was applied at the scalp over the left PPC (P3 of the International 10-20 System). A 2.0 mA current was delivered for 20 minutes through a 5 x 5 cm sponge electrode using a constant current stimulator (Phoresor PM850; Iomed, Salt Lake City, Utah). The circuit was completed with either a 5 x 5 cm or a 17.5 x 9 cm sponge electrode placed on the outer arm below the right elbow. The parietal electrode was connected to the anode or cathode of the stimulator for anodal or cathodal stimulation, respectively. The anodal electrode placement was used during a sham condition; however, the current was increased from 0 to 2.0 mA for the first 20 seconds and then decreased from 2.0 to 0 mA 30 seconds later and remained off for the remainder of the sham epoch.

Procedure

Participants received anodal, cathodal, and sham stimulation in separate sessions four days apart (Fig. 2). Stimulation order was counter-balanced across participants. Participants were not informed which stimulation condition they were receiving on each day. Each session began with two practice runs of the global/local task. Participants were prepared for EEG recording, and approximately 40 minutes later they completed a pre-stimulation run (“Pre”) of the task. Immediately following the pre-stimulation run, tDCS (or sham) was applied for 20 minutes. Participants began another run (“During”) of the task at 14 minutes of stimulation and received continuous tDCS (or sham) for the

duration of this run. After 20 minutes of stimulation, the stimulator was turned off and participants completed another run (“Post0”) of the global/local task. Participants rested for 15 minutes and then completed a final task run (“Post20”).

EEG recording

EEG recordings were collected from 128 electrodes during the pre-stimulation and the two post-stimulation task runs with a high-density EEG whole head array system (BioSemi Active Two system; BioSemi, Amsterdam, Netherlands). Data were collected at a sampling rate of 256 Hz, and electrode offsets were kept within +/- 25 μV throughout collection. Data were filtered with a one Hz high-pass filter and a 55 Hz low-pass filter and referenced to the average voltage of the electrode array. EEG data were down-sampled to 125 Hz for analysis offline.

Data Analysis

Behavioral Analysis

Behavioral data from runs Pre, During, Post0, and Post20 were analyzed. Data from each run were pre-processed. Inter-quartile box plots were created for all response times for each subject at each factor level, and reaction times were rejected when they deviated more than 1.5 box lengths (outlier responses). Additionally, blocks of compound feature trials following a target cue were rejected if the majority of trials in the block were incongruent and all subject responses to these incongruent trials were incorrect. Since the target cues were presented for only 80 ms, this procedure was followed to minimize the effects of failing to detect a target cue. The mean time to respond in milliseconds divided by the proportion of correct responses was the dependent variable [*cf* 16]. This combined variable was used to account for possible speed-accuracy trade-

offs and has been used in other studies, including studies examining responses to global/local compound stimuli [17, 18]. For clarification, accuracies are reported for omnibus effects. To determine the effects of tDCS on global/local switching, analyses were performed only on compound letter presentations immediately following a switch target cue. To examine global/local feature processing, a separate analysis was performed on trials that did not follow a target cue. Omnibus tests were repeated-measures multivariate analyses-of-variances (MANOVAs).

EEG Analysis

EEG data from runs Pre and Post0 were analyzed. EEG responses to global and local target cue presentations ("G" and "L") were analyzed from 200 ms prior to target cue presentation until 500 ms post presentation. Four posterior scalp regions were delineated for analysis (Fig. 3). Left and right parietal regions were assessed based on the average potentials of six electrodes from each hemisphere, and left and right occipital responses were assessed from the average of 11 electrodes per hemisphere. Frontal and midline responses were excluded from analyses.

Target cue trials were excluded from analysis if deflections of greater than +/- 50 μV were detected in any of the parietal or occipital electrodes during the 700 ms time window (noise trials). Trials where a response to the target cue was made were also excluded. ERP and frequency power analyses were performed on the remaining trials. Separate comparisons between anodal and sham (A *vs.* S) and cathodal and sham (*C vs.* S) ERP and oscillatory responses to target cues were assessed with repeated-measures multivariate analyses-of-variances.

ERP Analysis

To determine the evoked responses to target cues, peak voltage amplitudes and peak latencies of three ERP components were determined: The P1 component (defined as the peak positive voltage deflection between 50 and 150 ms after target cue presentation), the N2 component (the negative deflection between 150 to 210 ms post-presentation), and the P3 component (the positive deflection between 200 to 450 ms post-presentation). To determine the peak amplitudes of each component, the mean baseline voltage (from -200 to 0 ms prior to cue presentation) was subtracted from the time series, and the maximum or minimum voltage within each time window that defined each component was taken as the peak. Peak latencies were defined as the time point where the peak amplitude occurred.

Because P1 and N2 responses are maximal over occipital regions the peak amplitudes and latencies of these components were assessed over occipital electrodes. P3 responses are maximal over parietal regions so P3 amplitudes and latencies were evaluated over parietal electrodes.

Frequency Power Analysis

The power of three frequency bands in response to target cue presentations were assessed: The alpha frequency band (between 8 and 12 Hz), the beta frequency band (13 to 30 Hz), and the gamma band (31 to 50 Hz). EEG data were filtered within each frequency band by using high-pass and low-pass Fast Fourier Transform filters. Voltages from filtered data were squared at each sampling point in the time series to ascertain frequency power (in μV^2). Filtered data were then normalized to the baseline by dividing the frequency power of the total time series at each time point by the mean baseline

power (defined as the average from -200 to 0 ms prior to target cue presentations). Normalized alpha, beta, and gamma frequencies were then averaged separately across a time window from 50 to 350 ms post-presentation. Occipital and parietal frequency changes were assessed separately (Fig. 2).

RESULTS

Behavioral Results

Six subjects did not complete all testing conditions and were excluded from the analyses. Behavioral results from the remaining 14 subjects (5 women) are reported.

Global/Local Switch

There were approximately equal numbers of global-to-local and local-to-global switches per run (14 to16 each). The MANOVA included time (Pre, During, Post0, Post20), stimulation (anodal, cathodal, sham), and target switch (global target switch, local target switch) as within-subjects factors. Significant differences were assessed on the dependent variable (mean reaction time divided by proportion of correct responses). There was a significant main effect of target switch. Participants performed better on global switch trials compared to local switches [$F(1,13) = 19.37$; $p = 0.001$; (dependent variable (DV) means): global = 648.57, local = 715.74; (accuracy): global = 88.6%, local = 86.4%]. Main effects for time, stimulation, and interactions were not significant ($p > 0.05$, all cases).

Analysis of pre-stimulation trials revealed no significant main effects or interactions between anodal, cathodal, and sham conditions ($p > 0.05$ all cases). Pre-stimulation performances were then subtracted from During, Post0, and Post20 performances and comparisons were made separately for A *vs.* S and C *vs.* S conditions (Fig. 4).

A *vs.* S comparisons during stimulation (During) revealed a marginally significant interaction between stimulation and target switch [$F(1,13) = 6.104$; $p = 0.028$)]. A paired-samples t test showed that anodal tDCS significantly degraded global target switch

performance compared to sham [t(13) = 2.523, p = 0.025; (DV means): anod = 9.67, sham = -159.65]. There was no significant A *vs.* S local switch difference (p > 0.025).

