Anodal transcranial direct current stimulation reduces collinear lateral inhibition in normal peripheral vision

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Abstract

Peripheral vision is susceptible to crowding; difficulty in segregating a target object from adjacent objects. Crowding limits visual function in individuals with central vision loss who are forced to rely on their peripheral vision. Perceptual learning can reduce crowding in peripheral vision, however intensive training is required. To assess whether modulation of crowding can be achieved within a short time-frame, we tested the hypothesis that a single 25-minute session of primary visual cortex anodal transcranial direct current stimulation (a-tDCS) would reduce lateral inhibition in peripheral vision. Lateral inhibition occurs in the primary visual cortex and may contribute to crowding. Fourteen observers with normal vision performed a 2AFC contrast detection task with flankers positioned at a distance of 2λ (lateral inhibition) or 6λ (control condition). The stimuli were presented 6° to the left of a central cross and fixation was monitored with an infra-red eye tracker. Participants each completed two randomly sequenced, single-masked stimulation sessions; real anodal tDCS and sham tDCS. For the 2λ separation condition, a-tDCS induced a significant reduction in detection threshold (reduced lateral inhibition). Sham stimulation had no effect. No effects of a-tDCS were observed for the 6λ separation condition. This result suggests that a-tDCS may be useful as a visual rehabilitation tool for individuals with central vision loss who are reliant on peripheral vision.

Keywords: tDCS, crowding, collinear inhibition, lateral inhibition, peripheral vision.

Introduction

Peripheral vision is susceptible to a phenomenon called crowding, whereby it is difficult to segregate a target object from other objects that are in close proximity. [1–4] Crowding is a particular concern for patients with macular degeneration who lose central vision and are forced to rely on peripheral vision. These patients often develop a preferred retinal locus (PRL), a specific region of the peripheral retina that is used for fixation.[5–7] Crowding impairs spatial vision at the PRL leading to problems with everyday visual activates such as reading.

Crowding in peripheral vision involves cortical mechanisms that can be modulated. For example, perceptual learning can reduce letter crowding in central vision for observers with amblyopia[8,9] and in peripheral vision for observers with macular degeneration[10–13]. However, perceptual learning typically requires a large number of training trials [14] which may be a barrier for patients. In addition, the learning does not always transfer to non-trained stimuli.[15–17] Interventions that can directly modulate crowding mechanisms within visual cortex may complement perceptual learning techniques and enable improved vision in patients with central vision loss.

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique[18–20] that has the potential to modulate crowding. tDCS involves passing a weak 1-2mA electrical current through two head-mounted electrodes (the anode and cathode) and can induce regional changes in cortical excitability and neurotransmitter concentration that outlast the duration of stimulation. For example, anodal tDCS (a-tDCS) of the motor cortex increases cortical excitability[21] and causes a regional reduction in the concentration of the inhibitory neurotransmitter GABA [22–24]. When applied to the primary visual cortex, a-tDCS modulates contrast sensitivity[25,26], visually evoked potential amplitude[25] and the visual cortex BOLD response[26]. Of particular importance for crowding, a-tDCS can immediately improve Vernier acuity and reduce surround suppression within the near-periphery[27–29], possibly by modulating inhibition within the visual cortex.[27]

Lateral masking, a well-established psychophysical paradigm for the assessment of low-level mechanisms that may contribute to crowding, involves the presentation of a central target Gabor patch between two flanker patches[12]. When the patches have collinear orientation, contrast detection thresholds for the target can be increased (collinear inhibition or lateral masking) or reduced (collinear facilitation) depending on target/flanker separation. Collinear inhibition and facilitation arise within the primary visual cortex[30 31] and are present in central [8] and peripheral vision.[32,33] Maniglia et al. (2011) observed that collinear lateral inhibition could be reduced by ≈40% in normal peripheral vision after perceptual learning (20 sessions/week over 8 weeks), indicating that colinear inhibition mechanisms within the periphery are

plastic. In this study, we tested the hypothesis that a single session of visual cortex a-tDCS would induce an acute reduction in lateral inhibition. In support of this hypothesis, we observed that 20 min of visual cortex a-tDCS reduced lateral inhibition in the visual periphery of healthy observers by ≈30%.

