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Modulating attentional biases of adults with autistic traits using transcranial direct current stimulation: a pilot study.

Short title: TDCS alters attentional biases of High ALT adults

Authors: Michael C W English[1], Emma S Kitching[1], Murray T Maybery[1] and Troy A W Visser[1]

Affiliation: [1]School of Psychological Science, University of Western Australia, 35 Stirling Highway, Crawley, WA 6009, Australia

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Abstract: While neurotypical individuals over-attend to the left-side of centrally-presented visual stimuli, this bias is reduced in individuals with autism/high levels of autistic traits. Because this difference is hypothesized to reflect relative reductions in right-hemisphere activation, it follows that increasing right-hemisphere activation should increase leftward bias. We administered transcranial direct current stimulation (tDCS) over the right posterior parietal cortex to individuals with low levels (n = 19) and high levels (n = 19) of autistic traits whilst they completed a greyscales task. Anodal tDCS increased leftward bias for high-trait, but not low-trait, individuals, while cathodal tDCS had no effect. This outcome suggests that typical attentional patterns driven by hemispheric lateralization could potentially be restored following right-hemisphere stimulation in high-trait individuals.

Lay Summary: Attentional differences between individuals with and without autism may reflect differences in underlying activation of the left and right hemispheres. In this study, we combine an attentional task that reflects relative hemispheric activation with non-invasive cortical stimulation, and show that attentional differences between healthy individuals with low and high levels of autistic-like traits can be reduced. This outcome is encouraging, and suggests that other aspects of attention in autism (e.g. face processing) may stand to benefit from similar stimulation techniques.

Keywords: autism; autistic traits; spatial attention; lateralization; transcranial direct current stimulation (tDCS); right hemisphere

Introduction

Whilst neurotypical individuals tend to show pseudoneglect, an attentional bias towards stimulus features presented in the left hemifield (Jewell & McCourt, 2000) driven by the relatively greater lateralization of spatial attention to the right hemisphere (RH) (Siman-Tov et al., 2007), this attentional bias is reduced in individuals with autism spectrum conditions (ASC). Compared to controls, adults with ASC and infants with older ASC siblings show reduced eye-gaze to the left side of centrally-presented faces (Dundas, Best, Minshew, & Strauss, 2012; Dundas, Gastgeb, & Strauss, 2012), whilst adults with Asperger Syndrome show reduced leftward bias on face-identity matching (Ashwin, Wheelwright, & Baron-Cohen, 2005). Similar patterns are also found for neurotypical individuals with high levels of autistic-like traits (High ALT) viewing non-face stimuli (English, Maybery, & Visser, 2015, 2017).

Another aspect of attention linked to RH regions is global processing; the ability to integrate multiple independent stimuli into a coherent and meaningful whole (Hübner & Studer, 2009; Malinowski, Hübner, Keil, & Gruber, 2002; Weissman & Woldorff, 2005; Yamaguchi, Yamagata, & Kobayashi, 2000). Here too, individuals with ASC/High ALT show a reduction in global processing relative to neurotypical peers (for meta-analyses, see Cribb, Olaithe, Di Lorenzo, Dunlop, & Maybery, 2016; Van der Hallen, Evers, Brewaeys, Van den Noortgate, & Wagemans, 2015). In turn, this reduced global processing has been linked with poorer face identification and emotional recognition (Behrmann, Thomas, & Humphreys, 2006; Gross, 2005) – key elements of social processing.

It is possible that reductions in both pseudoneglect and global processing are the result of reduced right-side lateralization for spatial attention in individuals with ASC/High ALT. If that were the case, non-invasive transcranial direct current stimulation (tDCS) might be effective in shifting this imbalance and modulating associated attention-related task performance. TDCS has been previously used to elicit shifts in spatial attention by stimulating or disrupting posterior parietal cortex (PPC) activation in neurotypical individuals (Loftus & Nicholls, 2012; Roy, Sparing, Fink, & Hesse, 2015; Sparing et al., 2009) and to improve social functioning outcomes for individuals with ASC via disruption of the left dorsolateral prefrontal cortex (D'Urso et al., 2014, 2015). However, to our knowledge, no study has attempted to invoke attentional shifts using tDCS in individuals with either ASC or High ALT.

The present study aims to provide preliminary examination of the attentional changes induced via anodal and cathodal tDCS of the right PPC of neurotypical adults with Low and High ALT. Attentional changes as a result of tDCS were assessed by measuring performance on the greyscales task (Nicholls, Bradshaw, & Mattingley, 1999), which has been shown to be sensitive to differences in attentional bias between Low and High ALT groups (English et al., 2015, 2017).

