The effects of tDCS across the Spatial Frequencies and Orientations that comprise the Contrast Sensitivity Function

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Abstract

Transcranial Direct Current Stimulation (tDCS) has recently been employed in traditional psychophysical paradigms in an effort to measure direct manipulations on spatial frequency channel operations in the early visual system. However, the effects of tDCS on contrast sensitivity have only been measured at a single spatial frequency and orientation. Since contrast sensitivity is known to depend on spatial frequency and orientation, we ask how the effects of anodal and cathodal tDCS may vary according to these dimensions. We measured contrast sensitivity with sinusoidal gratings at four different spatial frequencies (0.5, 4, 8, and 12 cycles/°), two orientations (45° Oblique and Horizontal), and for two stimulus size conditions [fixed size (3 degrees) and fixed period (1.5 cycles)]. Only contrast sensitivity measured with a 45° oblique grating with a spatial frequency of 8 cycles/° (period = 1.5 cycles) demonstrated clear polarity specific effects of tDCS, whereby cathodal tDCS increased and anodal tDCS decreased contrast sensitivity. Overall, effects of tDCS were largest for oblique stimuli presented at high spatial frequencies (i.e., 8 and 12 cycles/°), and were small or absent at lower spatial frequencies, other orientations and stimulus size. Thus, the impact of tDCS on contrast sensitivity, and therefore on spatial frequency channel operations, is opposite in direction to other behavioral effects of tDCS, and only measurable in stimuli that generally elicit lower contrast sensitivity (e.g., oblique gratings with period of 1.5 cycles at spatial frequencies above the peak of the CSF).

239 words

Neuro-stimulation techniques have recently been combined with traditional psychophysical paradigms in an effort to obtain a measure of direct manipulation on spatial frequency channel operations in the early visual system (review: Antal, Nitsche, & Paulus, 2006). One technique that is gaining popularity due to its affordability and simplicity is transcranial Direct Current Stimulation (tDCS), a non-invasive brain stimulation technique that transiently modulates excitation and inhibition in the human brain via alterations in the membrane potential of neurons (Antal, Nitsche, & Paulus, 2001; Antal et al., 2006; Nitsche et al., 2008; Stagg & Nitsche, 2011; Stagg et al., 2009). The technique involves a stimulating device that delivers a mild direct current (DC) between two electrodes (anode and cathode) placed on the scalp of an observer, which creates a resistive DC circuit that induces a mild intra-cerebral electrical current from the anode where current enters cortex, to the cathode where current exits the cortex. The direction of current flow determines the effect of tDCS. Specifically, anodal stimulation (a-tDCS) generates a sub-threshold depolarization, while cathodal (c-tDCS) stimulation hyperpolarizes the membrane potential of neurons (Paulus, 2011; Pellicciari et al., 2013; Radman et al., 2009; Rahman et al., 2013; Reato et al., 2010; Stagg and Nitsche, 2011). Polarity specific behavioral effects of tDCS are well established in motor cortex (e.g., Jacobson et al., 2012). However, in primary visual cortex, it is typical to find either facilitatory or inhibitory effects due to a-tDCS or c-tDCS, but not both. Also, the polarity specific facilitation and inhibitory effects of tDCS may be opposite to those reported in motor cortex (Accornero et al., 2007; Antal et al., 2001; Chaieb et al., 2008; Lang et al., 2007; Peters et al., 2013; Pirulli et al., 2014; Spiegel et al., 2012). Part of the variability in tDCS effects for different cortical loci can be attributed to structural (e.g., cell type and morphology and the direction of current flow in relation to the somatodendritic axis), or functional differences between stimulated areas (Bikson et al., 2013; Radman et al., 2009; Reato et al., 2010; Rushton, 1927; Shipp, 2005; Ward and Weiskrantz, 1969). Given that the visual cortex is both structurally and functionally different from motor cortex, it should come as no surprise that the effects of tDCS over the visual cortex are less clear.

The application of a-tDCS over primary visual cortex has been shown to enhance contrast sensitivity in amblyopic persons (Spiegel et al., 2013) at spatial frequencies above the peak of the contrast sensitivity function (CSF) and near the peak of the CSF (Kraft et al, 2010) while inhibitory effects of c-tDCS (Antal et al., 2001; Chaieb et al., 2008) on contrast sensitivity have been found for spatial frequencies above the peak of the CSF. However, all previous studies of tDCS on contrast sensitivity presented a single spatial frequency to observers, and thus, the effect of tDCS on the shape of the contrast sensitivity function (Campbell et al., 1966; Graham, 1989; Peli et al., 1993), which involves multiple spatial frequencies, is currently unknown [1]. Furthermore, the influence

[1] The contrast sensitivity function is an index of sensitivity to contrast across multiple spatial frequencies, but previous studies that have used contrast sensitivity as a dependent measure of tDCS have restricted their stimulus to a single spatial frequency, orientation, and size. This can alter contrast sensitivity and thus alter tDCS effects. For example, CSFs measured with full-field gratings (well localized in Fourier space) generally have narrower bandpass shape and peak at a higher spatial frequency (~4 cycles/°) than CSFs measured with gratings localized both in spatial frequency and space (i.e., Gabors), which peak at about 1 cycle/° (Peli et al., 1993). Similarly, CSFs measured with cardinally oriented gratings have higher contrast sensitivity values at spatial frequencies above the peak of the CSF than when measured with obliquely oriented gratings (Campbell et al., 1966).

of stimulus orientation on tDCS induced changes in contrast sensitivity has not been investigated.

The goal of the current study was to assess how the effects of tDCS vary according to the stimulus dimensions (spatial frequency and orientation) used to measure contrast sensitivity. Given the known functional organization of the early visual system, and the properties of the DC circuit generated by tDCS, certain predictions as to the interaction of tDCS and stimulus dimension can be made. First, the effects of tDCS on contrast sensitivity should be greatest at higher spatial frequencies, and diminish with decreasing spatial frequency. This is because tDCS exerts its greatest effect at cortical sites closet to the skull (Miranda et al., 2006, 2013; Rahman et al., 2013) and V1 neurons at the occipital pole (close to the skull) have higher preferred spatial frequencies than those located deeper within the calcarine sulcus (Engel et al., 1997; Foster et al., 1985; Henriksson et al., 2008; Horton, 2006; Tootell et al., 1981, 1988; De Valois et al., 1982; Yu et al., 2010). Cells further from the occipital pole have receptive fields located peripherally in the visual field, which means that stimuli presented further than 2° eccentricity from fovea may not be affected as strongly by tDCS than stimuli presented in the central visual field (Kraft et al., 2010; but see Costa et al., 2015 for a contrasting view). Stimulus orientation may also influence the effect of tDCS on contrast sensitivity. Contrast sensitivity to oblique gratings is lower than that to horizontal gratings (the "Oblique Effect"; Appelle, 1972; Essock, 1980; Campbell et al., 1966). Therefore, contrast sensitivity to oblique gratings may be more susceptible to the facilitatory effects of a-tDCS whereas horizontal gratings may be more susceptible to the inhibitory effects of c-tDCS. This, in essence, should decrease the magnitude of the “Oblique Effect”. Thus, we measured changes in contrast sensitivity from a non-stimulation baseline under both a-tDCS and c-tDCS to gratings of four different spatial frequencies that spanned the contrast sensitivity function (0.5, 4, 8, and 12 cycles/°) and two stimulus orientations (45° oblique or Horizontal).

Method

Participants

Twenty-six undergraduate students participated at baseline, out of which 20 continued onto the tDCS portion of this study. All observers but two were naïve to the goals of the experiment. Observers were prevented from moving onto the tDCS sessions when their contrast detection thresholds measured just prior to the application of tDCS exceeded 2 standard deviations of their average thresholds measured at baseline. Participants that continued onto the tDCS sessions were separated into two groups; 10 (N_{female} = 7, M_{age} = 20.2) participants were presented with oblique gratings while the other 10 (N_{female} = 5, M_{age} = 20.5) saw horizontal gratings. Two of the participants in the oblique orientation group completed the experiment at Concordia University (Montreal, Quebec, Canada), while data for all other participants in this study were collected at Colgate University (Hamilton, New York, USA). All participants had normal, or corrected-to-normal visual acuity (Snellen cutoff = 20/25) and no astigmatism. Written informed consent was obtained from all participants and all were treated in accordance to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans

(Medical Research Council of Canada, 2003) and the ethical standards of the Federal Code of Regulations Title 45 (Public Welfare) and Department of Health and Humans Services, Part 46 (Protection of Human Subjects). All participants were compensated financially for their time.

Apparatus

All stimuli were presented on 22.5" Viewsonic (G225fB) monitors driven by a dual core Intel® Xeon® processor (1.60GHz x2) equipped with 4GB RAM and a 256MB PCIe x16 ATI FireGL V7200 dual DVI/VGA graphics card with 8-bit grayscale resolution at Colgate University and an Apple Mac Pro (2 X 2.66GHz processor) equipped with 8GB of RAM and a 1GB PCIe x16 ATI Radeon HD 5770 Graphics card with 8-bit grayscale resolution. The color management settings for the graphics card (i.e., 3D display settings) were adjusted such that the luminance "gain" of the green gun was twice that of the red gun, which was set to twice that of the blue gun. A bit-stealing algorithm (Bex et al., 2007; Tyler, 1997) was employed to yield 10.8 bits of luminance (i.e., grayscale) resolution (i.e., 1785 unique levels) distributed evenly across a 0-255 scale. Stimuli were displayed using a linearized look-up table, generated by calibrating with a Color-Vision Spyder3 Pro sensor. Maximum luminance output of both display monitors was 100 cd/m^2 (50 cd/m^2 mean luminance after calibration). The frame refresh rate was set to 85 Hz (100 Hz at Concordia), and the resolution was set to 1600 x 1200 pixels (1024 X 768 pixels at Concordia). Single pixels subtended .0134° (.0381° at Concordia) of visual angle, i.e., 0.80 arc min. (2.28 arc min. at Concordia) as viewed from 1.0 meter. Head position was maintained with a chin rest. Participants viewed the display monitor from 2 meters in a dark room through an aperture (16° of visual angle in diameter) of a large black circular mask that was fit to the monitor bezel in order to obscure any monitor or room orientation cues.

Transcranial Direct Current was generated with a 9V battery driven direct current stimulator (Chattanooga Ionto, USA) and delivered via a pair of carbon-rubber electrodes (The Magstim Company Ltd., UK). The electrodes were encased in potassium chloride soaked Spontex sponge pockets (The Magstim Company Ltd., UK). The size of the stimulating electrode was 6 × 8 cm, and the size of the reference electrode was 12 × 8 cm. The larger size of the reference electrode renders it inert due to low current density (Nitsche et al., 2007; Spiegel et al., 2012). Both electrodes were held in place with four Magstim rubber headbands (The Magstim Company Ltd., UK), applied in a manner that maximized complete electrode sponge surface contact over the targeted scalp regions.