A *vs.* S comparisons following stimulation (Post0 and Post20) revealed no significant stimulation or stimulation by target switch interactions (p > 0.025 in all cases). However, paired-samples t tests showed a trend toward diminished global switch performance at Post0 [t(13) = 2.132; p = 0.053; (DV means): anod = 82.43, sham = -83.45] and marginally significantly diminished global switch performance at Post20 [t(13) = 2.510; p = 0.026; (DV means): anod = 41.07, sham = -160.20]. A *vs.* S local switch differences weren't significant at either post-stimulation time point (p > 0.025 both cases).

C *vs.* S comparisons during stimulation (During) revealed a significant main effect of stimulation. Cathodal switch performance was significantly worse than sham [F(1,13) = 7.450; p = 0.017; (DV means): cath = 44.10; sham = -64.69]. The target switch (global *vs.* local) by stimulation interaction was not significant (p > 0.025).

C *vs.* S comparisons following stimulation (Post0, Post20) revealed no significant stimulation effects or interactions (p > 0.025 all cases).

Global/Local Feature Processing

Analysis of non-cued feature processing trials included time (Pre, During, Post0, Post20), stimulation (anodal, cathodal, sham), globality (global target stimuli, local target stimuli), and congruency (congruent stimuli, incongruent stimuli) as within-subjects factors. There were significant main effects for globality [F(1,13) = 5.175, p = 0.041] and congruency [F(1,13) = 93.296, p < 0.001], consistent with other studies [10, 19]. Participants performed better on global than local trials [(DV means): global = 482.44,

local = 505.39; (accuracy): global = 92.6%, local = 93.2%] and better on congruent than incongruent trials [(DV means): cong = 452.27, incong = 535.55; (accuracy): cong = 96.3%, incong = 89.6%]. The main effect for time was also significant [$F(3,11) = 5.903$, $p = 0.012$], and a paired-samples t test revealed significant improvement in performance between Pre and Post20 [$t(13) = 4.173$; $p = 0.001$; (DV means): Pre = 512.68, Post20 = 479.55] indicating a practice effect. However, there were no significant effects of stimulation or stimulation interactions ($p > 0.05$, all cases). Pre-stimulation trials revealed no significant effects or interactions ($p > 0.05$). Additional A *vs.* S and C *vs.* S comparisons were made (after subtracting pre-stimulation trials) at the During, Post0, and Post20 time points. Effects of stimulation and stimulation interactions weren't significant at any of these time points ($p > 0.025$; all cases).

EEG Results

Several subjects did not have a sufficient number of EEG responses to target cues in some conditions (< three trials) once trials were excluded due to noise. Results are reported for the eight remaining subjects (two women).

ERP Results

To assess the effects of tDCS on the P1, N2, and P3 components in response to target cues, separate A *vs.* S and C *vs.* S analyses where time (Pre *vs.* Post0), stimulation (A *vs.* S or C *vs.* S), target cue (global target cue *vs.* local target cue), and hemisphere (left *vs.* right) were factors were performed for each amplitude and latency.

A *vs.* S MANOVAs revealed no significant effects of DC stimulation on the peak latencies or amplitudes for any of the ERP components ($p > 0.05$, all tests).

The C *vs.* S MANOVA of the P1 peak amplitude revealed a significant stimulation by time interaction [$F(1,7) = 8.292$; $p = 0.024$; Figs. 5 and 6]. Pre-stimulation responses were then subtracted from Post0 responses. P1 amplitude responses to cue stimuli increased following cathodal stimulation when compared to sham [(means) cath = 1.28 μV, sham = -1.19 μV]. There were no significant C *vs.* S differences in P1 peak latency ($p > 0.05$).

Evaluation of N2 peak amplitudes and latencies revealed no significant C *vs.* S differences ($p > 0.05$, both cases).

The C *vs.* S MANOVA of the P3 peak amplitude revealed a significant stimulation by time by target cue interaction [$F(1,7) = 8.467$; $p = 0.023$); Figs 7, 8, 9]. Pre-stimulation differences between cathodal and sham conditions weren't significant ($p > 0.05$). To detect the nature of the interaction, responses were collapsed across hemispheres and pre-stimulation responses were subtracted from Post0 responses. Cathodal responses to global cues were greater than responses to local cues following stimulation, while the opposite pattern emerged following sham [(means) cath global - local = 1.153 μV, sham global - local = -1.185 μV]. A paired-samples t test revealed that cathodal P3 responses to global cues were greater than sham global responses, but this trend did not reach significance [$t(7) = 2.253$; $p = 0.059$; (means) cath global = 0.986 μV, sham global = -1.21 μV].

Analysis of P3 peak latencies revealed no significant differences between cathodal and sham stimulation ($p > 0.05$).

In addition to separate analyses of behavioral and ERP results, exploratory correlations of attentional switch responses between ERP amplitudes and behavioral

measures were made. None of these correlations reached significance. Correlations and results are presented in Appendix A1.

Frequency Power Results

Frequency power changes in response to target cue stimuli were assessed for each frequency band separately with MANOVAs that used stimulation (A *vs.* S or C *vs.* S), time (Pre *vs.* Post0), target cue (global target cue *vs.* local target cue), and hemisphere (left *vs.* right) as factors. Separate MANOVAs were performed for occipital and parietal regions.

A *vs.* S MANOVAs revealed no significant alpha, beta, or gamma frequency power differences in parietal or occipital regions ($p > 0.025$, all tests).

C *vs.* S comparisons of alpha frequency power changes were not significant in occipital or parietal regions ($p > 0.025$, both cases).

C *vs.* S beta frequency comparisons were not significant over occipital regions ($p > 0.025$); however, comparisons over parietal regions revealed a significant four-way interaction ($F(1,7) = 22.921$; $p = 0.002$). To assess the interaction, pre-stimulation power was subtracted from Post0 power and comparisons were made at each level of stimulation, target cue, and hemisphere (Fig. 10). A paired-samples t test revealed that left hemisphere changes following cathodal stimulation resulted in significantly decreased beta power in response to global cues when compared to local cues [$t(7) = -3.082$; $p = 0.018$; (means) global = -0.255, local = 0.085]. Cathodal left hemisphere responses to global cues were also significantly decreased compared to right hemisphere responses [$t(7) = -2.697$; $p = 0.031$, (means) left global = -0.255, right global = 0.103]. These decreases were not detected in the sham condition ($p > 0.05$). Left hemisphere

differences between global and local responses were greater in the cathodal condition and in the opposite direction compared to sham. This effect was marginally significant [$t(7) = -2.356$; $p = 0.051$; (means) cath global - local = -0.340, sham global - local = 0.268].

No significant C *vs.* S differences were observed in gamma frequency power in occipital or parietal regions ($p > 0.025$, both cases).

DISCUSSION

The purpose of this study was to investigate the effects of parietal tDCS on global/local attentional switching and feature processing. TDCS was applied to the left PPC while a global/local compound letter task was performed. During the task, some compound stimuli were preceded by a target cue indicating a global/local switch while the remaining stimuli didn't follow a cue. This design permitted the dissociation of the effects of tDCS on cued target switching from the effects on global/local feature discrimination. It was found that cathodal tDCS degraded performance on all cued switch trials during stimulation. Anodal stimulation selectively degraded performance only on trials requiring a switch from local-to-global targets. This effect persisted up to 20 minutes after stimulation. There were no significant effects of tDCS on global/local feature processing.