Methods

Apparatus and visual stimuli

14 participants with best corrected visual acuity of ≤20/20 agreed to participate in the study. All participants provided written, informed consent. The study was approved by the University of Waterloo research ethics committee. All the procedures involved in this research adhered to the tenets of the Declaration of Helsinki. Participants were instructed to fixate a 0.2°central cross and respond to visual stimuli by pressing a key on a keyboard. Visual stimuli were created using PsychoPy[34,35] (available for free download: http://www.psychopy.org). The stimuli were presented on a 27" LCD (ASUS - https://www.asus.com/ca-en/Monitors/ROG-SWIFT-PG278QR/) placed at the distance of 50cm from a chinrest. The LCD background luminance was 32 cd/m^2.

The visual stimuli consisted of a central target, Gabor patch (size: 1° and spatial frequency: 7 cpd) presented 6° to the left of the fixation cross. Two flanker Gabor patches (7 cpd, 0.8 contrast) were presented above and below the target. The flanker Gabor patches were positioned at a distance of 2λ (lateral inhibition) or 6λ (control). Throughout the procedure, fixation was monitored using an infrared video-based eye tracker (EyeLink II, SR Research, Osgoode, Canada, 500 Hz sampling rate).

Psychophysical task

The 2AFC lateral masking task involved the measurement of contrast detection thresholds for the central target Gabor patch. The initial contrast of the central Gabor patch was set at 0.5 and its contrast was altered using a 2 down and 1 up staircase procedure with a fixed step size of 0.05. The staircase was terminated either after 50 trials or 5 reversals. The contrast detection threshold was determined as the mean of the last 4 reversals. The same procedure was followed for both flanker distances of 2λ and 6λ. These particular flanker distances were selected based on a previous study reporting colinear inhibition for 2λ but not for 6λ[32] and our own pilot data supporting this observation. The 2λ separation was our experimental condition and the 6λ condition was a control condition to test for any general effects of a-tDCS on contrast sensitivity for the target stimulus.

Brain-stimulation (tDCS)

tDCS was delivered by a DC Stimulator MC from NeuroConn gmbh (https://www.rogue-resolutions.com/catalogue/neuro-modulation/dc-stimulator-tes/) using a pair of rubber electrodes (5mm x

5mm) placed inside saline soaked sponges. The electrodes were secured in place by the head strap of the eye tracker over electrode positions Oz (anodal electrode) and Cz (cathodal electrode) as shown in Figure 1. Participants each completed two randomly sequenced stimulation sessions; real 0.2mA anodal tDCS of the primary visual cortex for 20 minutes and sham tDCS where the current was ramped up and then immediately ramped down with the electrodes kept in place to 20 minutes. Participants were masked to the type of stimulation. During each test session, participants completed a block of four threshold measurements for each flanker distance pre-, during-, 5mins post- and 30mins post-stimulation. The sequence of 2λ and 6λ separation measurements was randomized within each test block.