Stimuli

Stimuli consisted of foveally presented sinusoidal gratings generated at one of two orientations: either oblique (45°) or horizontal (90°). All gratings were windowed by a 2D Gaussian, which ramped down the contrast to mean luminance. Stimulus spatial frequency was 0.5, 4, 8, or 12 cycles/°, with a period of 1.5 cycles (fixed period condition). The electrical field generated by tDCS is prominently focused onto the surface of the visual cortex, which limits the spatial extent of the visual field modulated

196 by tDCS to the central 1-2° of the visual field (Kraft et al., 2010)[2]. As the effects of tDCS
197 change as both a function of spatial frequency and stimulus area, we added a second
198 stimulus condition and measured contrast sensitivity with a fixed stimulus size (3°), and
199 adjusted the period of the stimulus with spatial frequency (fixed stimulus size condition).
200 All stimuli were surrounded by a low contrast ring (Michelson Contrast = 10%) 1 pixel in
201 size, 0.78° away from the border of the grating, and paired with a low frequency tone;
202 both served to minimize participant doubt as to the location and/or presence of the
203 stimulus on the screen. Stimulus contrast was expressed as Michelson contrast =
204 $[(\boldsymbol{L_{max}} - \boldsymbol{L_{min}})/(\boldsymbol{L_{max}} + \boldsymbol{L_{min}})]$ scaled to have zero mean and then normalized to 1.0.
205
206 **Psychophysical Procedure**
207
208 The within-subject stimulus conditions for this experiment consisted of four
209 spatial frequencies (0.5, 4, 8, and 12 cycles/°), and two period conditions (fixed period
210 and fixed size). Observers were grouped according to the stimulus orientation (45°
211 oblique or horizontal). The psychophysical procedure for both the training and test phases
212 were identical. The stimulus presentation consisted of a 2-Interval Force Choice (2-IFC)
213 procedure where participants had to indicate the interval, either the first or the second,
214 which contained the target. Target contrast was controlled by a 2-up, 1-down staircase
215 setup and controlled by the *PAL_AMUD_setupUD* and the *PAL_AMUD_updateUD*
216 functions from the Palamedes toolbox for MATLAB (Kingdom and Prins, 2010; Prins
217 and Kingdom, 2009). Threshold was approached from above with a target contrast step
218 size of 0.05% Michelson contrast. Each staircase ran until 12 reversals were observed and
219 the averaged target contrast value of the last 5 reversals was used as an estimate of target
220 contrast threshold (70.71% correct on the psychometric function).
221
222 All staircases completed by observers began with an instruction screen that
223 informed them of the spatial frequency and size condition of the stimulus (orientation
224 never changed within observers). Each trial began with a black fixation dot (0.1°)
225 presented at the center of the screen. The fixation dot served both to remind the observer
226 a stimulus will appear shortly and the location of said stimulus. The fixation screen
227 (300ms) was followed by a blank screen (150ms) set to mean luminance, followed by the
228 first stimulus interval (onset followed a square-wave function) presented for 150ms. This
229 sequence was repeated for the second stimulus interval (see **Figure 1**). One interval
230 contained the stimulus, surrounded by a low-contrast ring, while the other interval
231 contained only a low-contrast ring. Participants indicated, via keyboard press, the interval
232 that they believed contained the target. The duration of the response interval was
233 unlimited, and participants received no feedback on their accuracy.
234
235 FIGURE 1
236
237 Each spatial frequency by stimulus size block was repeated 10 times by observers
238 in the baseline portion of the study (total of 80 staircase blocks), which approximately
239 took 5 hours to complete over multiple one-hour sessions completed on different days

[2]We note that these results stem from a single study, which has yet to have been replicated.

(approximately five sessions over two weeks). All staircase blocks were randomly interleaved for each observer, and only the final 8 stimulus blocks were stored for data analysis. The contrast sensitivity of observers across each sequential measurement for all spatial frequency and stimulus size conditions is shown in **Figure A1** (see **Supplemental Material A**), separated by orientation group. The 20 observers (10 per orientation group) that continued onto the tDCS portion of this study showed no statistically significant increment or decrement in contrast sensitivity across the final 8 stimulus blocks completed during baseline (the slope of the line of best fit across all 8 stimulus blocks was not statistically different from 0, all *p*s > .05). This is consistent with other studies that have shown either small (Li, Polat, Makous, & Bavelier, 2009; Sowden, Rose, & Davies, 2002), or no change in the CSF over sequential measurements in healthy adults (Adini et al., 2002, 2004; Dorais and Sagi, 1997; Maehara and Goryo, 2007).

tDCS Procedure

Transcranial Direct Current Stimulation is known to be a safe neuro-stimulation technique with no long lasting negative side effects, it is nevertheless important to limit the duration of stimulation to no more than 30-35 minutes (Bikson et al., 2009; Fertonani et al., 2015; Nitsche et al., 2003b; Poreisz et al., 2007; Russo et al., 2013). In order to meet this time restriction, the number of repetitions for each spatial frequency by stimulus size block was set to two. The total number of staircases completed by observers while receiving tDCS was 16 (four spatial frequencies by two stimulus size conditions by two repetitions). Prior to receiving either a-tDCS or c-tDCS, participants completed two staircases for each spatial frequency by stimulus size blocks, which were combined with the 8 stimulus blocks from the baseline portion of this study and used as a pre-stimulation baseline (see **Supplemental Material A, Figure A2**). If contrast detection thresholds exceed their average baseline thresholds by at least two SDs, participants were asked to repeat the pre-stimulation baseline measurements. If thresholds following the repetition remained two SDs away from average thresholds, participants were excused from the study.

Immediately following baseline measurements, participants repeated the 16 staircases while receiving tDCS (time to complete: $M = 21.05$ minutes, $SD = 2.74$). All observers completed two stimulation sessions (anodal and cathodal, counterbalanced across participants) with no less than 48 hours between sessions. As both a-tDCS and c-tDCS have been shown to produce differential effects on contrast detection performance (see Antal et al., 2001; Jacobson et al., 2012; Spiegel et al., 2012; Kraft et al., 2010), we used both stimulation conditions to serve as a control of the other. Specifically, we prioritize any relative effects whereby tDCS polarity differentially modulated contrast sensitivity for a particular stimulus dimension within our observers. This allowed us to avoid certain confounds that have been associated with sham in neurostimulation designs (for review: Duecker & Sack, 2015). Specifically, while observers are typically unable to differentiate between a-tDCS and c-tDCS, they have been shown to easily detect the sham condition, which may alter their response pattern and thus, serves as a poor control for neurostimulation (Kessler et al., 2012; Minhas et al., 2011; O'Connell et al., 2012).

Injecting current was set to 2mA, which yielded a stimulation current density of 0.042 mA/cm^2 over primary visual cortex. The stimulation and reference electrode were positioned over Oz and Cz respectively, in accordance with the 10-20 EEG system (Antal et al., 2004a; Chatrian et al., 1985). The current was initially ramped up, over a period of 30 seconds and participants waited for a minute once the current ramped-up so the experimenter could verify comfort levels. When participants completed the 16 staircases, the current was ramped back down to zero over a period of 30 seconds. Once the experimental session was completed, participants completed a post-stimulation checklist to verify for any minor side-effects (Nitsche et al., 2008) – none were reported.

Statistical Analyses

Contrast detection thresholds ($c_{threshold}$) were transformed to dB sensitivity units $\boldsymbol{Contrast\ Sensitivity}_{\boldsymbol{db}} = \mathbf{20log_{10}}(\mathbf{1}/\boldsymbol{c_{threshold}})$ prior to analyses. The first statistical analysis conducted for all stimulus block conditions (stimulus orientation by stimulus period condition), was a 2 (tDCS polarity) × 4 (spatial frequency) repeated measures ANOVA on the difference contrast sensitivity values (stimulation – pre-stimulation), which tested for any spatial frequency dependent or polarity specific effect of tDCS on contrast sensitivity. All statistically significant interactions were followed by simple effect analyses. ANOVA output tables for all analyses are reported in **Supplemental Material B**.

Additionally, this study was designed to serve as a potential reference for future experiments that aim to use contrast sensitivity as a dependent measure of tDCS effects, but direct comparison between studies is complicated when only *p*-values are reported (see Kline, 2004 - Chapter 3 - for an in-depth description of the issues associated with null-hypothesis significance testing and *p*-values). Thus, we report an additional effect size analysis, which measured the magnitude of effects both at the group level (Hedge's g) and at the case level (e.g., Left Tail Ratios). The advantage of effect size measures is that their expected values are independent of sample size and thus they simplify the interpretation of results (particularly in regards to comparisons with other studies) and promote replication. The magnitude of an effect size should be interpreted in context to the relevant literature (Cohen, 1988). Thus, we interpret effect size magnitude according to the meta-analysis findings of Jacobson and colleagues (2012). They reported average effect sizes (g) of approximately 1.11 (CI [0.53 – 2.04]) of a-tDCS and 0.56 (CI [0.04 – 1.22]) of c-tDCS in cognitive studies (i.e., studies that measured the impact of tDCS on language, attention/perception, executive function, and memory). Any effect size that exceeds the average effect of either a-tDCS or c-tDCS is considered large, while effect sizes below the average values are moderate or small. Left-Tail Ratios (LTRs) are a case level analysis designed to assess the relative proportion of contrast sensitivity measurements recorded during stimulation to those of pre-stimulation in the left-tail of the combined distribution (see **Supplemental Material B**). Under assumptions of normality, homogeneity of variance, and large and equal group sizes, case-level proportions are functions of the magnitude of effect size at the group-level (Kline, 2004). However, when these assumptions are not met, group-level and case-level analyses will both offer separate information on the obtained effects. Given that the current that enters

cortex with tDCS is several orders of magnitude less than what is required to elicit action potentials, any influence of tDCS on psychophysical performance will be relatively small, and may only be large enough in a sub-group of our sample (see Spiegel et al., 2013). Thus, the combination of group-level and case-level analyses offer a thorough descriptive approach of the data by quantifying effects in both central tendency and spread of the distribution of contrast sensitivity values. LTRs are calculated with the largest proportion as the numerator (regardless of time-point affiliation); values marked by an asterisk (*) indicate that the pre-stimulation contrast sensitivity values were over-represented in the left tail of the combined distribution. Finally, interval estimates reported for Hedge's g effect size measures are exact 95% confidence intervals calculate from the non-central t distribution (see **Supplemental Material B**; Cumming & Finch, 2001; Kline, 2004). Interval estimates for η_p^2 variance accounted for effect sizes are not reported, as their distribution in correlated designs are complex and do not follow a central nor a non-central distribution (Cumming and Finch, 2001; Kline, 2004).

Results

Two observers in the oblique condition completed the study at Concordia University, and thus, we first verified that their contrast sensitivity values were similar to those of the Colgate University sample (see **Figure 2**). We report U1 (see **Supplemental Material B;** Cohen, 1988), a statistic of overlap with range [0 1]: values of 0 indicate complete overlap between both samples, while values of 1 indicate no overlap whatsoever. At baseline, there was significant overlap between contrast sensitivity measures collected at both testing facilities (U1 never exceeded .27). Both a-tDCS and c-tDCS measures showed similar results to those of baseline, except for the fixed size stimuli with spatial frequency of 4 cycles/°, U1 = .87. This shows little overlap between scores from the Colgate and Concordia samples. However, given that contrast sensitivity values were discrepant for a single stimulus condition block, we average contrast sensitivity values collected at both testing locations for all subsequent analyses.