To assess the underlying electrophysiology involved in the effects of tDCS on global/local switching, the ERP and oscillatory responses to global and local switch cues were evaluated. Cathodal tDCS increased the amplitude of the P1 ERP component in response to all switch cues. Additionally, cathodal stimulation reversed the pattern of P3 ERP component responses to global and local cues, marked by an increased response to global cues following stimulation.

While assessing changes in the power of EEG frequencies resulting from stimulation, it was found that cathodal tDCS led to altered left hemispheric differences in responses to global and local cues in the beta frequency band (13 - 30 Hz). There was significantly reduced parietal beta power in response to global cues in the left hemisphere compared to local cue responses and right hemisphere responses. The opposite pattern of

left hemisphere global/local beta frequency responses was observed following sham. No significant ERP or EEG frequency changes were detected following anodal stimulation.

TDCS was induced with an active electrode that covered regions of the left PPC including the superior and inferior parietal gyri (SPG & IPG), and the intraparietal sulcus (IPS) [20]. Neuroimaging studies indicate that regions of the PPC are engaged by cued target orienting in global/local tasks. Weissman *et al.*, report several left parietal foci activated by global/local cued attentional orienting, including the SPG and IPG [21], and this finding has been replicated across multiple studies [7, 22]. The present results affirm the functionality of these regions during global/local switch.

Recently, Qin and Han investigated global/local switching by applying repetitive TMS (rTMS) to the PPC [9]. They stimulated the same left parietal area as in this study, but failed to detect a significant effect of rTMS on target level switching. Their alternative finding may reflect differences in experimental design and stimuli. These researchers used compound letters that were comprised of target letters and distractors and assessed global/local switching by frequently changing the level at which the target letters were presented. This deviates from the present design in that target switch cues were presented which may engage separate preparatory control mechanisms.

Qin and Han suggest that one of the reasons they failed to achieve a significant result is that global/local attentional shifts are mediated in the temporal-parietal junction. However, the Qin and Han paradigm may have confounded global/local switching and feature processing. In an fMRI study, it was found that cue-related activity resulted in cortical hemispheric differences in the IPS, while feature processing resulted in hemispheric differences in the IPG/superior temporal gyrus [7]. It has also been reported

that bottom-up attentional shifts are mediated in the temporal-parietal junction while top-down/cued shifts are mediated in the SPG [23]. So left PPC participation in attentional switch may depend on whether the switch involves bottom-up feature processing or top-down preparatory control processes. The possibility that cued attentional switching and global/local feature processing are mediated by different cortical networks might explain why significant behavioral differences were observed in cued attentional switching while global/local feature processing was left undisturbed by tDCS in the present study.

Cathodal tDCS increased P1 ERP amplitudes in occipital regions in response to both global and local cue stimuli. Increased P1 responses following cathodal stimulation have been previously reported. In a study examining the effects of DC stimulation over primary visual cortex, increased P1 amplitudes were observed in response to low contrast sinusoidal luminance gratings, although these increases didn't reach significance [11]. The significant P1 amplitude increases observed here were in response to both global and local cue stimuli. Given that P1 is associated with early visual processing and that increases were observed in response to both visual cues following tDCS, it may be that increased early responses are a general feature of the effects of cathodal tDCS on visual evoked potentials.

Cathodal tDCS reversed P3 ERP amplitude responses over parietal cortex in response to global and local cues. The P3 ERP component has been linked to visual feature identification and discrimination in several studies, including studies of global/local attentional switching and feature processing [8, 24]. There is a substantial body of evidence that tDCS can effectively alter perceptual discrimination in several modalities. For example, it has been demonstrated that cathodal tDCS can detrimentally

affect the discrimination of sound pitch [4], tactile discrimination [25], and can enhance visual motion discrimination [26]. Here, it is shown that tDCS alters discrimination of target cues necessary for downstream feature processing of global/local compound letters. This effect may be reflected in the observed alteration of the P3 response. If so, this would be the first evidence that tDCS directly alters an electrophysiological marker important for perceptual discrimination in a behaviorally relevant task. Late-latency alterations in cortical responses may be a predominant feature of DC stimulation's effects on perceptual discrimination and bears investigation in future tDCS studies.

P1 and P3 component differences were accompanied by a left hemispheric effect of cathodal stimulation on oscillatory activity in the beta frequency range. It was observed that 13 to 30 Hz frequencies were reduced in response to global cue stimuli over the area covered by the tDCS electrode. Beta frequency increases have been shown to play an important role in attention, particularly when coupled with gamma frequency increases [27]. It has been hypothesized that beta activity shifts cortical systems to an attentional state that permits gamma synchronization. Although gamma frequency changes were not observed in the present study, the reduced power of beta frequencies following cathodal stimulation might contribute to the deficits observed in cued attentional shifts.

Reductions of beta frequency following tDCS have been observed previously [12, 15]. In one study, cathodal stimulation reduced beta and gamma frequencies elicited while subjects viewed sinusoidal luminance gratings [12]. The present study showed a complex pattern of beta frequency changes across cortical hemispheres and in response to different attentional cues. This finding suggests that cathodal tDCS may elicit different

patterns of oscillatory activity depending on the nature of the tasks involved or on the dynamics of the cortical areas affected.

It should be noted that cathodal tDCS acutely affected performance during stimulation and that this effect was no longer significant following stimulation when significant ERP and oscillatory differences were observed. The necessity for accurate placement of the tDCS electrode and the EEG electrodes over left PPC prevented simultaneous tDCS administration and EEG recording. Therefore, it is possible that the behavioral and physiological effects observed were unrelated. However, this seems unlikely. The electrophysiological effects of tDCS reported in other studies are present both during and after stimulation [11, 12, 15]. Additionally, differences in EEG measures following tDCS that can last up to 20 minutes after stimulation, while after-effects on task performances usually diminish shortly after stimulation [for examples, see refs 3 & 26]. It seems reasonable to conclude that the tDCS induced physiological alterations detected immediately following stimulation were present during tDCS and that these changes contributed to the significantly diminished behavioral performances observed.

The behavioral and electrophysiological results indicate that anodal and cathodal tDCS have differential effects on attentional switching. Anodal tDCS had a weaker effect that selectively targeted global cued attentional switching while cathodal stimulation had a stronger effect on cued switching across global and local trials. Further, the altered electrophysiological responses following cathodal stimulation were not observed following the anodal condition. Previous reports have noted weaker anodal effects on visual evoked potentials when compared to cathodal tDCS [11]. It has also been observed

that reductions in cortical excitability are easier to induce than increases in animals *in vivo* [28]. It has been suggested that the visual system is already optimally tuned, such that increases in excitability following anodal stimulation have minimal effects on perception [11]. A similar effect may be occurring here. Putatively, cortical hemispheric asymmetries exist in global and local processing: local feature processing is dominated by left hemisphere regions, while global features predominantly engage the right hemisphere [29, 30]. These asymmetries may also extend to global/local attentional shifts [8]. Given this asymmetry, it may be that the left hemisphere is optimally tuned for local feature processing but suboptimal for global processing. Therefore, global cued switching may be susceptible to the effects of left hemisphere anodal stimulation while local switching is not.