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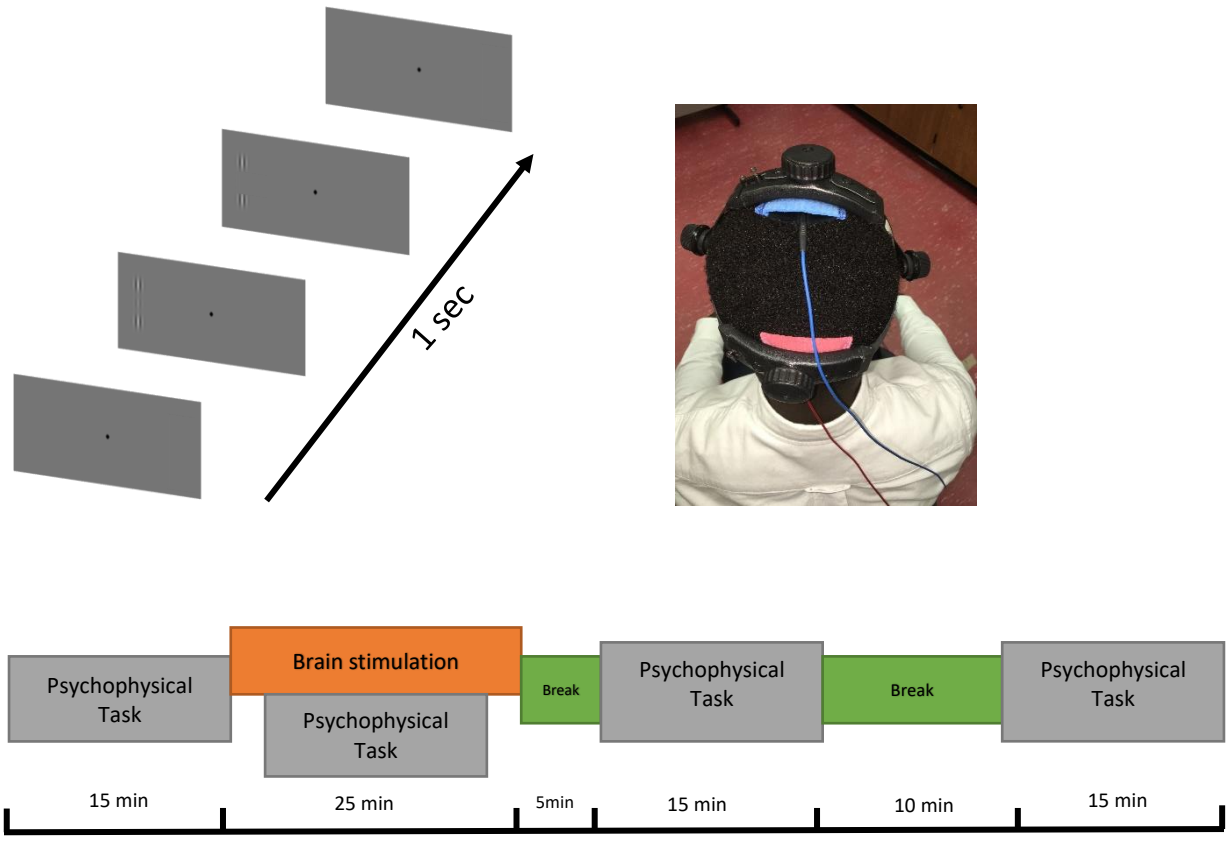

Figure 1: Stimuli and procedure.

A) Collinear configuration of Gabor patches that have the same orientation and phase. B) Sample picture of a participant wearing the eye tracker and the electrodes (pink-anodal and blue-reference) of tDCS secured using the head strap of the eye tracker. C) Timeline of the experiment. The same timeline was used for anodal and sham stimulations.

Data Analysis

A mixed ANOVA with within-subject factors of stimulation type (anodal vs. sham) and time (pre-, during-, 5 minutes post- and 30 minutes post-stimulation) was applied to the log contrast thresholds. Post-

hoc Tukey HSD was used to compare the log contrast thresholds between different stimulation sessions. A p value of <0.05 was considered statistically significant.

Results

Baseline contrast detection thresholds for the central Gabor patch differed significantly between the two flanker separation conditions, with higher thresholds for the 2λ separation than the 6λ separation (mean ± SEM; 2λ 0.36±0.03, 6λ 0.14±0.02, $t_{12} = 8.2$, $p < 0.001$). This is consistent with previous observations of collinear inhibition within peripheral vision at a target/flanker separation of 2λ[31,33] but not at a 6λ separation.