FIGURE 2

Fixed period oblique and horizontal stimuli

The average effects of both a-tDCS and c-tDCS on fixed period oblique and horizontal gratings are shown in **Figure 3**. Contrast sensitivity measured with oblique fixed period gratings showed a statistically significant interaction between tDCS polarity and spatial frequency, $F(3, 27) = 8.10$, $p < .001$, $\eta_p^2 = .474$, which stemmed from a contrast sensitivity decrease under a-tDCS and increase under c-tDCS at a spatial frequency of 8 cycles/°, $F(1, 9) = 20.79$, $p < .001$, $\eta_p^2 = .698$. There was no statistically significant interaction between spatial frequency and tDCS type on contrast sensitivity measured with horizontal fixed period gratings, $F(3,27) = 1.97$, $p = .585$, $\eta_p^2 = .179$.

FIGURE 3

The effect size analysis also showed the polarity specific effect of tDCS on contrast sensitivity measured to an 8 cycles/° oblique grating (**Figure 3C**). Contrast sensitivity decreased by a third of a standard deviation under a-tDCS (8 cycles/°: g = -0.32, 95% CI [-0.60 -0.03]) while it increased by a quarter of a standard deviation under c-tDCS (g = 0.24, 95% CI [-0.03 0.50]). Additionally, we found a-tDCS to decrease contrast sensitivity by a similar amount at spatial frequencies of 4 cycles/° (g = -0.40, 95% CI [-0.78 -0.03]) and 12 cycles/° (g = -0.36, 95% CI [-0.70 -0.01]). At the group level, a-tDCS induced decreases in contrast sensitivity remained stable across spatial frequency, but at the case-level, we found that observers were progressively more likely to have contrast sensitivity values one standard deviation below the grand mean than pre-stimulation contrast sensitivity values as spatial frequency increased. This would suggest that these decrements in contrast sensitivity under a-tDCS are accentuated with spatial frequency (see **Table 1**). Thus, the effects of a-tDCS may be spatial frequency dependent, and increase in magnitude in accordance with an increase in spatial frequency.

The effects of a-tDCS and c-tDCS on horizontal fixed period gratings were small in comparison to those of its oblique counterpart. We did find a moderate increment in contrast sensitivity under c-tDCS at a spatial frequency of 12 cycles/° (g = 0.35, 95% CI [-0.02 0.71]). This effect may be spatial frequency dependent, as the both the effect size and LTRs (see **Table 1**) showed that the benefit of c-tDCS on contrast sensitivity increased with spatial frequency: from 4 cycles/° (g = 0.13, 95% CI [-0.17 .42]) and 8 cycles/° (g = 0.19, 95% CI [-0.11 0.48]), which reached significance at 12 cycles/°. Thus, the results of the fixed period condition show that the effects of a-tDCS may be most pronounced on oblique gratings while those of c-tDCS on horizontal gratings, both for spatial frequencies above the peak of the CSF.

TABLE 1

Fixed size oblique and horizontal stimuli

The average effects of both a-tDCS and c-tDCS on oblique gratings of a fixed size are shown in **Figure 4**. There were no statistically significant interactions between spatial frequency and tDCS polarity for contrast sensitivity measure with either oblique, $F(3, 27) = 0.65$, $p = .585$, $\eta_p^2 = .068$, or horizontal, $F(3,27) = 2.83$, $p = .057$, $\eta_p^2 = .239$, gratings. There was a main effect of tDCS polarity on contrast sensitivity measured to oblique gratings, $F(1, 9) = 9.23$, $p = .014$, $\eta_p^2 = .506$. Anodal tDCS decreased and c-tDCS increased contrast sensitivity for all spatial frequencies. Effects of tDCS collapsed across spatial frequency are not particularly informative, and thus, we turn to our effect size analysis to measure if any changes in contrast sensitivity can attributed to tDCS.

FIGURE 4

Overall, effect sizes in the fixed size condition were small and had large confidence intervals. There is an indication of a polarity specific effect of tDCS on contrast sensitivity measured to an oblique grating at 12 cycles/°. This effect has a similar direction to the polarity specific effect obtain in the fixed period condition: a-tDCS

decreased contrast sensitivity (g = -0.33, 95% CI [-0.65 0.01]) while c-tDCS increased sensitivity (g = 0.21, 95% CI [-0.10 0.51]). The influence of a-tDCS here does not seem to increase with spatial frequency. LTRs were similar for both 4 and 8 cycles/° conditions, and decreased slightly at 12 cycles/°, which suggest a narrowing of the contrast sensitivity distribution of a-tDCS (see **Table 2**). We found no meaningful effects of a-tDCS on contrast sensitivity measured with horizontal gratings, but did find an abnormal increase in contrast sensitivity under c-tDCS to a horizontal grating of 8 cycles/° (g = 0.51, 95% CI [0.06 0.93]). While this may be indicative of an actual facilitation in contrast sensitivity, the effects of c-tDCS in this stimulus condition seem independent of spatial frequency. Additionally, the LTR value for this condition was small in comparison to the magnitude of the effect size, which should be considered when interpreting this result.

TABLE 2

Orientation Dependent Effects of tDCS

Given that the effects of tDCS reported above varied according to the orientation of the stimulus, we opted compared the these effects directly by calculating effect size measures for the difference in contrast sensitivity between horizontal and oblique gratings for all stimulus and stimulation conditions (see **Figure 5**). Baseline contrast sensitivity, in both stimulus size conditions followed the well-defined "Oblique Effect" (Appelle, 1972; Campbell et al., 1966). Horizontal contrast sensitivity exceeded that of oblique at higher spatial frequencies in the fixed period (8 cycles/°: 12 cycles/°: g = 0.62, 95% CI [-0.29 1.51]) and fixed size conditions (8 cycles/°: g = .90, 95% CI [-0.04 1.81]; 12 cycles/°: g = 1.16, 95% CI [0.20 2.10]). However, the overlap between confidence intervals for baseline and tDCS suggest tDCS had no measureable impact on the magnitude of the Oblique Effect. Thus, while the effects of tDCS are orientation dependent (as shown above), they do not influence contrast sensitivity sufficiently to diminish or increase the magnitude of the Oblique Effect.

FIGURE 5

Effects of tDCS on low spatial frequency contrast sensitivity

Finally, we note that while contrast sensitivity to a grating with a spatial frequency of 0.5 cycles/° can be affected by tDCS, these effects are unlikely to be indicative of a true modulation. The 0.5 cycles/° grating were identical in both the fixed period and fixed size condition, and attributing contrast sensitivity to either condition was arbitrary in our analysis. When contrast sensitivity values from both stimulus size conditions (fixed period and fixed size) were combined, and the effects of tDCS reanalyzed, we find that both a-tDCS (g = 0.46, 95% CI [0.05 0.85], LTR = 1.61*) and c-tDCS (g = 0.44, 95% CI [0.02 0.85], LTR = 4.44*) increased contrast sensitivity from baseline equally. As both a-tDCS and c-tDCS had an identical influence on contrast sensitivity values, neither can serve as a control for the other, which clouds any meaningful effects we may have obtained at lower spatial frequencies. We had not

anticipated any modulation of contrast sensitivity under tDCS for our lowest spatial frequency grating as it differed from all others used in this study. At 0.5 cycles/°, a grating is part of the low spatial frequency rollover in the CSF, and is presumably subject to additional inhibition than the other gratings (Meese and Hess, 2004; Webster and Miyahara, 1997). If the application of tDCS over primary visual cortex creates an imbalance in the interactive properties of neurons (i.e., excitatory and inhibitory interactions), regardless of polarity, then contrast sensitivity to low spatial frequency gratings may be affected differently by the current generated with tDCS than to high spatial frequencies. Our findings here suggest that the application of a current, regardless of polarity, will increase contrast sensitivity to low spatial frequencies. Why this is, however, remains unclear.

Discussion

The goal of the current study was to assess whether the stimulus dimensions of gratings (spatial frequency, and orientation) could modulate the influence of tDCS on contrast sensitivity. We observe that the effects of both a-tDCS and c-tDCS were most pronounced on contrast sensitivity to obliquely oriented gratings of higher spatial frequency (i.e., above the peak of the CSF), and were absent at spatial frequencies below the peak the CSF. Generally, we found that a-tDCS decreased contrast sensitivity, while c-tDCS increased contrast sensitivity. However, these effects were small, and varied greatly across both stimulus spatial frequency, orientation and size conditions. In all but one stimulus condition, we found the influences of tDCS to be selective for polarity; only a-tDCS or c-tDCS had a large enough effect to influence contrast sensitivity. That said, when measured with an 8 cycles/° oblique grating (fixed period condition), contrast sensitivity was affected differently according to tDCS polarity: a-tDCS decreased while c-tDCS increased contrast sensitivity. Thus, while polarity specific effects of tDCS may be uncommon in vision studies (Accornero et al., 2007; Antal et al., 2001; Chaieb et al., 2008; Lang et al., 2007; Peters et al., 2013; Pirulli et al., 2014; Spiegel et al., 2012), we found that polarity specific influences of tDCS can be obtained under certain stimulus conditions (e.g., high frequency oblique gratings with small periods). Moreover, the effects of a-tDCS and c-tDCS on contrast sensitivity measured with fixed period gratings seem tied to orientation. Contrast sensitivity measured with oblique gratings was most subject to the influence of a-tDCS, while contrast sensitivity measured with horizontal gratings was most influenced by c-tDCS. While this did not affect the magnitude of the "Oblique Effect" (Appelle, 1972; Campbell et al., 1966; Essock, 1980), it may be indicative of an anisotropy of tDCS effects in vision, similar to the reported effects of Hansen and colleagues (2015).

The behavioral effects of tDCS result from an interaction between the electrical components of stimulation (Miranda et al., 2006; Paulus, 2011), the neuroanatomy of the stimulated area (Bikson et al., 2013; Radman et al., 2009; Shipp, 2005), the task completed by observers (Lapenta et al., 2013), and their cognitive state (Miniussi et al., 2010). While this allows for the broad acting effects of tDCS on cortex to be narrowed, or guided by the task, it also emphasizes that stimulus design should take into consideration the cortical area stimulated by tDCS. In primary visual cortex, the superficial layers near

the apex of the calcarine sulcus contain neurons with higher preferred spatial frequencies than cells further from the apex (Engel et al., 1997; Foster et al., 1985; Henriksson et al., 2008; Horton, 2006; Tootell et al., 1981, 1988; De Valois et al., 1982; Yu et al., 2010). Additionally, the magnitude of the electric field generated by tDCS is greater at the cortical surface (Bikson et al., 2013; Miranda et al., 2006; Nitsche et al., 2007). Thus, it is plausible the effects of tDCS on contrast sensitivity were greatest when higher spatial frequency gratings were used as neurons with higher preferred spatial frequencies would be most influenced by tDCS. Likewise, the peak in current density at the apex of the primary visual cortex suggest the effects of tDCS may be restricted to the central visual field, which is retinotopically mapped to the apex of the calcarine sulcus (Engel et al., 1997; Grill-Spector and Malach, 2004; Horton, 2006; Tootell et al., 1988). There is a study that corroborates this hypothesis (Kraft et al., 2010), however, other factors may influence the localization of tDCS effects in the visual field, as a recent study by Costa and colleagues (2015) has failed to replicate the findings of Kraft and colleagues (2010). Nevertheless, if the effects of tDCS are greatest within the central 2° of the visual field, as proposed by Kraft et al., (2010), it may explain why contrast sensitivity to fixed size gratings, which extend beyond the area affected by tDCS, was only mildly altered by tDCS. Additional psychophysical mechanisms (e.g., summation effects; Graham, Robson, & Nachmias, 1978; Legge, 1978; Meese & Summers, 2007; Peli et al., 1993) may have contributed to the lack of tDCS influence on contrast sensitivity to large gratings of high spatial frequency, as they also raise contrast sensitivity and potentially restricts any measurable influence of tDCS.