One limitation of the current study was the paucity of EEG data used in the analyses. Because of the infrequency of the global and local switch cues (presented every four to eight trials) and the transitory after-effects of tDCS, only 14 to 16 switch cues of each type were available from each run of the global/local task. Once trials were rejected due to artifacts, such as subject blinks or channel noise, the amount of viable EEG data was further limited. Such a deficit may be amended in future research by selecting a more suitable method of data acquisition, such as magnetoencephalography (MEG). MEG data generally possesses a greater signal-to-noise ratio than EEG [31], and there exist sophisticated tools for MEG artifact rejection. This modality may also permit simultaneous DC stimulation and acquisition of electrophysiological data. More data of better quality could be collected, which would permit other types of analyses such as

current source modeling or analyses of phase relationships within and across oscillatory frequencies.

Another potential issue concerns differences between behavioral and EEG analyses. In examining the behavioral effects of tDCS on global/local switch, responses to compound stimuli immediately following a switch cue were analyzed, while EEG analyses focused on responses to the switch cues themselves. It was argued that parietal DC stimulation modulates preparatory control mechanisms, which justifies the assessment of electrophysiological responses to cue stimuli, and such analyses are consistent with other studies examining cued attentional switch [e.g. 7, 8]. However, it was impossible to behaviorally monitor preparatory control in itself. This raises the possibility that the behavioral effects observed confounded preparatory control and feature processing. Although attentional shift was measured indirectly in the behavioral analyses, there were differences between compound stimuli responses occurring after target cue presentations and responses to stimuli that did not follow a target cue. These findings, coupled with the significant alterations detected in the EEG analyses, suggests that processing of the target cues themselves was at least partially compromised. Comparisons with future tDCS studies, designed to modulate bottom-up or stimulus driven shifts in global/local attention, may elucidate the extent to which the present design specifically altered preparatory control.

There is evidence from the present study that tDCS might induce changes throughout a visual attentional network. For example, significant changes were detected in P1 amplitudes over occipital areas that were not directly stimulated. This study did not include an investigation of potential ERP sources. However, additional research, using

sensitive electrophysiological measures collected in conjunction with DC stimulation, might permit an examination of the brain sources affected by tDCS and reveal the contributions made by different areas in the preparatory control network.

Although subjects were not informed which stimulation condition they received during each session, it should be noted that at the completion of all sessions most subjects were able to identify when they had received stimulation and when they had received sham. Such a finding is rarely reported in the tDCS literature, but it has implications for future designs [32]. Attempts were made to maintain the blind study condition, such as modifying the dimensions and placement of the reference tDCS electrode, but it seemed clear that any stimulation over 1.5 mA was consciously perceptible by most subjects (12 out of 15). The extent to which subject awareness contributed to the present findings is unknown. However, subjects were unable to discriminate between the anodal and cathodal conditions, and these conditions produced differential results. Additionally, preliminary research, where tDCS was applied at a lower and undetectable amperage (1.5 mA), produced similar deficits in attentional switch [unpublished pilot data]. Therefore, it seems conceivable that the differences observed in the current study were primarily the result of tDCS rather than the result of potential placebo effects. Future tDCS research might explore various amperage and electrode configurations to obtain the optimal parameters for minimizing subject awareness while preserving stimulatory effects.

Results from this study indicate that parietal tDCS can significantly affect behavioral and electrophysiological responses to cued attentional shifts while preserving global/local feature processing. As has already been mentioned, cued attentional switching and feature processing may be subserved by distinct cortical networks in

global/local paradigms [7, 23]. An interesting question is whether tDCS, applied over other areas such as the temporal-parietal junction, would alter global/local feature processing while leaving cued attentional shift undisturbed. Another interesting issue is the extent to which preparatory control and global/ local feature processing occur in distinct or over-lapping cortical networks. Future studies, aimed at manipulating different aspects of global/local attention with tDCS and monitoring the subsequent electrophysiological changes, may be able to parse the distinct and complex processes that underlie these phenomena.

CONCLUSION

This is the first report of significant modulation of global/local attentional switch resulting from DC stimulation. It was observed that anodal and cathodal stimulation of left parietal cortex led to deficits in the ability to shift attention between the global and local features of compound stimuli. This effect was accompanied by significant alterations in evoked and oscillatory cortical responses following cathodal stimulation, suggesting that the effects of tDCS on perceptual performance are mediated by directly observable changes in cortical activity.

These results support a functional role of left parietal cortex in global/local attentional shifts and underscore the efficacy of tDCS as a tool for exploring neurocognitive function at both the behavioral and physiological levels.

FIGURES

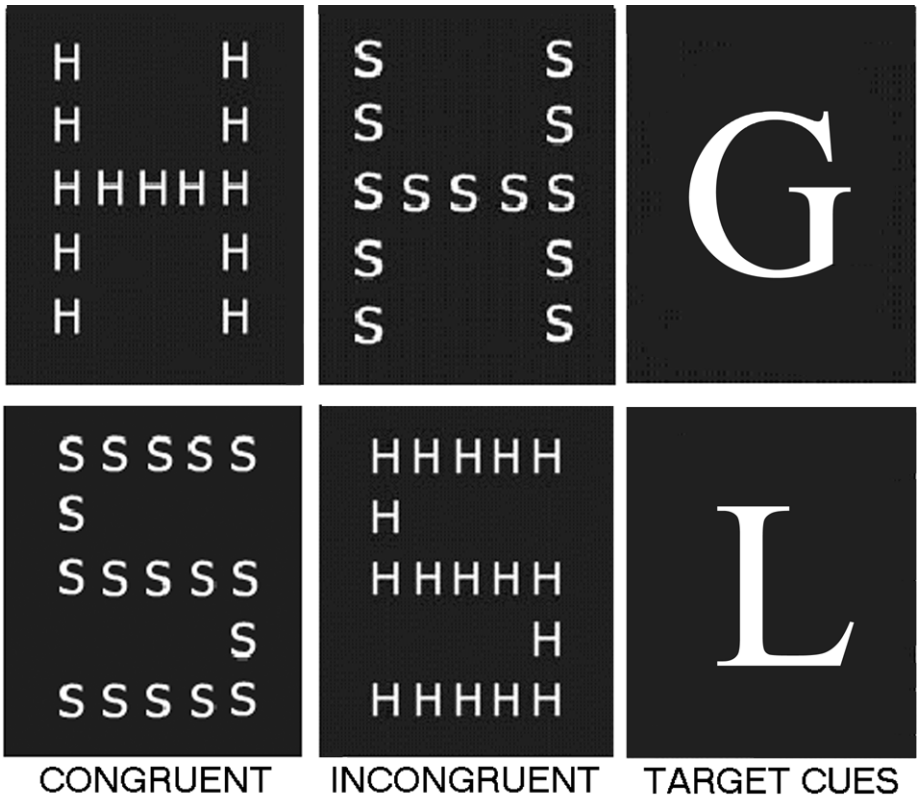

Figure 1. **Examples of compound letter and target cue stimuli.**

PRACTICE RUNS	EEG SETUP	PRE-STIMULATION (PRE) RUN| EEG	TDCS | RUN (DURING) @ 14 MIN OF STIM	POST-STIMULATION (POST0) RUN| EEG	REST	POST-STIMULATION (POST20) RUN| EEG
10 minutes	~ 40 min	5 min	20 min | (During 5 min)	5 min	15 min	5 min