Figure 2 shows baseline-normalized group means (panels A and B) and raw individual participant data (panels C-H) for the a-tDCS and sham stimulation sessions for the 2λ (left column) and 6λ (right column) flanker separation conditions. For the 2λ separation, a-tDCS significantly improved contrast detection thresholds for the central target (reduced colinear inhibition) whereas sham stimulation had no effect. There was a significant interaction between stimulation type [anodal vs. sham] and time [pre, during, post 5 min, post 30 min] ($F_{3, 36} = 2.95$, $p=0.045$), with post-hoc Tukey HSD comparisons revealing significantly reduced contrast thresholds relative to baseline for the a-tDCS session during stimulation ($p=0.003$) and 30 min post stimulation ($p=0.004$). Thresholds at the 5 min post stimulation timepoint did not differ significantly from baseline ($p=0.09$). Thresholds within the sham stimulation session did not differ from baseline for any timepoint. For the 6λ separation, there was no significant interaction between stimulation type and time ($F_{3, 33} = 0.59$, $p=0.62$) indicating no difference between a-tDCS and sham on contrast detection thresholds.

Discussion

The purpose of the study was to test the hypothesis that anodal tDCS would reduce collinear lateral inhibition in peripheral vision of observers with normal vision. The hypothesis was based on previous reports of improved peripheral Vernier acuity, Snellen acuity and contrast sensitivity[29] along with reduced center-surround suppression[27] following occipital lobe a-tDCS in participants with normal vision. Enhanced contrast sensitivity and modulation of visual cortex activity following a-tDCS have also been observed in patients with amblyopia.[25,26] We observed a significant reduction of collinear inhibition during and 30 min after a single 20 min application of a-tDCS to the occipital lobe. The effects of single a-tDCS sessions are transient, but this result suggests that a-tDCS is able to modulate low-level lateral interactions in early visual cortex that may contribute to crowding in peripheral vision.

A number of explanations have been proposed for the effects of visual cortex a-tDCS. These include changes in response gain[29], stochastic resonance leading to increased signal strength[36], and reduced GABA-mediated inhibition[22,24]. Our results are most clearly aligned with a reduction in cortical inhibition as we observed an effect for the lateral inhibition condition but not the control condition that would have also benefitted from response gain and stochastic resonance changes. Our results also support previous work indicating that lateral inhibition takes place in V1[31,37], the primary target of our stimulation.

Previous studies have observed that collinear lateral inhibition can be reduced using perceptual learning in observers with normal vision[12] and observers with macular degeneration[10]. Maniglia et al.[12] reported an approximately 40% reduction of peripheral collinear lateral inhibition after training in healthy observers. However, in order to achieve this reduction, each participant underwent 160 sessions over the course of 8 weeks (≈ 7600 trials/week). In this study, we observed that a single session of anodal tDCS reduced collinear lateral inhibition by approximately 30%. This suggests that a-tDCS may enhance the effects of perceptual learning paradigms designed to reduce colinear lateral inhibition. Indeed, a very recent study of healthy adults by Contemori et al. observed that the combination of a different tDCS protocol, transcranial random noise stimulation, and perceptual learning reduced peripheral crowding for trigram stimuli to a greater extent than perceptual learning alone[38]. Furthermore, tDCS increased the transfer of learning to other tasks. Taken together, the present results and the results of Contemori et al.[38] provide a strong foundation for the application of non-invasive brain stimulation to the rehabilitation of patients with central vision loss, for whom crowding is a major cause of visual disability [39].

One limitation of our study is that there is no consensus on whether lateral masking and crowding are associated, although they share similar features such as increasing strength with eccentricity[40]. In particular, the mechanism of crowding is likely to involve higher visual processing centers[40]. Nonetheless, it is plausible that enhancing the early stages of visual processing by reducing collinear inhibition will improve higher-level visual processing of crowded stimuli [41,42].