Changes in the stimulus characteristics presented to observers can have large contrasting tDCS effects on the same psychophysical measure. We opted to represent this with effect sizes to characterize changes in central tendency, and LTR, to define changes in the tail of the distribution (Feingold, 1995). While these may be considered uncommon statistical approaches, they are ideally suited to infer the meaningfulness of a change in behavior attributed to tDCS. For example, effects of tDCS in the tails of a distribution are to be expected as not all observers are affected equally by tDCS (Datta et al., 2009; Spiegel et al., 2013; Wagner et al., 2007). Thus, we used LTR to better define our dataset and characterized not only average effects (group-level) but also account for individual differences. Our analyses demonstrated that while the changes in contrast sensitivity induced by tDCS were sufficiently large to shift the central tendency of a distribution, certain effects were most apparent in the tails of the distribution. The decrease in contrast sensitivity under a-tDCS to fixed period gratings was of a similar magnitude for spatial frequencies of 4, 8, and 12 cycles/°, but the proportion of contrast sensitivity values in the left tail of the distribution increased with spatial frequency. This suggests observer contrast sensitivity, generally, was much more likely to show an influence of a-tDCS in higher spatial frequency conditions than when the spatial frequency neared the peak of the CSF. Furthermore, we calculated 95% confidence intervals of effect size measures to obtain an estimate of the sampling error in our effects. While most effect sizes were of moderate size, many had large confidence intervals that contained both positive and negative values. As 95% of all confidence intervals calculated in this way will contain the true effect size of a-tDCS and c-tDCS on contrast sensitivity measurements, both increments and decrements in contrast sensitivity appear equally valid directions in many

conditions evaluated here. Hence, the expected directionality of tDCS polarity - a-tDCS excites while c-tDCS inhibits - which stems predominantly from findings in motor cortex (Jacobson et al., 2012; Nitsche et al., 2003a, 2007; Pellicciari et al., 2013; Stagg et al., 2009), should be disregarded for cortical areas that are functionally and structurally different (Shipp, 2005, 2007).

tDCS Polarity and Psychophysical Performance

We found facilitatory and inhibitory effects of tDCS on low-level visual function, but our findings contrast those of other, similar studies (Antal et al., 2001; Chaieb et al., 2008; Kraft et al., 2010; Peters et al., 2013; Spiegel et al., 2013). It well established that the a-tDCS excitatory, c-tDCS inhibitory effect is only truly valid when measured in motor cortex, while in visual cortex the behavioral outcome of tDCS cannot necessarily be predicted by its polarity (Accornero et al., 2007; Antal et al., 2004a; Hansen et al., 2015; Miniussi et al., 2013; Pirulli et al., 2014). There are many factors that contribute to the net influence of current on cell activity that may explain the different outcomes between stimulation in motor and primary visual cortex (e.g., neuroanatomy and functional anatomy; Bikson et al., 2013; Peterchev et al., 2012; Radman et al., 2009; Rahman et al., 2013). Still, if cells in primary cortex are similarly influenced by tDCS as those of motor cortex, an additional mechanism must be defined to account for the variability in behavioral outcomes of tDCS in vision studies. For tasks that involve the detection of a stimulus, facilitatory effects of c-tDCS may stem from an increase in signal-to-noise ratios that result from a decrease in cell excitability (Antal et al., 2004b; Miniussi et al., 2013; Pirulli et al., 2014). An increase in the signal-to-noise ratio could minimize stimulus uncertainty (Pelli, 1985), which will increase the detectability of the stimulus. Similarly, a-tDCS could worsen performance by injecting additional noise and decreasing the signal-to-noise ratio. That said, tDCS is a continuous neurostimulation procedure and its effects on neuronal behavior cannot be as simple as an increment in excitability under a-tDCS and decrement in excitability under c-tDCS (Miniussi et al., 2013; Pirulli et al., 2014). The continuous current generated by tDCS may instead alter the balance of excitation and inhibition in neurons affected by the current (Pirulli et al., 2014). Balance of excitation and inhibition is a known neuro-mechanism responsible for the tuning characteristics of visually responsive cells (it serves to narrow the bandwidth of tuning curves and regulates their responses to contrast; Blin et al., 1993; Edden et al., 2009; Ferster and Miller, 2000; Rose and Blakemore, 1974; Li et al., 2008; Katzner et al., 2011). Thus, the psychophysical performance change under tDCS obtained in vision studies, such as the one presented here, may lie in low-level gain mechanisms that adjust the responses of a cell to a given level of contrast.

Limitations

Our tDCS stimulation protocol used large electrodes (48 cm^2 over Oz and 96 cm^2 over Cz), which most likely covered both primary visual and secondary visual cortical areas. As these areas differ in their cortical folding (Horton, 2006; Rosa et al., 1997a, 1997b), the alignment between the current generated by tDCS to the somatodendritic axis of the cell will vary and potentially alter the polarizing effects of tDCS (Radman et al.,

2009; Rahman et al., 2013; Rushton, 1927). It is unclear how the stimulation of both primary and secondary visual cortex may have impacted our findings here, however, more focal approaches that use smaller electrodes (HD-tDCS; Miranda et al., 2013; Rahman et al., 2013), may help prevent the simultaneous stimulation of multiple visually responsive cortical sites in future studies.

Conclusion

The effects of tDCS on contrast sensitivity are largest when measured with high spatial frequency oblique oriented gratings of a fixed period (1.5 cycles). Additionally, we found that the magnitude of a-tDCS and c-tDCS effects may be anisotropic, as c-tDCS generally elicited larger effects with horizontal gratings, while a-tDCS with oblique gratings. Finally, the overall magnitude of tDCS effects on contrast sensitivity were small, and spatial frequency dependent effects vanished when contrast sensitivity was measured with larger gratings of variable period. The effects of tDCS on low-level visual function is evidently subject to the particular stimulus attributes presented to observers, and further demonstrates the susceptability of this stimulation technique to the activity of cells within the cortical area it stimulates. In regards to contrast sensitivity, we find that under certain stimulus condition, tDCS effects may be facilitatory or inhibitory within a particular group of observers, regardless of stimulation polarity. Consequently, careful use of stimuli that reliably elicit tDCS polarity specific effects should be favored when implementing tDCS in vision studies.

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Table 1. Left-Tail Ratios of contrast sensitivity measures in the fixed stimulus period condition

		Spatial Frequency (cycles/°)			
Stimulus Dimensions		0.5	4	8	12
45° Oblique					
	a-tDCS	2.50*	4.34	12.67	124.19
	c-tDCS	6.47	1.02*	1.66	16.48
Horizontal					
	a-tDCS	1.74*	1.34*	1.23	3.39
	c-tDCS	2.56*	24.80	7.52	1.70

Note. Values marked with an asterisk (*) are ratios with the proportion of scores from the pre-stimulation distribution as the numerator.

Table 2. Left-Tail Ratios of contrast sensitivity measures in the fixed stimulus size condition

		Spatial Frequency (cycles/°)			
Stimulus Dimensions		0.5	4	8	12
45° Oblique					
	a-tDCS	4.60	36.28	34.84	14.25
	c-tDCS	1.04	15.65	1.29*	2.37*
Horizontal					
	a-tDCS	2.07	109.22	2.61	4.17
	c-tDCS	4.70*	1.05	1.60*	26.57

Note. Values marked with an asterisk (*) are ratios with the proportion of scores from the pre-stimulation distribution as the numerator.

Figure Captions

Figure 1. General psychophysical procedures completed by all observers in this study. **(A)** Stimulus presentation sequence (see text for details). **(B)** Contrast sensitivity was measured for both stimuli of a fixed size and fixed period, at 4 different spatial frequencies (0.5, 4, 8, and 12 cycles/°). Groups (n = 10 per group) were split according to stimulus orientation (45° oblique, and horizontal). Stimuli in the fixed period condition do not represent the actual change in size of our stimuli during the staircase, and are a graphical representation of the different stimulus dimensions used in this study. Stimuli of a fixed size subtended 3° of visual angle while stimuli of a fixed period had a period of 1.5 cycles.

Figure 2. Average contrast sensitivity values collected from the Colgate University (solid lines) and Concordia University (dashed lines) at baseline (gray) and tDCS sessions. For all conditions, contrast sensitivity values from both samples overlapped significantly and averaged for all subsequent analyses.

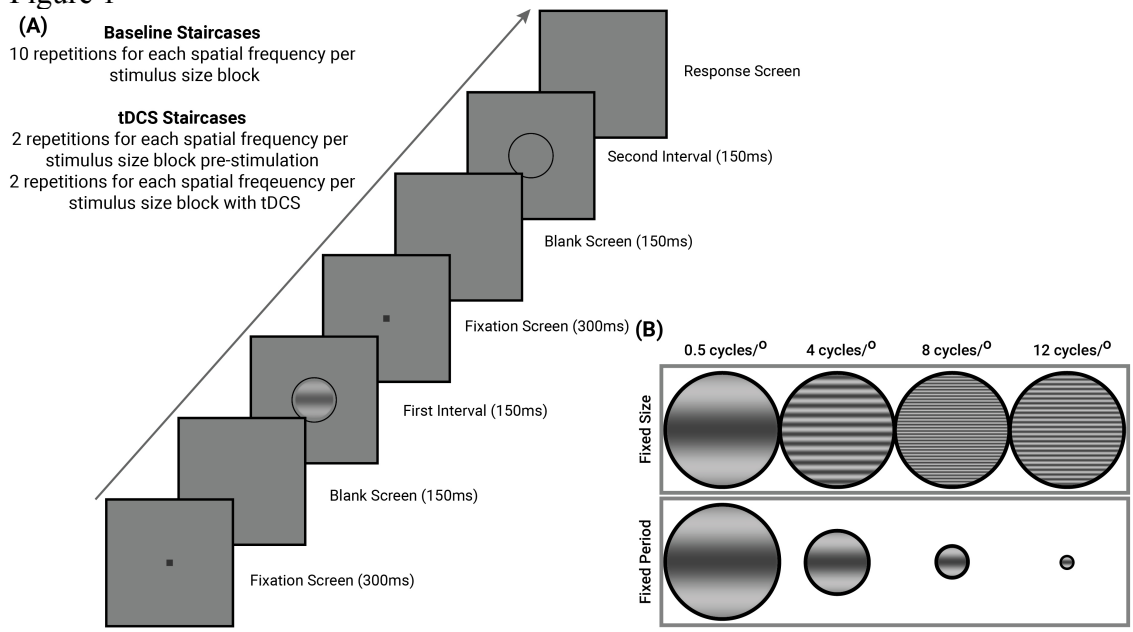
Figure 3. Average pre-stimulation (grey) and stimulation contrast sensitivity functions for both a-tDCS (red) and c-tDCS (blue) measured with the oblique (**A**) and horizontal (**B**) fixed period gratings (at spatial frequencies of 0.5, 4, 8, and 12 cycles/°). Contrast sensitivity is presented in decibels (dB). Error bars represent the standard error of the mean difference calculated across observers. **C** and **D** show the effect size measures of the mean difference contrast sensitivity measured at stimulation and at pre-stimulation for oblique and horizontal conditions, respectively. For oblique gratings**,** contrast sensitivity measured at 8 cycles/° showed a polarity specific effect of tDCS, whereby a-tDCS decreased and c-tDCS increased contrast sensitivity. Error bars represent the exact 95% confidence interval of the effect size. We used error bar overlap to assess the magnitude of tDCS effects on contrast sensitivity. Thus, error bars that do not contain 0 and do not overlap with changes in contrast sensitivity with the other tDCS polarity are considered "significant".