EXPERIMENTAL SESSION

Figure 2. **Experimental procedure. During each session, subjects were given two practice runs of the global/ local task, prepared for EEG recording, and given a pre-stimulation run of the task. TDCS (or sham) was administered for 20 minutes and another run of the global/local task was given after 14 minutes (during stimulation). Two post-stimulation runs were given, separated by 15 minutes of rest. EEG activity was recorded during the pre-stimulation and two post-stimulation runs. Each subject completed three experimental sessions (one anodal session, one cathodal session, and one sham session). Sessions were separated by four days.**

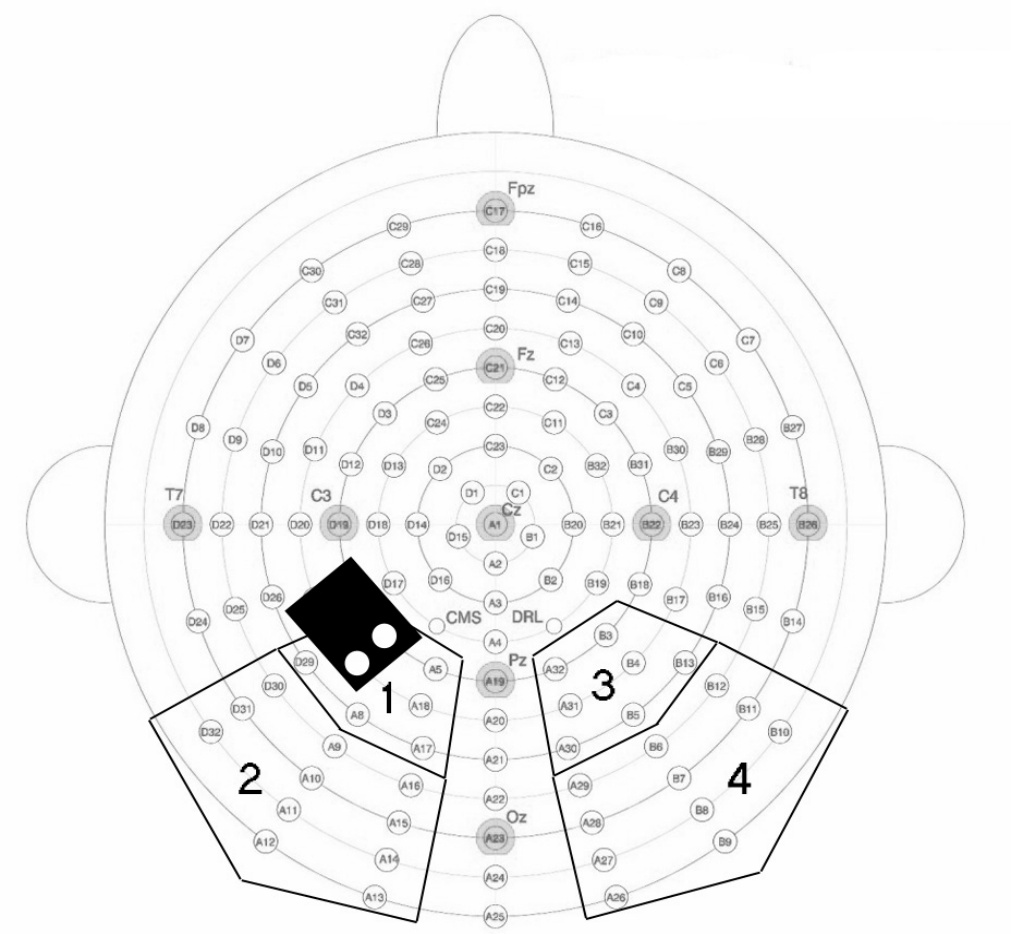

Figure 3. **Posterior scalp regions used for ERP and frequency analyses. Regions 1 and 3 represent left and right parietal electrodes used in analysis. Regions 2 and 4 represent left and right occipital electrodes. Black rectangle represents placement of tDCS stimulating electrode.**

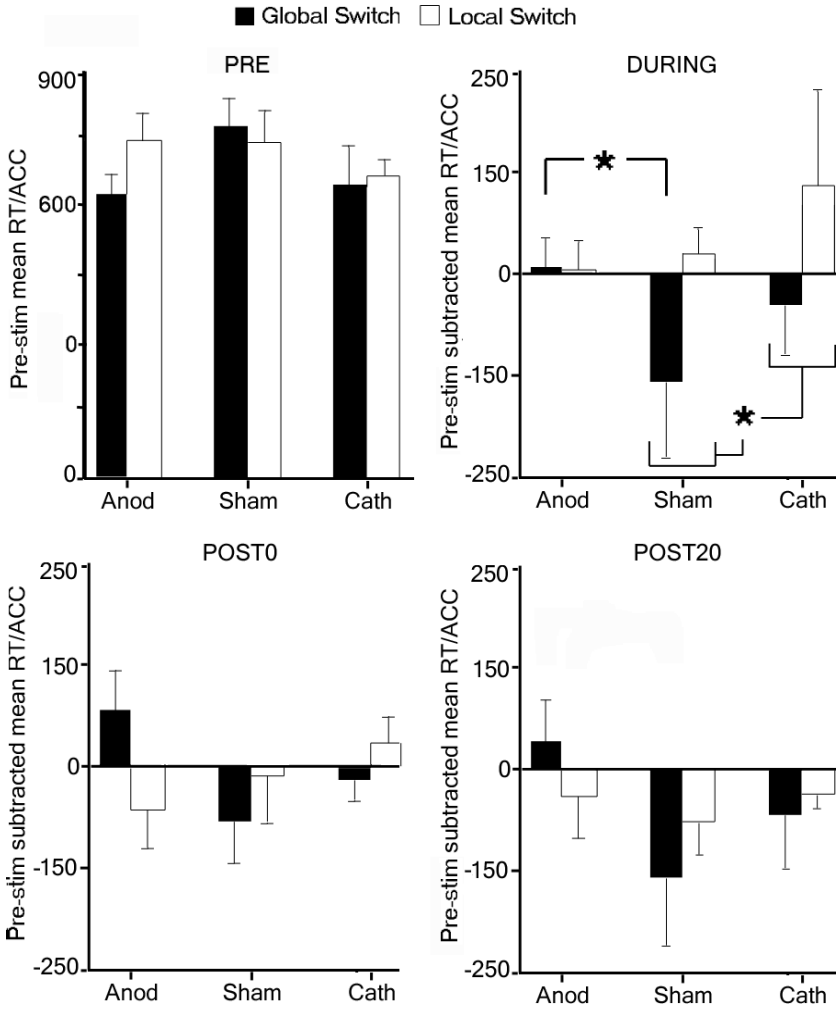

Figure 4. **Cued global/local switch responses across tDCS conditions. Mean RT/ACC = mean reaction time in millisecond divided by proportion correct. (Top Left) Mean pre-stimulation responses to global and local switch cues. Differences between pre-stimulation conditions were not significant. (Top Right) Switch responses during stimulation (minus pre-stimulation responses). Cathodal stimulation degraded target switching. Anodal stimulation significantly degraded global switch. (Bottom Left) Switch responses immediately after stimulation (minus pre-stim). (Bottom Right) Switch responses 20min after stimulation (minus pre-stim). Anodal stimulation marginally degraded global switch (p = 0.026).**
*P < 0.025, significant differences between tDCS and sham conditions.