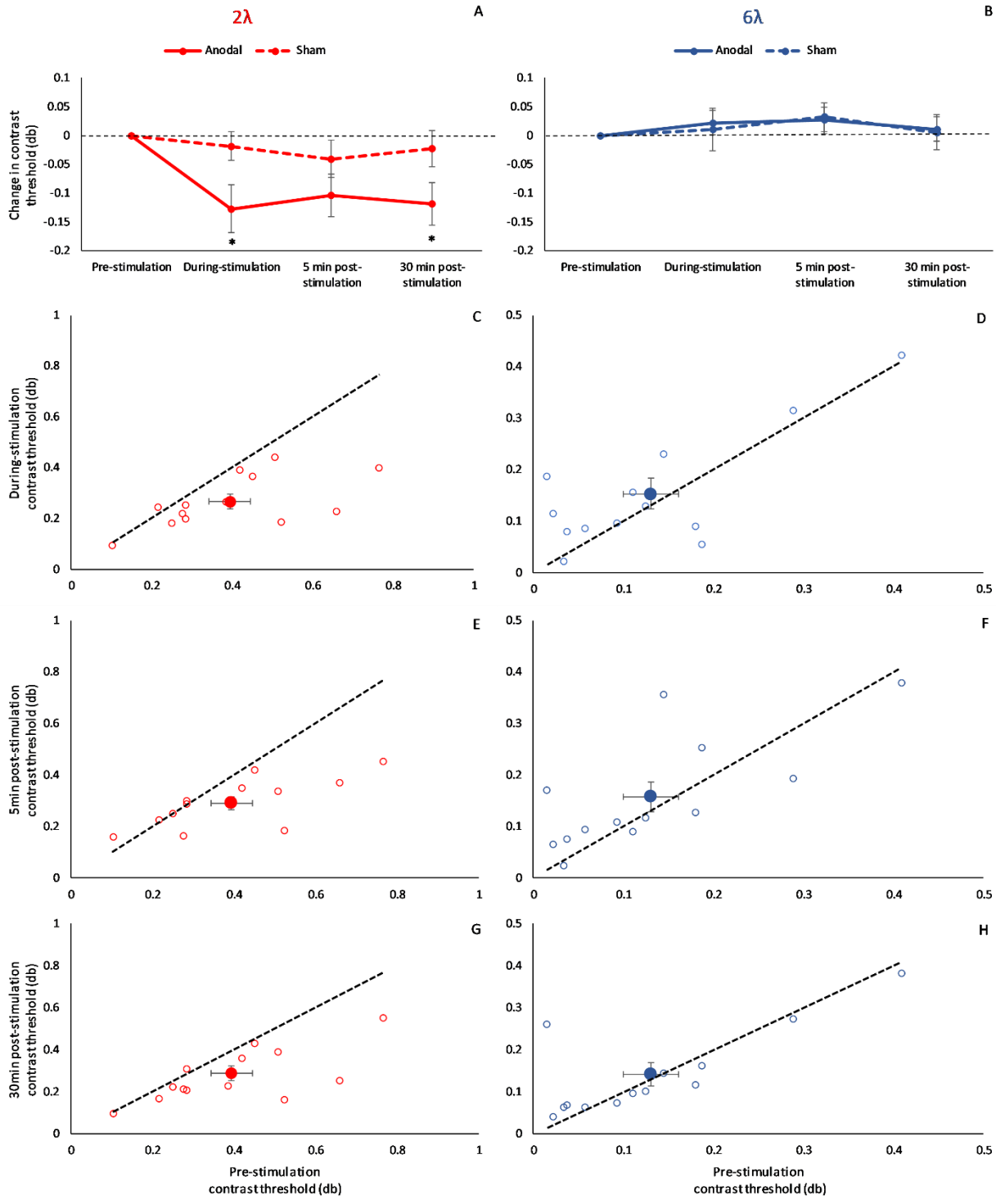

Figure 2:Reduction of collinear inhibition using anodal-tDCS..

A & B) Mean change in contrast detection threshold from the baseline for the 2λ (red) and 6λ (blue) flanker distances for anodal (solid line) and sham (dashed line). error bars represent ±1 SEM and asterisk symbols represent statistical significance ($p<0.05$). C, E & G) Individual pre-stimulation contrast detection thresholds plotted as a function of during-, 5min post- and 30min post-stimulation contrast detection thresholds for the 2λ flanker a-tDCS condition. Data points below the dotted line indicate reduced contrast detection thresholds (reduced collinear lateral inhibition), during- and post-stimulation. D, F & H) Individual

pre-stimulation contrast detection thresholds as a function of during-, 5min post- and 30min post-stimulation contrast detection thresholds for the 6λ flanker a-tDCS condition.

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