Figure 4. Average pre-stimulation (grey) and stimulation contrast sensitivity functions for both a-tDCS (red) and c-tDCS (blue) measured with the oblique (**A**) and horizontal (**B**) fixed size gratings (at spatial frequencies of 0.5, 4, 8, and 12 cycles/°). Contrast sensitivity is presented in decibels (dB). Error bars represent the standard error of the mean difference calculated across observers. **C** and **D** show the effect size measures of the mean difference contrast sensitivity measured at stimulation and at pre-stimulation for oblique and horizontal conditions, respectively. We found a large increase in contrast sensitivity measured with the 8 cycles/° horizontal, fixed size grating under c-tDCS, and a potential polarity specific effect of tDCS on contrast sensitivity measured to oblique gratings at a spatial frequency of 12 cycles/°. Error bars represent the exact 95% confidence interval of the effect size. As in Figure 4, we used error bar overlap to assess the magnitude of tDCS effects on contrast sensitivity.

Figure 5. Effect size of the mean difference between contrast sensitivity measured with horizontally orientated gratings and oblique orientated gratings. Grey bars represent the respective pre-stimulation baseline for either a-tDCS (red) or c-tDCS (blue) contrast

959 sensitivity difference between horizontal and oblique gratings. We do find a-tDCS to
960 increase the difference between contrast sensitivity measured to horizontal gratings and
961 that of oblique gratings at a spatial frequency of 4 cycles/° and for c-tDCS to have a
962 similar effect at a spatial frequency of 12 cycles /°. Error bars represent the exact 95%
963 confidence interval for the mean difference effect size.
964

965 Figure 1



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969 Figure 2

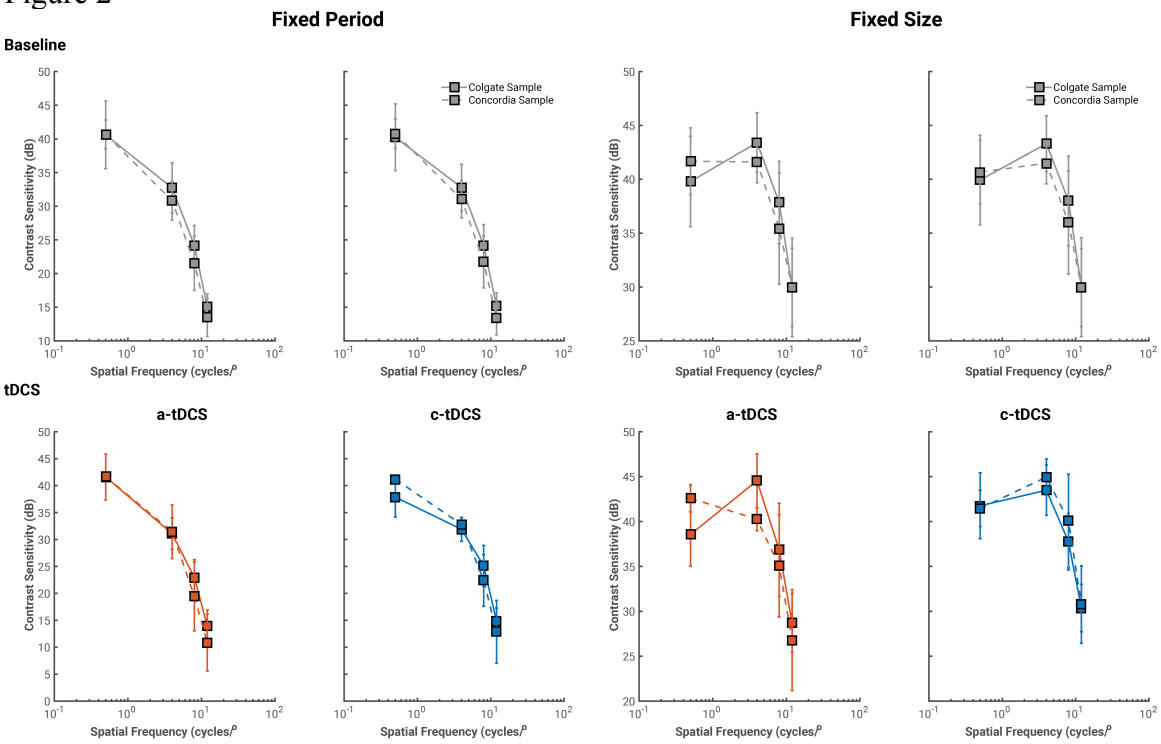

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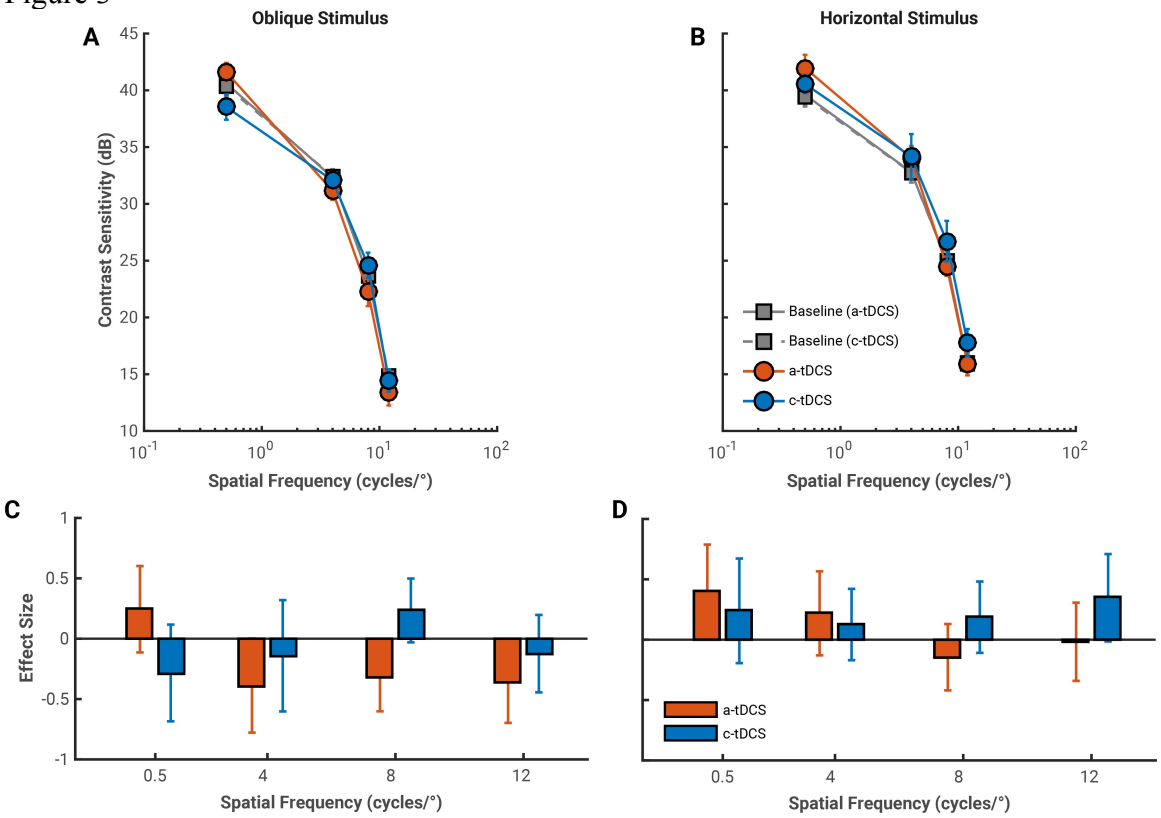
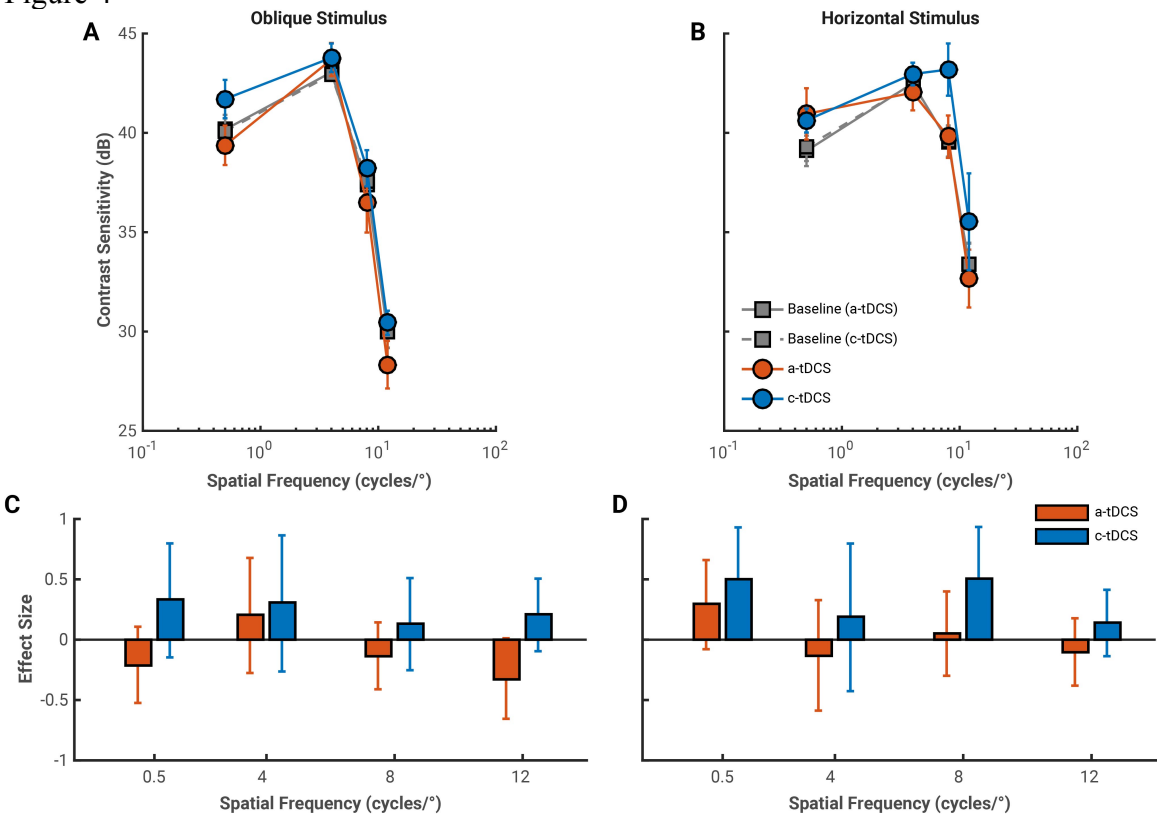
Figure 3