Method

Participants

Thirty-eight right-handed undergraduate students from the University of Western Australia participated in the study in exchange for partial course credit. All participants provided informed consent and ethical approval for the experimental procedures was obtained from the University's Human Research Ethics Office.

Materials

Questionnaires

ALT levels were assessed using the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), a 50-item self-report questionnaire, scored using Austin's (2005) 1-4 method. Handedness was assessed using the ten-item Edinburgh Handedness Inventory (Oldfield, 1971).

Greyscales Task

The task was adapted from English et al. (2015). Stimuli were generated using Presentation software (Version 17.0, Neurobehavioral Systems) and presented on a 24" BenQ XL2420T monitor. Participants were seated approximately 50cm from the display. Trials consisted of a central fixation cross presented for 1500ms, followed by two horizontal bars presented above and below the display's centre. From the left, one bar was shaded white-to-black, with the number of black pixels increasing evenly across the stimulus. The other bar was shaded similarly but in the reverse direction (Figure 1). Finally, one bar was 'darker, achieved by randomly replacing 100 white pixels with black pixels evenly across the bar, and similarly replacing 100 black pixels with white pixels across the other bar. The top/bottom positions of the left-to-right shaded bar and the overall darker bar were varied randomly but counterbalanced across trials. Participants were instructed to select the bar they perceived was 'darker' overall by pressing the T ("top") or B ("bottom") keys. Participants had 5s to make their response – if no response was recorded, the trial was repeated after the remaining trials.

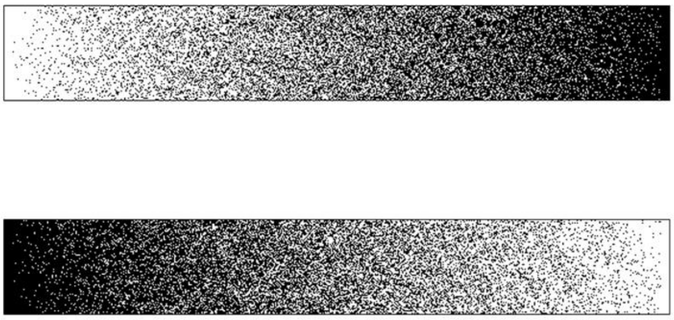

Figure 1. Example of a stimulus presented in the greyscales task.

Transcranial Direct Current Stimulation (tDCS)

Stimulation was applied to the right PPC using a battery-driven stimulator (Dupel Iontophoresis System, MN) via a pair of 6x4cm electrodes placed on the scalp in saline-moistened sponge pouches. Electrode configuration followed that used in prior work (Loftus & Nicholls, 2012; Roy et al., 2015; Sparing et al., 2009). During anodal stimulation, the reference was placed at the Cz position according to the International 10-20 System (Klem, Lüders, Jasper, & Elger, 1999), and the active electrode at P4. This configuration was reversed for cathodal stimulation. For anodal and cathodal stimulation, the current was gradually ramped up to 2mA over 30s and maintained at this level for the duration of the session. Mean stimulation duration was 9.76 min (*SD*=2.06) and a repeated measures analysis of variance (ANOVA) showed that durations did not differ across stimulation conditions or ALT groups (all $ps>0.55$, all $\eta_p^2s<0.02$).

Procedure

Participants completed the experiment over two days separated by a minimum 24-hour period (see Figure 2 for a diagram of the experimental flow). On each day, participants completed two 168-trial sessions of the greyscales task. There were four session types. In the initial practice session, participants completed the task without wearing the tDCS apparatus. In the anodal and cathodal sessions, the respective stimulation was applied during the task. In the sham (placebo) condition, the current was ramped up to 2mA, but immediately ramped down again over 30s. This was intended to create a physical experience like anodal and cathodal stimulation with minimal or no effect on neural excitability (Loftus & Nicholls, 2012; Sparing et al., 2009). The administration order of the anodal and cathodal conditions was counterbalanced across participants and always followed the practice/sham sessions to avoid carry-over stimulation effects between sessions.