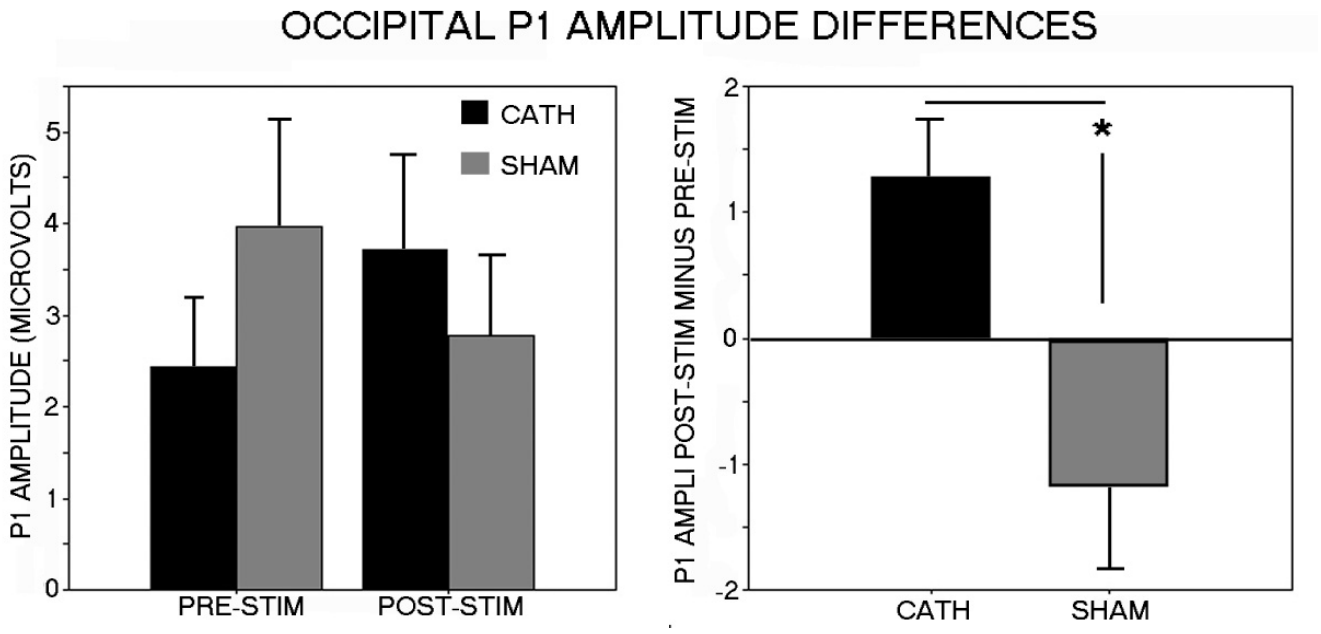

Figure 5. **Occipital P1 amplitude comparisons between cathodal and sham stimulation. (Left) Pre-stimulation and post-stimulation comparisons. (Right) Post-stimulation P1responses (minus pre-stimulation). Cathodal tDCS significantly increased P1 amplitude following stimulation compared to sham.**
* P = 0.024.

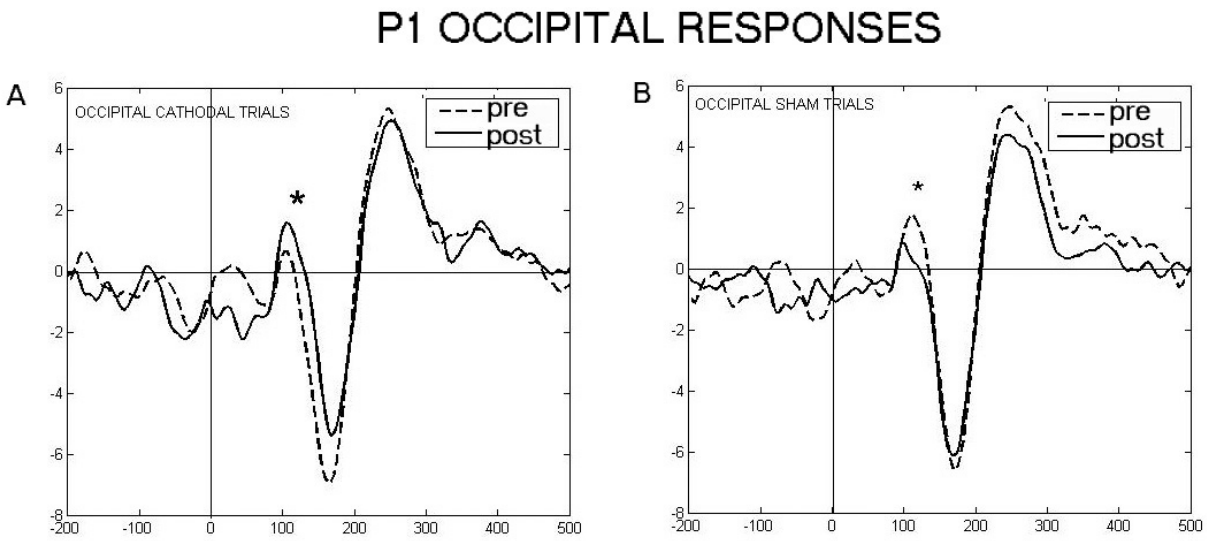

Figure 6. **Grand Averaged occipital ERP waveform comparisons. Graphs represent responses in occipital electrodes collapsed across hemispheres and target cue types. A) Cathodal pre-stimulation vs. post-stimulation comparisons. B) Sham pre-stimulation vs. post-stimulation comparisons. Asterisks indicate pre-stimulation vs. post-stimulation differences in P1 responses. Note that average amplitudes expressed in the graphs differ from those reported in the results and Fig. 5, because the peak amplitudes were computed separately for each subject in each condition and then averaged to perform the statistical analyses. However, the directions of significant effects in the P1 amplitudes are still visible in the figure.**