A
Oblique Stimulus
Contrast Sensitivity (dB)
Spatial Frequency (cycles/°)
B
Horizontal Stimulus
Baseline (a-tDCS)
Baseline (c-tDCS)
a-tDCS
c-tDCS
Spatial Frequency (cycles/°)
C
Effect Size
Spatial Frequency (cycles/°)
D
a-tDCS
c-tDCS
Spatial Frequency (cycles/°)

975 Figure 4



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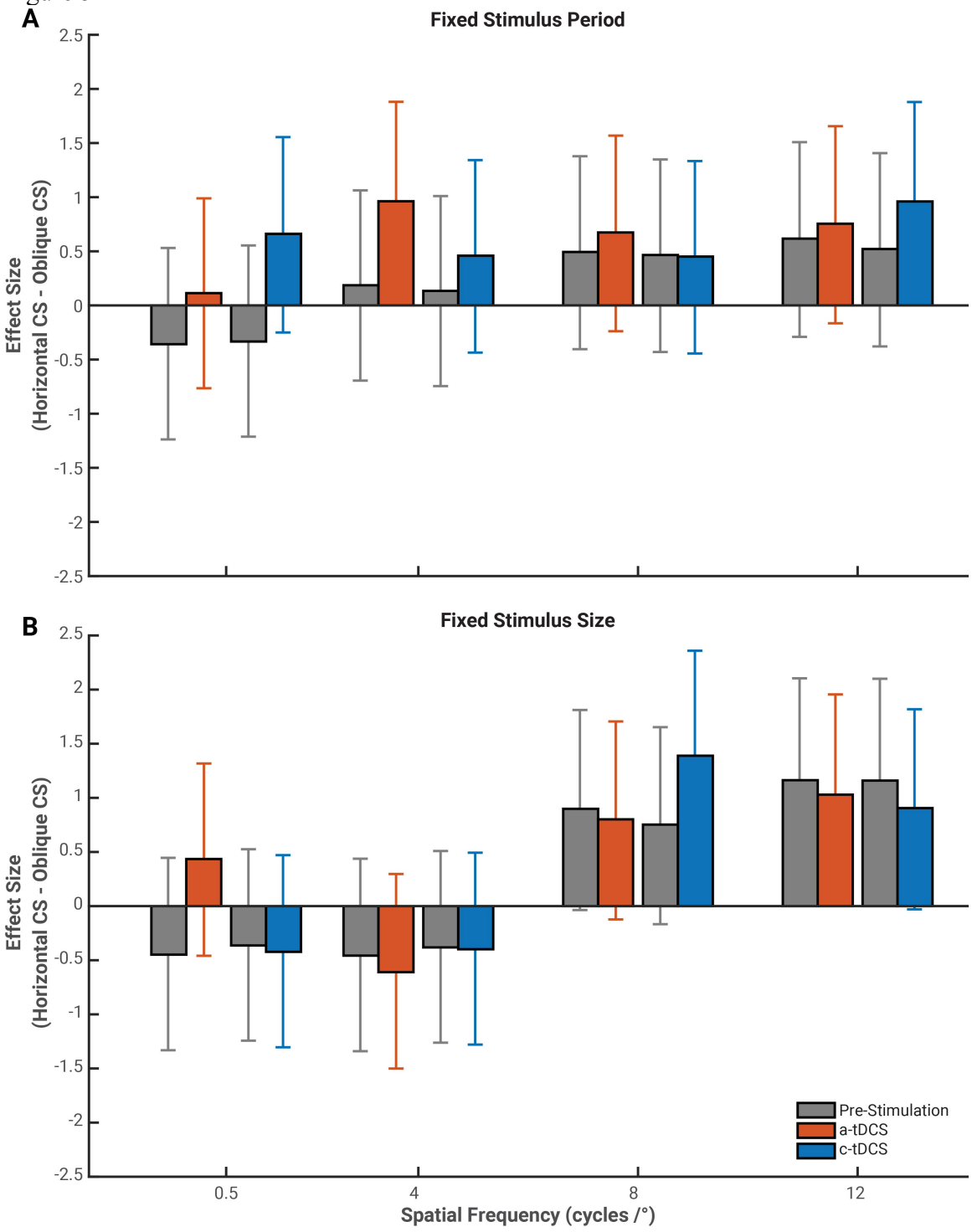
978 Figure 5



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Supplementary Material A

The effects of tDCS across the Spatial Frequencies and Orientations that comprise the Contrast Sensitivity Function

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Baseline Sequential Measurement in Time Data

The baseline portion of this study, completed by all observers, measured their contrast sensitivity to each spatial frequency by size stimulus blocks 10 times. The first two repetitions were practice staircases and removed prior to data analysis. Contrast sensitivity values for all observers in this study (both 45° oblique and horizontal orientation groups) for the final 8 staircases completed during baseline are shown in **Figure A1**. As described in text, we calculated the linear regression line of best fit for all observers across the 8 sequential measurements in time for all stimulus dimensions (solid lines in **Figure A1**) and found that no slope deviated from 0. Therefore, contrast sensitivity value for all 20 observers remained relatively stable across the final 8 repetitions of baseline measurements.

We opted to combine both the contrast sensitivity measured during baseline and the pre-stimulation contrast sensitivity measures to use as a pre-stimulation baseline in our data analyses reported in text. There is evidence that same-day and different-day baseline measures may alter the relative effects of tDCS (Peters et al., 2013), however, as observers were constrained to perform similarly to their baseline contrast sensitivity measurements prior to undergoing stimulation, we found no differences in our effects when using either different-day baseline measures or same-day baseline measures alone or combined (see **Figure A2**).

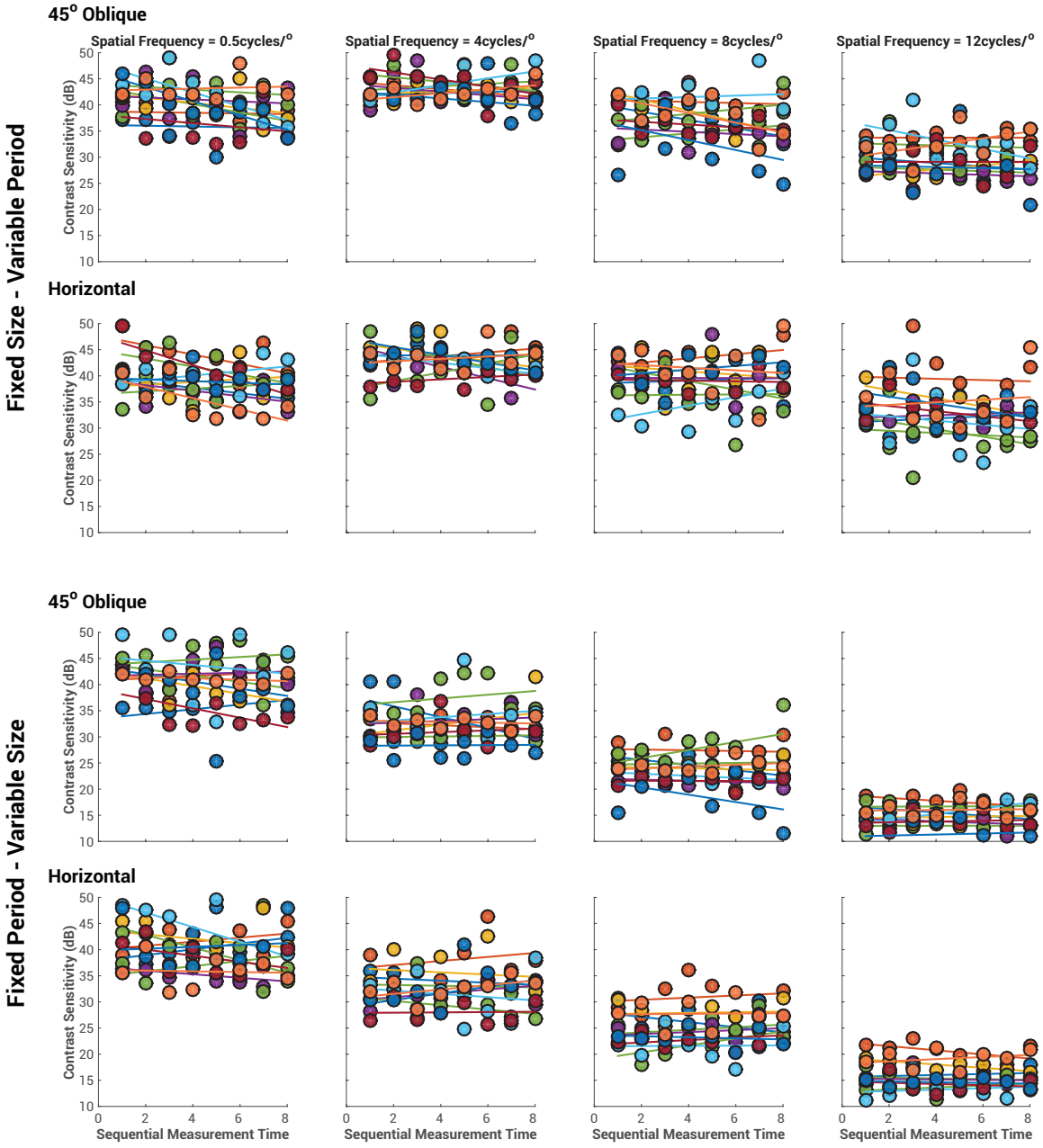

Figure A1. Observers in the 45° oblique grating group and horizontal grating group showed no statistically significant difference across the sequential measurements in time for all stimulus dimensions used in this study (all *p*s > 0.05). Each color in the figure represents the contrast sensitivity value for an individual observer for the final 8 measurements of contrast sensitivity (in decibels) completed in the baseline portion of the study.