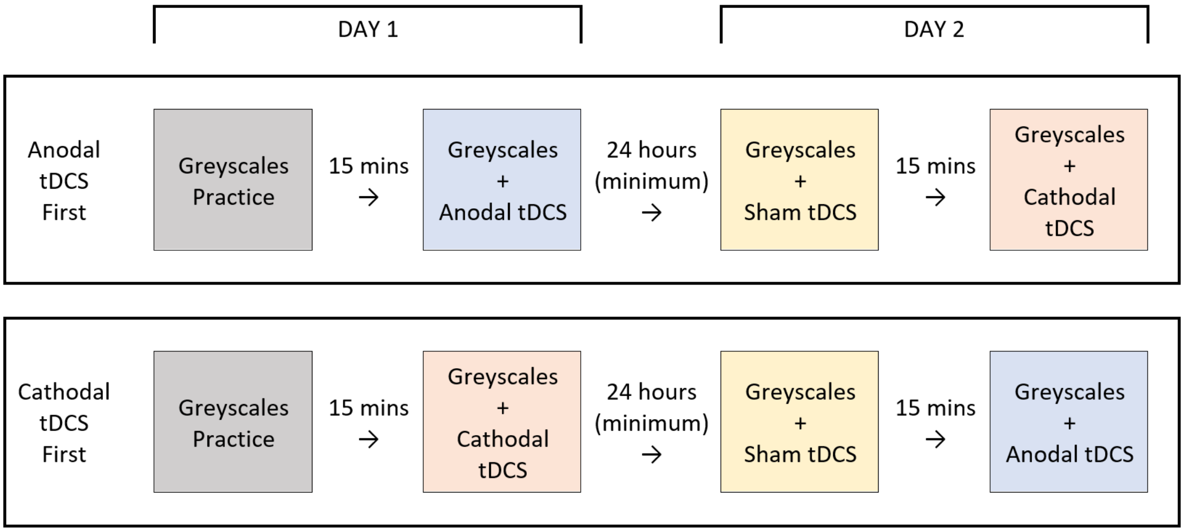

Figure 2. Order of administration of the tDCS conditions, with half of the sample receiving the first order and half the second.

Results

Low- and High-ALT groups were created using a median split of AQ scores (median = 107) following previous methodology (English et al., 2015). Accuracy was calculated as the percentage of trials on which participants selected the darker stimulus. Pseudoneglect was calculated as the percentage of trials on which participants selected the bar with most black pixels oriented towards the left side of the screen.

Four participants (1 Low ALT, 3 High ALT) data were omitted because their pseudoneglect scores across the anodal, cathodal and sham sessions were identified as multivariate outliers (Mahalanobis Distance: $\chi^2>7.82$, $p<0.05$). The remaining participants' descriptive statistics are presented in Table 1. An independent-samples t-test confirmed that AQ scores differed between Low- and High-ALT groups, $t(32)=8.20$, $p<0.001$, $d = 2.90$.

Table 1. Descriptive statistics for the Low and High ALT groups (standard deviations presented in parentheses).

	Low ALT (n=18)	High ALT (n=16)
Sex	8 male, 10 female	10 male, 6 female
Mean age (years)	21.28 (1.23)	21.19 (2.00)
Mean AQ	95.67 (9.75)	120.63 (7.72)

A one-sample t-test verified that mean task accuracy (M=55.25%, SD=5.87%) was significantly greater than chance levels (50%), $t(31)=5.21$, $p<0.001$, $d=1.68$. We also verified that any changes in pseudoneglect were not attributable to variations in accuracy by submitting mean accuracy scores to a 2 (ALT Group; Low or High) x 3 (Stimulation Type; anodal, sham and cathodal) repeated-measures ANOVA. No main effects or interactions were found (all p's > 0.23, all η_p^2's < 0.04). To determine whether pseudoneglect differed between ALT groups in the absence of stimulation, Sham condition pseudoneglect scores were submitted to an independent samples t-test, which revealed no significant difference ($p = 0.22$, $d = 0.43$).

To test our main research question, mean pseudoneglect scores were submitted to a 2 (ALT Group) x 3 (Stimulation Type) x 2 (Sex) ANOVA (Type III sums of squares). Mean pseudoneglect scores are illustrated in Figure 3. This analysis revealed no main effect of ALT Group, $p=0.34$, $\eta_p^2=0.03$, but a main effect of Stimulation Type, $F(2,34)=16.36$, $p<0.001$, $\eta_p^2=0.29$, and, importantly, an ALT Group x Stimulation Type interaction, $F(2,34)=7.00$, $p<0.01$, $\eta_p^2=0.12$. There was no main effect of Sex and Sex did not interact with any other variables (all ps>0.23, all η_p^2s<0.04). To determine the source of the ALT Group x Stimulation Type interaction, we used paired-samples t-tests (Bonferroni corrected) to compare pseudoneglect scores in the sham condition relative to the anodal and cathodal conditions separately for each ALT group. Bayes factors were also calculated with *JASP* (JASP Team, 2017), using a default Cauchy prior width of $r=0.707$. The results of these analyses are summarized in Table 2.