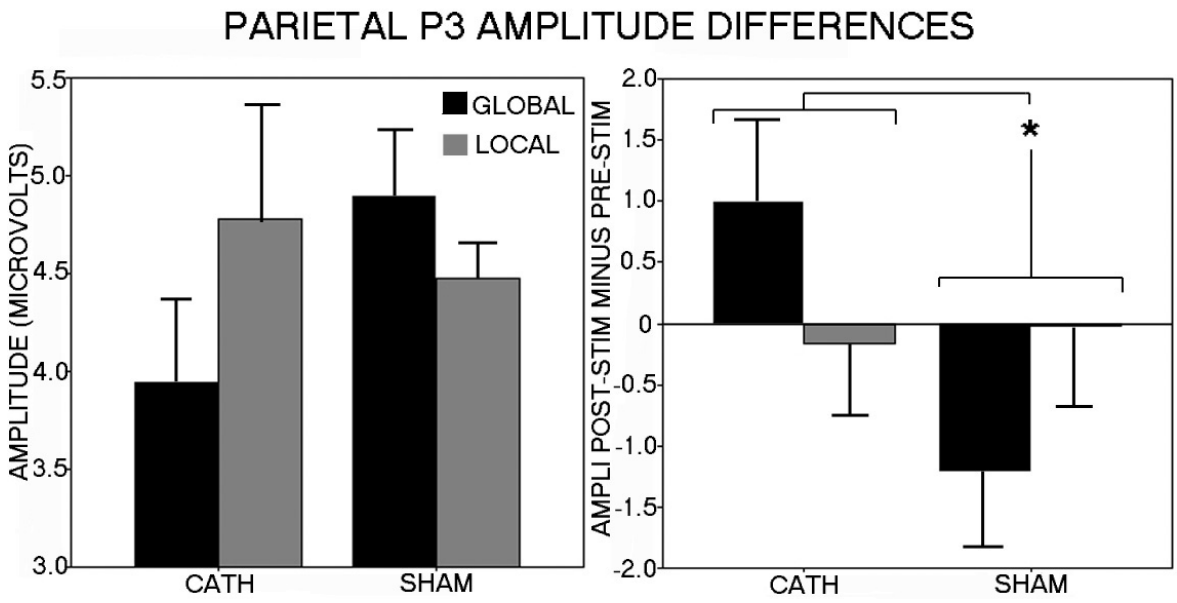

Figure 7. **Parietal P3 responses to global and local target cues in sham and cathodal conditions. (Left) Pre-stimulation P3 amplitudes for global and local cues. Pre-stimulation differences were not significant. (Right) Post-stimulation (minus pre-stimulation) P3 amplitude changes in response to global and local cues. Global/ local differences were significantly different between cathodal and sham conditions.**
*P = 0.023.

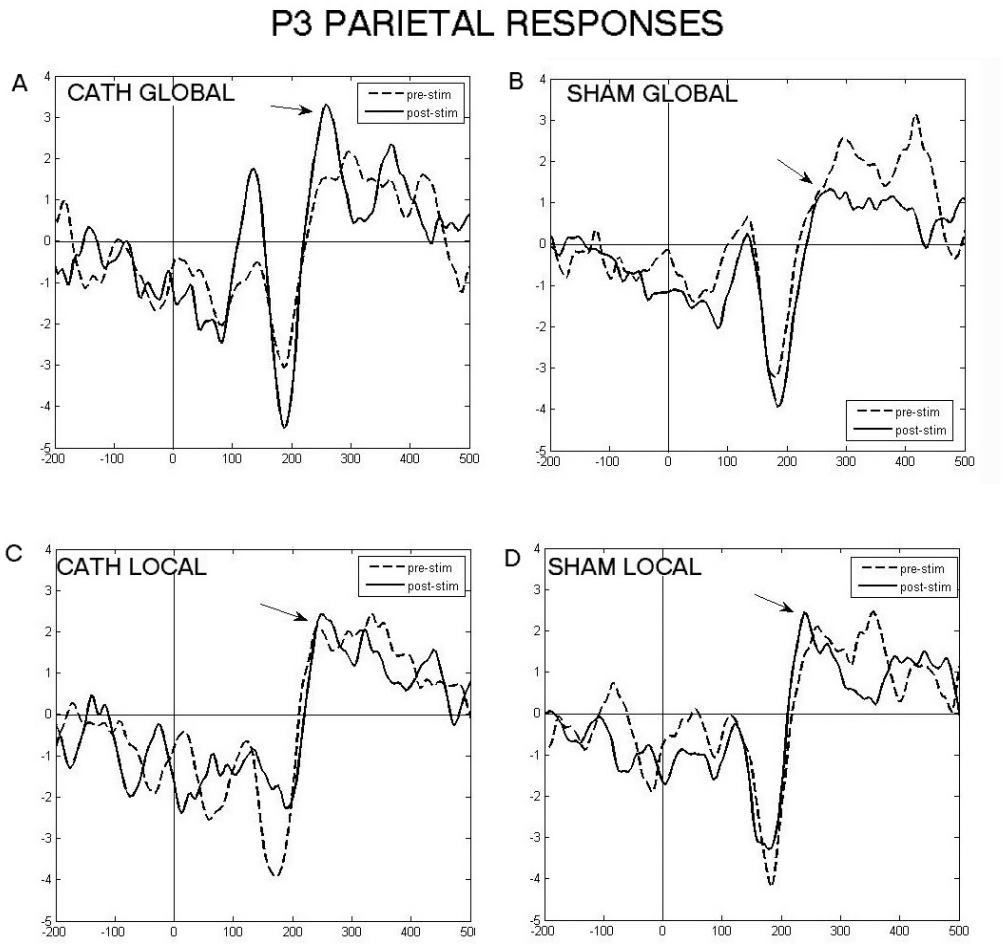

Figure 8. **Grand average parietal ERP waveform comparisons. Pre-stimulation vs. post-stimulation comparisons for cathodal and sham global and local responses. A) Cathodal parietal ERP responses to global cues. B) Sham parietal ERP responses to global cues. C) Cathodal parietal ERP responses to local cues. D) Sham parietal ERP responses to local cues. Arrows point to post-stimulation peak P3 amplitudes. Note the increased P3 response to global cues following cathodal stimulation (A). Waveforms show directions of significant effects reported in Figure 7.**