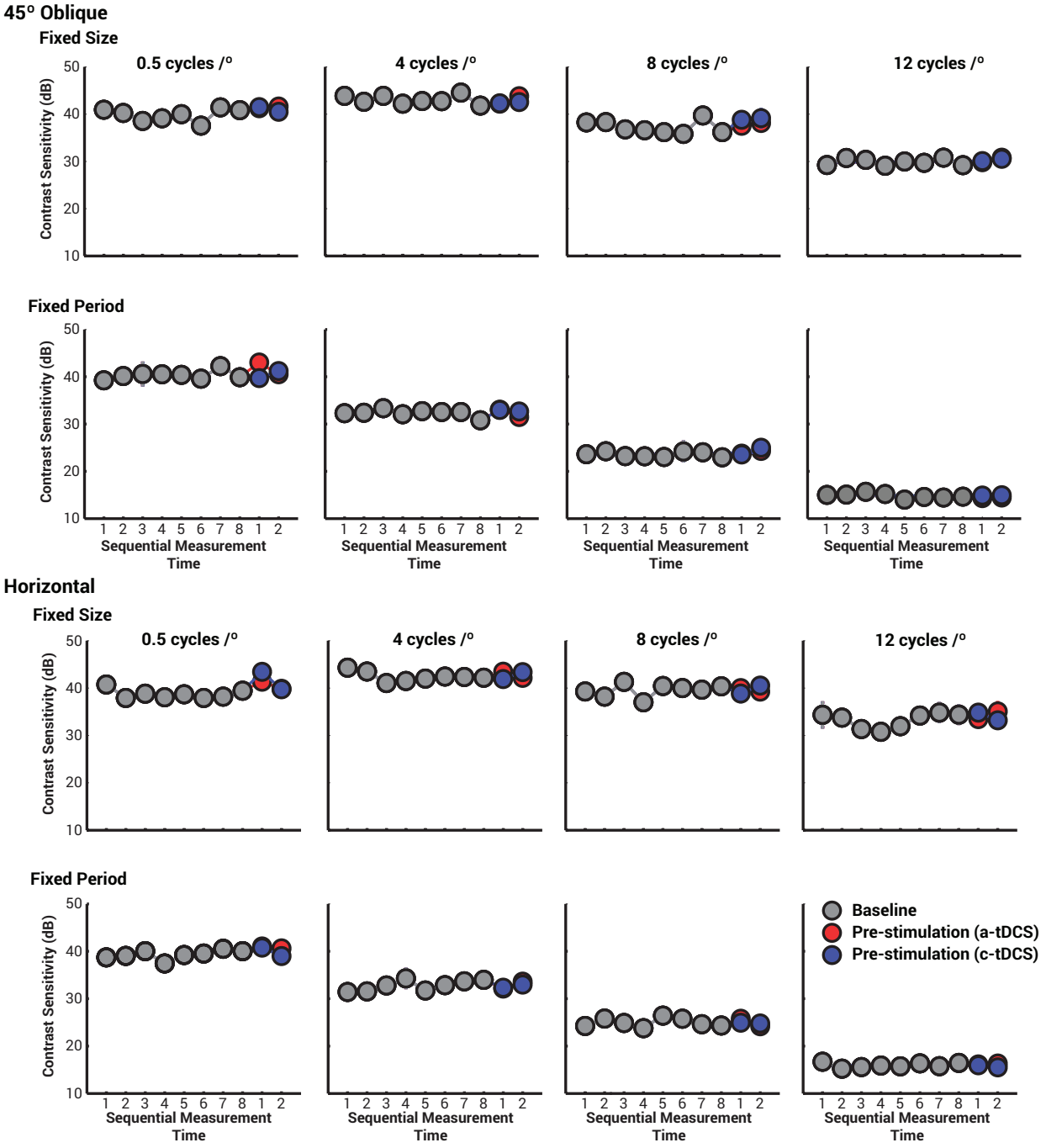

Figure A2. Average contrast sensitivity values (n = 10 observers per data point) for the last 8 spatial frequency by stimulus size blocks (fixed period and fixed size) of the baseline session, and the pre-stimulation contrast sensitivity values for both for a-tDCS (red) and c-tDCS (blue) sessions. The figure is split by stimulus orientations. Average contrast sensitivity values did not change significantly between baseline measurements sessions or pre-stimulations. Error bars represent 1 standard error of the mean (note that many data points have error bars smaller than the marker).

References

Peters, M. A. K., Thompson, B., Merabet, L. B., Wu, A. D., and Shams, L. (2013). Anodal tDCS to V1 blocks visual perceptual learning consolidation. *Neuropsychologia* 51, 1234–1239. doi:10.1016/j.neuropsychologia.2013.03.013.

Supplementary Material B

The effects of tDCS across the Spatial Frequencies and Orientations that comprise the Contrast Sensitivity Function

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Description of Statistical Analyses

This appendix offers a brief description of analyses used in this study to estimate the magnitude of both a-tDCS and c-tDCS effects on contrast sensitivity. We begin with a complete table of U1 statistics used to assess overlap between the Colgate University and Concordia Samples, and subsequently offer an overview of building exact [(1-α)*100] confidence intervals around the Hedge's g effect size, and define the computation of Left Tail Ratios (LTRs). Further details on these analyses and calculations can be found in Kline (2004) and Cumming and Finch (2001). Finally, we report the output of all repeated-measures ANOVA from our experiment.

Measures of overlap

Given the large discrepancy in sample size between the Colgate (n = 8) and Concordia (n = 2) samples, we opted to assess overlap between the two prior to averaging their data with a simple measure of overlap, U1, which defines the proportion of scores between two sampling distribution that do not overlap (Cohen, 1988). U1 is calculated as follows: 1) count the total number of scores in one group outside the range of scores in the other group and 2) divide that number by total sample size (N). If the mean contrast between both groups is 0, then U1 is also 0, while it is 1 if both samples do not overlap whatsoever (see **Table B1**).

Table B1. Measures of overlap between the Colgate and Concordia samples (U1) for all stimulus block and time points (Baseline / tDCS) of the study.

	Baseline		tDCS	
	a-tDCS	c-tDCS	a-tDCS	c-tDCS
Spatial Frequency		Fixed Stimulus Period		
0.5	0.15	0.15	0.38	0.13
4	0.28	0.20	0.06	0.06
8	0.15	0.16	0.31	0.19
12	0.05	0.05	0.25	0.00
		Fixed Stimulus Size		
0.5	0.05	0.05	0.06	0.19
4	0.16	0.13	0.88	0.19
8	0.11	0.13	0.25	0.00
12	0.03	0.03	0.13	0.13

Group-Level Analyses

Traditionally, confidence intervals are constructed in order to estimate the mean of the sampling distribution of the parameter of interest (μ), as the mean of the sampling distribution will be within the confidence interval [(1-α)*100] percent of the time. There are, other approaches to build confidence intervals, which are more intuitive when building a confidence interval around an effect size measure. Instead of defining the confidence intervals as capturing μ [(1-α)*100] percent of the time, the confidence interval is built by defining plausible values of μ. Therefore, the lower limit of the confidence interval is defined as all plausible values of μ having a [(1- α/2)*100] probability below a certain value of x, while the upper limit is defined as all plausible values of μ having a [(α/2)*100] probability below x. In this form, the confidence intervals can be calculated by finding the mean of the distribution for which [(1-α/2)*100] of its proportion lies below the effect size measure (the lower limit) and the mean of a distribution for which [(α/2)*100] of its proportion falls below the effect measure (the upper limit; see **Figure B1**).

The sampling distribution of effect sizes (g) is a non-central *t* distribution: a probability density function defined by two parameters, the degrees of freedom (*df*) and a non-centrality parameter (Δ). The non-centrality parameter reflects the degree to which the null hypothesis is false. If Δ = 0, the resulting distribution is a symmetrical central *t* distribution with the same *df*, while it will be positively skewed when Δ > 0 and negatively skewed when Δ < 0. In an independent samples design, the effect size between two sample means is related to the non-centrality parameter as follows:

$$\Delta = \delta \sqrt{\frac{n_1 n_2}{n_1 + n_2}} \qquad \textbf{Equation B1}$$

When building confidence intervals around an effect size for a dependent samples design, as we have done here, exact confidence intervals can only be defined when the mean difference is standardize by the standard deviation of the difference scores (s_D). Effect sizes standardized by the within-group pooled standard deviation or by the standard deviation of a single group are too complex and do not follow a central or non-central *t* distribution. In a dependent samples design, the effect size is related to the non-centrality parameter as follows:

$$\delta = \Delta\sqrt{\frac{2s_D^2}{n\left(s_1^2 + s_2^2\right)}} \qquad \textbf{Equation B2}$$

Whereby the variance of the difference scores (s_D^2) is defined as

$$s_D^2 = s_1^2 + s_2^2 - 2\,\mathrm{cov}_{12}$$
$$\mathrm{cov}_{12} = r_{12}s_1s_2 \qquad \textbf{Equation B3}$$

where cov_{12} is the covariance of the observed scores across conditions and is the product of the cross condition correlation and the within condition standard deviations.

As both the non-centrality parameter and effect size are linked, we can build confidence intervals around an effect size measure by first building a confidence interval for the non-centrality parameter and then transforming it into the effect size units. For a given *t* statistic (independent: $t = m_1 - m_2 \big/ s_{m_1 - m_2}$; dependent: $t = M_D \big/ s_{m_D}$), we can search for the non-central *t* distribution with Δ such that [1- α/2]*100 falls below the *t* statistic (the lower limit, Δ_L) and conversely find the non-central *t* distribution with Δ such that [α/2]*100 falls below *t* (the upper limit, Δ_U). **Figure B1** illustrates this concept for an independent sample design with values taken from Kline (2004). When both the Δ_L and Δ_U have been found, they can easily be converted into effect size values (**equation B1** or **equation B2**).