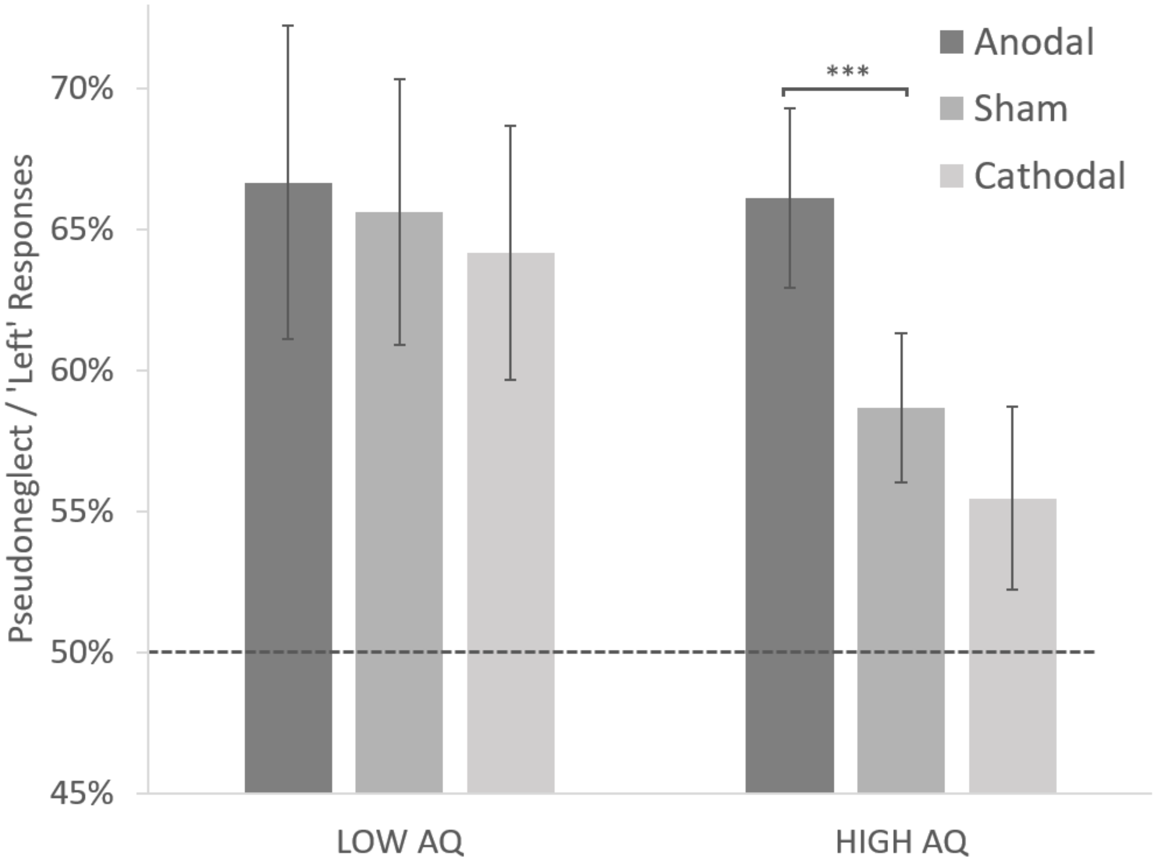

Figure 3. Pseudoneglect levels associated with each of the three types of stimulation (error bars represent one standard error of the mean). The dashed line highlights the level at which no pseudoneglect is present. *** p < 0.001.

Table 2. Summary of results from paired-sample t-tests conducted to evaluate differences in pseudoneglect as a function of Stimulation Condition for the two ALT groups.

	t	*p*	*d*	BF_{10}
Low ALT (n = 18)				
Anodal vs Sham	0.58	0.57	0.14	0.28
Sham vs Cathodal	0.95	0.35	0.23	0.36
Anodal vs Cathodal	1.26	0.23	0.30	0.48
High ALT (n = 16)				
Anodal vs Sham	4.09	< 0.001	1.02	39.13
Sham vs Cathodal	2.05	0.06	0.51	1.33
Anodal vs Cathodal	5.65	< 0.001	1.41	562.27

For the Low ALT group, no comparisons were statistically significant, indicating that there was no effect of tDCS for this group. Supporting this suggestion, BF_{10} scores for these comparisons were less than 1 indicating that the data supported an interpretation favoring the null hypothesis (Jeffreys, 1961; Raftery, 1995). By comparison, for the High ALT group, the Anodal-Sham and Anodal-Cathodal comparisons were statistically significant. In addition, BF_{10} scores exceeded 1 for all comparisons indicating that the data supported an interpretation that favors the alternative hypothesis (i.e. an effect of tDCS on pseudoneglect scores). In particular there was strong/very strong evidence ($BF_{10} > 30$) for the alternative hypothesis for the Anodal-Sham comparison and very strong/decisive evidence ($BF_{10}>150$) for the alternative hypothesis for the Anodal-Cathodal comparison. There was also weak/anecdotal evidence (BF_{10} = 1–3) for the alternative hypothesis for the Sham-Cathodal comparison (Jeffreys, 1961; Raftery, 1995).