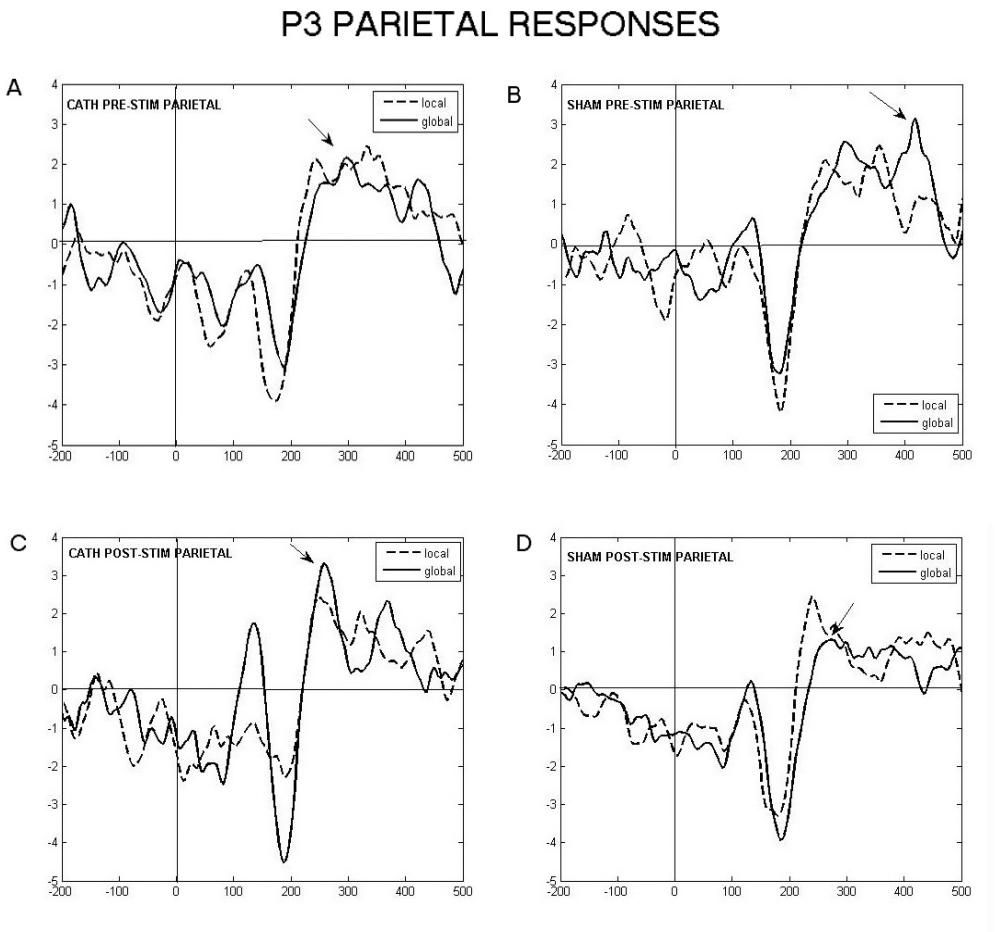

Figure 9. **Grand average parietal ERP waveform comparisons. Global vs. local comparisons before and after cathodal and sham tDCS. A) Cathodal parietal ERP responses before tDCS. B) Sham parietal ERP responses before tDCS. C) Cathodal parietal ERP responses following tDCS. D) Sham parietal ERP responses following tDCS. Arrows point to peak P3 amplitudes in response to global cues. Waveforms are equivalent to those presented in Fig. 8 but directly contrast global vs. local responses. Compare to Figures 7 and 8.**

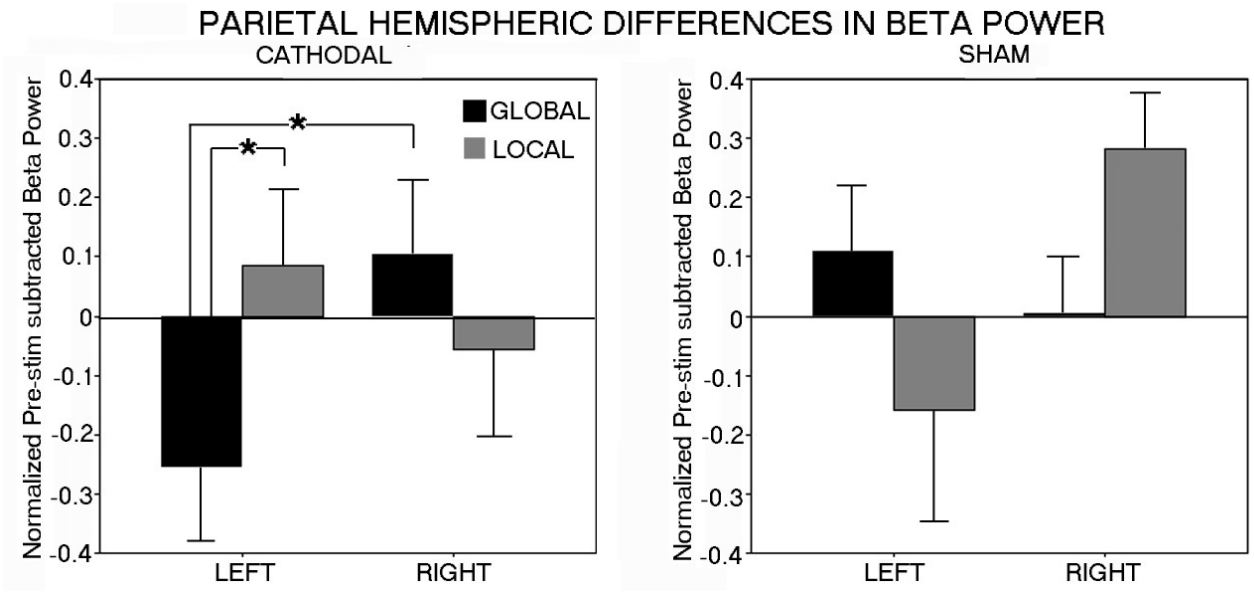

Figure 10. **Parietal hemispheric changes in normalized average beta frequency (13 to 30 Hz) from 50 to 350 ms after presentation of global and local switch cues following sham and cathodal stimulation. (Left) Cathodal left and right hemisphere comparisons between global and local stimuli. Left hemisphere beta frequency responses to global cues were significantly reduced following stimulation compared to left hemisphere local responses and right hemisphere global responses. (Right) Changes in average beta frequency following the sham condition. Left hemisphere global/local responses were marginally significantly different between the cathodal and sham conditions (p = 0.051).**
*P < 0.025.

APPENDIX A-1

ANALYSIS	N	Pearson Correlation (r)	p-value
P1 ampli + Beh DV (all conditions)	64	-0.036	0.78
P1 ampli + Beh DV (global trials only)	32	0.095	0.60
P1 ampli + Beh DV (local trials only)	32	-0.185	0.31
P1 ampli (Left Hemisphere) + Beh DV	64	-0.042	0.74
P1 ampli (right Hemisphere) + Beh DV	64	-0.026	0.84
P1 ampli + Beh DV (pre-stim trials only)	32	-0.095	0.61
P1 ampli + Beh DV (post-stim trials only)	32	0.024	0.90
P1 ampli + Beh DV (post-stim - pre-stim)	32	-0.176	0.34
P1 ampli + Beh DV (cathodal trials only)	32	-0.113	0.54
P1 ampli + Beh DV (sham trials only)	32	0.020	0.91
P3 ampli + Beh DV (all conditions)	64	0.016	0.90
P3 ampli + Beh DV (global trials only)	32	0.147	0.42
P3 ampli + Beh DV (local trials only)	32	-0.183	0.32
P3 ampli + Beh DV (global - local)	32	-0.184	0.31
P3 ampli + Beh DV (Cath global only)	16	0.196	0.47
P3 ampli + Beh DV (Cath global - Cath local)	16	-0.340	0.20
P3 ampli + Beh DV (Sham global - Sham local)	16	0.060	0.83
P3 ampli + Beh DV (pre-stim trials only)	32	0.133	0.47
P3 ampli + Beh DV (post-stim trials only)	32	-0.090	0.62
P1 ampli + Beh DV (post-stim - pre-stim)	32	0.135	0.46
P1 ampli + Beh DV (global post-stim - global pre-stim)	16	0.200	0.46
P1 ampli + Beh DV (local post-stim - local pre-stim)	16	0.066	0.81

Figure A-1. **Exploratory correlations between behavioral and ERP measures.**

Correlations were made between the P1 or the P3 amplitudes (in μV) and behavioral responses (in RT/ prop. correct) at several different levels and factors. Amplitudes are in response to target cues and behavioral measures are in response to compound letter stimuli immediately following a target cue (switch trials). All responses are from the pre-stimulation (Pre) and post-stimulation (Post0) task runs. All correlations were made for the combined sham and cathodal conditions unless otherwise specified. None of the tested correlations reached significance.

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