Finding the appropriate non-central *t* distribution is simple in MATLAB, as the non-central *t* distribution is defined by the *nctcdf* function (requires the statistics toolbox, see attached MATLAB code). Statistical software, including SAS and STATISTICA also include non-central *t* distribution calculators that allow building exact confidence intervals around an effect size, and the Real Statistics Excel Resource Pack (http://www.real-statistics.com/) also contains a non-central *t* distribution calculator. We strongly encourage the construction of confidence intervals around effect sizes, as the effect, just as any other statistics, will always be subject to estimation error. Estimated confidence intervals for effect sizes can be calculated with more traditional (estimating the mean of the sampling distribution that will capture a value [(1-α/2) *100] percent of the time) by using the z distribution (see **Equation B4**).

$$g \pm z_{\alpha/2} s_d$$

$$s_d = \sqrt{\frac{g^2}{2df} + \frac{1}{n_1} + \frac{1}{n_2}}$$

Equation B4

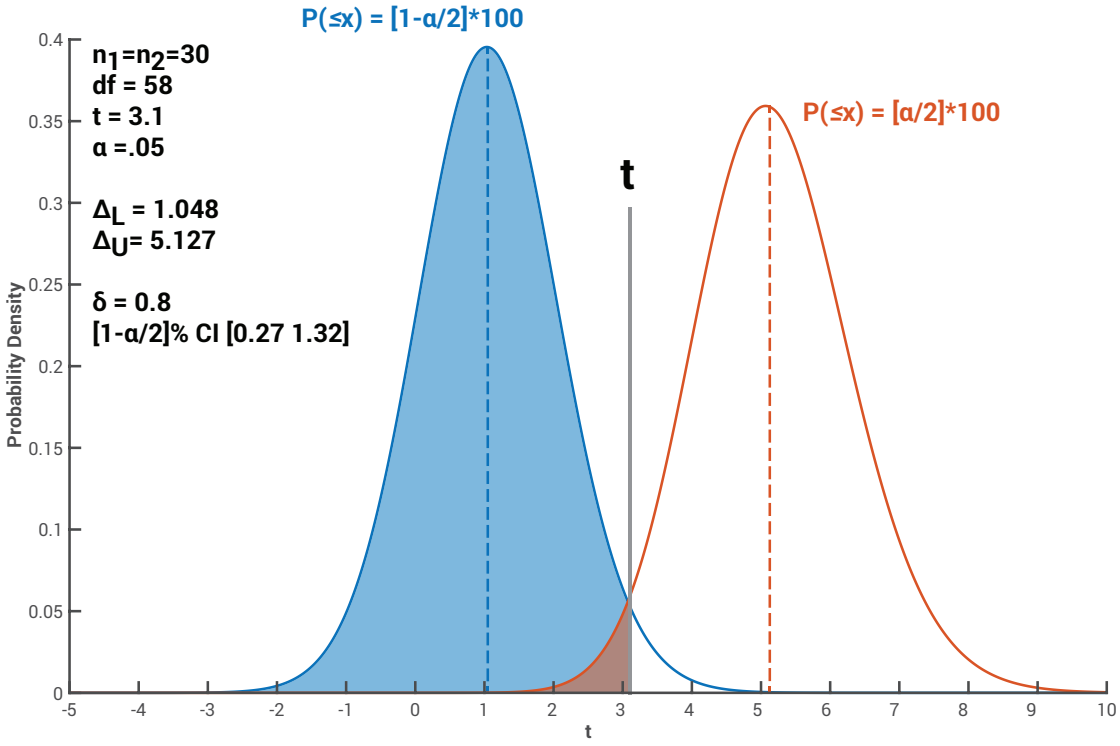

Figure B1. Finding the two non-central *t* distributions with best fitting non-centrality parameters (Δ_L and Δ_U). The blue *pdf* is the non-central t distribution with the best fitting Δ_L for which a cumulative density of [1-α/2]*100 falls below *t*. The orange distribution is the best fitting Δ_U for which a cumulative density of [α/2]*100 falls below *t*. Values taken from Kline (2004).

Case-Level Analyses

Transcranial Direct Current Stimulation in human observers are subject to a variety of factors that include the skull density, and alignment of cortical gyri with the electrodes that will moderate the effects of stimulation and vary significantly between observers (Miranda et al., 2006; Datta et al., 2009; Sadleir et al., 2010). Furthermore, given the magnitude of the non-shunted direct current that enters cortex is several orders of magnitude less than what is required to elicit action potentials (Rahman et al., 2013; Peterchev et al., 2012; Creutzfeldt et al., 1962), we expected contrast sensitivity values obtain during stimulation of have different variance than those obtain prior to stimulation (as some observers may respond more drastically than others to stimulation). Previous attempts to account for individual variability between observers receiving tDCS have predominantly focused on the removal of "non-responders" (observers that shown small or effects in the opposite direction typically reported for a tDCS polarity), we opted to implement case-level analyses, which allowed us to keep all observers that underwent

tDCS in our data analysis. Case-level analyses can be particularly beneficial when the variance between two samples (here pre-stimulation and stimulation) is believed to differ significantly, but their central tendency may not (see **Figure B2)**. Case-level analyses are therefore ideally suited to quantify the effects of neuro-modulators, including tDCS, as the effects of stimulation are known to be small (Jacobson et al., 2012) at the level of central tendency, but may induce large effects in certain observers more susceptible to neuro-stimulation. There are many forms of case-level analyses (see Kline, 2004), however, given that our data showed large suppressive effects of a-tDCS, we opted to measure the Left-Tail Ratios for all stimulus dimensions presented in the results section.

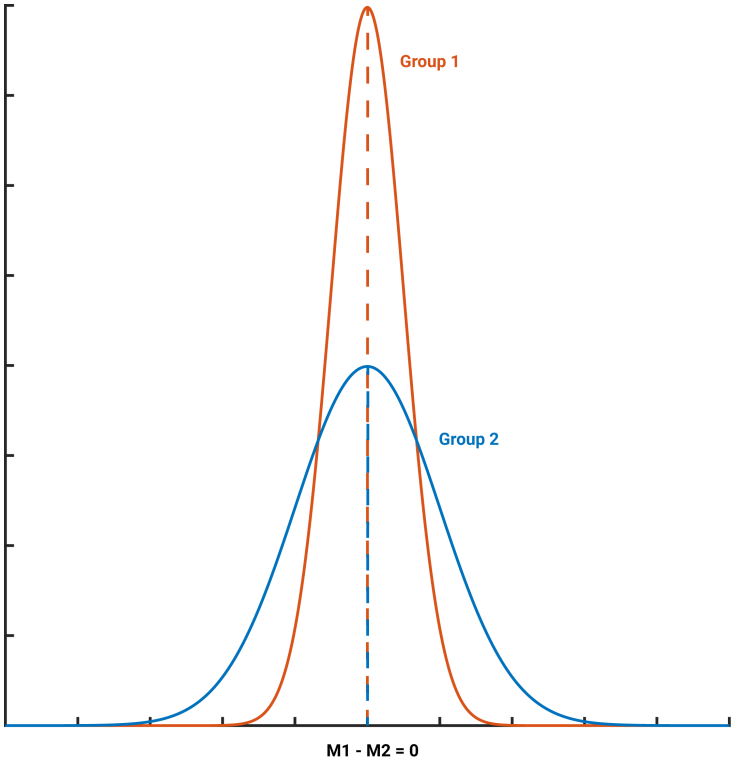

Figure B2. In this scenario, two sample distributions have identical means, but different variance values. The effect size of the mean difference value here is 0, however, this does not mean that these two distributions are identical. LTRs, which calculate the proportion of scores with the tails of a combined distribution (the "average" distribution of both samples) would identify the difference between these two samples. The combination of both effect size measures and tail ratios ensures that any effect that leads to a change in the sample distribution is properly characterized.

A Left-tail ratio is the relative proportion of scores from two different groups (here contrast sensitivity collected prior to and during tDCS) that fall in the lower extreme (left-tail) of the combined frequency distribution. Tail ratios are always calculated with the largest value as the numerator and are therefore always larger than 1. We computed left-tail ratios based on a cut-off point relative to the mean (M_t) and standard deviation (s_T) of the combined distribution (pre-stimulation and stimulation) for each stimulus dimension presented to observers in this study. The mean and standard deviation of the combined distribution are calculated as follows.

$$M_T = \left[n_1 M_1 + n_2 M_2 \right]$$
$$SS_T = n_1 \left(M_1 - M_T \right)^2 + n_2 \left(M_2 - M_T \right)^2 + df\left(s_1^2 \right) + df\left(s_2^2 \right) \quad \textbf{Equation B4}$$
$$s_T = \sqrt{\frac{SS_T}{df}}$$

The cut-point for left tail ratios is defined as one standard deviation below the grand mean. The distance between the cut-off score ($M_T - s_T$) and the mean of each sample is then converted into a z-score and the proportion of scores that fall below this z-score under the normal distribution is calculated. The left-tail ratio is then simply the ratio between both proportions, with the largest proportion always placed as the numerator.

$$z_1 = \frac{\left(M_T - s_T \right) - M_1}{s_1}$$
$$z_2 = \frac{\left(M_T - s_T \right) - M_2}{s_2} \quad \textbf{Equation B5}$$
$$LTR = \frac{P(\geq z_1)}{P(\geq z_2)}$$

Repeated Measures ANOVA Tables

Table B2 – Repeated Measures ANOVA – Fixed Period Stimulus Conditions

Factors	SS	*df*	MS	F	*p*	η_p^2
			Oblique			
tDCS	1.98	1	1.98	0.52	0.489	0.055
SF	5.19	3	1.73	0.29	0.830	0.032
tDCS x SF	72.30	3	24.10	8.10	0.001	0.474
Subjects	57.57	9	6.40			
tDCS x Subjects	34.17	9	3.80			
SF x Subjects	159.36	27	5.90			
tDCS x SF x Subjects	80.29	27	2.97			
Total	410.85	79	5.20			
			Horizontal			
tDCS	12.27	1	12.27	1.08	0.325	0.107
SF	14.26	3	4.75	0.58	0.631	0.061
tDCS x SF	39.13	3	13.04	1.97	0.142	0.179
Subject	284.48	9	31.61			
tDCS x Subject	101.86	9	11.32			
SF x Subject	219.68	27	8.14			
tDCS x SF x Subject	178.88	27	6.63			
Total	850.56	79	10.77			

Table B3 – Simple Effect Comparison - Fixed Period Oblique Stimuli

Factors	SS	*df*	MS	F	*p*	η_p^2
tDCS $_{\text{at SF = 0.5 cpd}}$	39.90	1	39.90	4.72	.058	.344
Subjects	98.72	9	10.97			
tDCS X Subjects	76.06	9	8.45			
Total	214.67	19	11.30			
tDCS $_{\text{at SF = 4 cpd}}$	3.34	1	3.34	1.57	.242	.149
Subjects	36.60	9	4.07			
tDCS X Subjects	19.12	9	2.12			
Total	59.06	19	3.11			
tDCS $_{\text{at SF = 8 cpd}}$	26.35	1	26.35	20.79	0.001	0.698
Subjects	34.83	9	3.87			
tDCS X Subjects	11.41	9	1.27			
Total	72.58	19	3.82			
tDCS $_{\text{at SF = 12 cpd}}$	4.70	1	4.70	5.37	.046	.374
Subjects	46.77	9	5.20			
tDCS X Subjects	7.88	9	0.88			
Total	59.35	19	3.12			

1223 **Table B4 –** Repeated Measures ANOVA – Fixed Size Stimulus Conditions

Factors	SS	*df*	MS	F	*p*	η_p^2
			Oblique			
tDCS	48.45	1	48.45	9.23	0.014	0.506
SF	20.46	3	6.82	1.35	0.278	0.131
tDCS x SF	14.41	3	4.80	0.66	0.585	0.068
Subjects	64.89	9	7.21			
tDCS x Subjects	47.25	9	5.25			
SF x Subjects	135.93	27	5.03			
tDCS x SF x Subjects	197.21	27	7.30			
Total	528.60	79	6.69			
			Horizontal			
tDCS	56.38	1	56.38	4.80	0.056	0.348
SF	45.33	3	15.11	0.97	0.423	0.097
tDCS x SF	48.72	3	16.24	2.83	0.057	0.239
Subject	278.77	9	30.97			
tDCS x Subject	105.70	9	11.74			
SF x Subject	421.96	27	15.63			
tDCS x SF x Subject	154.98	27	5.74			
Total	1111.84	79	14.07			

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