Discussion

Following behavioral evidence that reduced levels of pseudoneglect and global processing in individuals with ASC/High ALT potentially reflect relatively lower activation of the RH (English et al., 2015, 2017), the present study examined whether tDCS applied over the right PPC could alter attentional biases in these individuals. Consistent with this hypothesis, anodal tDCS significantly increased pseudoneglect in our High ALT group relative to sham stimulation, while not yielding a significant increase in pseudoneglect in our Low ALT group. Such a pattern of results would be expected as the result of baseline pre-stimulation differences in RH activation between the two groups (English et al., 2015; Loftus & Nicholls, 2012). That is, the increased cortical excitability arising from anodal tDCS would more effectively increase RH activation in our High ALT group with lower pre-stimulation baseline, than in the Low ALT group, with relatively higher pre-stimulation RH activity. In turn, this would yield greater increases in levels of pseudoneglect in the High ALT group than in the Low ALT group.

Our findings also offer a fresh perspective on the failure of Loftus and Nicholls (2012) to observe an effect of right-PPC anodal stimulation on pseudoneglect in an ALT-unselected neurotypical sample. While the authors proposed that this outcome reflected generally high levels of right PPC pre-stimulation activation, our results suggest that this explanation may not adequately account for individual differences in levels of autistic traits. Put differently, it is likely that testing an unselected neurotypical sample which, collectively, likely had relatively high levels of RH activation, masked effects of anodal tDCS – effects which may be more readily apparent in a subset of individuals with relatively higher levels of autistic traits (and thus lower RH baseline activation).

Cathodal tDCS failed to produce any significant reductions in pseudoneglect for either ALT group. One plausible explanation is that factors other than baseline activation more strongly modulate the impact of cathodal stimulation. Indeed, effects of cathodal stimulation have not been observed in numerous studies (for a review, see Jacobson, Koslowsky, & Lavidor, 2012), and a multitude of factors, including stimulation duration, location and intensity, as well as task complexity, seem to contribute to situations where anodal and cathodal stimulation do not lead to systematic changes (Vallar & Bolognini, 2011). Given that the effects of cathodal stimulation are generally less robust than those arising from anodal stimulation, we suggest that further research is required to better understand the possible implications of the lack of cathodal stimulation effects on pseudoneglect.

That said, this interpretation should be taken somewhat cautiously because evidence for the absence of a baseline group difference in hemispheric activation in the present study is equivocal. Examination of Figure 3 suggests that baseline differences trended in the expected direction (i.e. greater baseline levels of pseudoneglect for the Low ALT group). Thus, it is possible that the present analysis was simply underpowered and that testing a larger sample would have revealed a significant difference. This conjecture is further supported by the results of Bayesian analysis of the Low ALT group where the Sham-Cathodal and Anodal-Cathodal results both showed only anecdotal/weak evidence in favor of the null hypothesis. Nevertheless, it is also the case that the main aim of the present study was to determine if High ALT individuals respond to tDCS in the context of a task that indexes spatial bias, and the current sample size was sufficient to show that this is the case.

In summary, this study is the first to our knowledge to show that atypical attentional biases in individuals with High ALT may be modulated using non-invasive cortical stimulation. If pseudoneglect can be shifted (at least, temporarily), what other aspects of attention could be similarly altered regarding autism? Spatial processes that have a relatively greater reliance on regions in the RH, such as global processing, potentially stand to benefit from techniques such as tDCS. For example, tDCS could assist with increasing otherwise low levels of RH activation that may be contributing to slowed global processing in autism (Van der Hallen et al., 2015), which is itself linked with less accurate/efficient processing of socially relevant information such as faces (Behrmann, Avidan, et al., 2006; Gross, 2005). Furthermore, determining the extent to which attentional modulations in individuals with ASC/High ALT can be made to persist over time will help establish the scope of changes that could arise from techniques to stimulate RH activity. A limitation of the present study that could be addressed in future work is the relatively small sample size observed, and a replication with a larger sample would assist in confirming the present findings. Finally, it is also critical to confirm the present findings using a sample with ASC as while individuals with High ALT are susceptible to attentional modulations following tDCS, this may not be true of individuals with ASC.

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