Author's Accepted Manuscript

Anodal-tDCS over the human right occipital cortex enhances the perception and memory of both faces and objects

Marica Barbieri, Marcello Negrini, Michael A. Nitsche, Davide Rivolta



 PII:
 S0028-3932(15)30270-0

 DOI:
 http://dx.doi.org/10.1016/j.neuropsychologia.2015.12.030

 Reference:
 NSY5841

To appear in: Neuropsychologia

Received date:21 October 2015Revised date:10 December 2015Accepted date:28 December 2015

Cite this article as: Marica Barbieri, Marcello Negrini, Michael A. Nitsche and Davide Rivolta, Anodal-tDCS over the human right occipital cortex enhances the perception and memory of both faces and objects, *Neuropsychologia*. http://dx.doi.org/10.1016/j.neuropsychologia.2015.12.030

This is a PDF file of an unedited manuscript that has been accepted fo publication. As a service to our customers we are providing this early version o the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain

Anodal-tDCS over the human right occipital cortex enhances the

perception and memory of both faces and objects

Marica Barbieri, MSc^{1,2}*, Marcello Negrini, MSc^{1,2}*, Michael A. Nitsche, MD^{3,4} & Davide

Rivolta, PhD¹

1. School of Psychology, University of East London (UEL), London, UK.

2. Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy

red m

3. Department of Psychology and Neuroscience, Leibniz Research Center for Working Environment and Human Factors (*IfADo*), Dortmund, Germany.

4. Department of Neurology, University Medical Hospital Bergmannsheil, Bochum, Germany

* Shared first authorship

Corresponding author:

Dr Davide Rivolta

School of Psychology, University of East London (UEL), Water Lane, E15 4LZ, London, UK

Phone: +44(0)2082234737; Email: d.rivolta@uel.ac.uk

Running title: tDCS increases face and object processing

Abstract

Accurate face processing skills are pivotal for typical social cognition, and impairments in this ability characterise various clinical conditions (e.g., prosopagnosia). No study to date has investigated whether transcranial direct current stimulation (tDCS) can causally enhance face processing. In addition, the category- and the process- specificity of tDCS effects, as well as the role of the timing of neuromodulation with respect to the execution of cognitive tasks are still unknown. In this single-blind, sham-controlled study, we examined whether the administration of anodal-tDCS (a-tDCS) over the right occipital cortex of healthy volunteers (N = 64) enhances performance on perceptual and memory tasks involving both face and object stimuli. Neuromodulation was delivered in two conditions: *online* (a-tDCS during task execution) and offline (a-tDCS before task execution). The results demonstrate that offline atDCS enhances the perception and memory performance of both faces and objects. There was no effect of online a-tDCS on behaviour. Furthermore, the offline effect was site-specific since a-tDCS over the sensory-motor cortex did not lead to behavioural changes. Our results add relevant information about the breadth of cognitive processes and visual stimuli that can be modulated by tDCS, and about the design of effective neuromodulation protocols, which have implications for advancing theories in cognitive neuroscience and clinical applications.

Keywords: face perception, object perception, face memory, object memory, tDCS

1. Introduction

Our ability to learn and recognise hundreds of faces is crucial for typical social interactions. The dramatic consequences of atypical face processing can be seen, for instance, in congenital prosopagnosia (CP), a disorder characterised by the inability to recognise people from their faces (Behrmann & Avidan, 2005; Duchaine, 2000; Rivolta, Palermo, & Schmalzl, 2013; Rivolta, Palermo, Schmalzl, & Coltheart, 2012). Face processing aberrations are also reported in neurodevelopmental disorders such as autism (Tang et al., 2015) and schizophrenia (Rivolta, Castellanos, et al., 2014), and in patients with acquired brain lesions such as in acquired prosopagnosia (Barton, 2008). Since face processing impairments characterise a variety of neurological and psychiatric conditions, it is of paramount importance to find strategies that are effective in ameliorating deficits in face-processing skills.

One way to potentially enhance human cognitive skills is via a non-invasive brain stimulation technique called *transcranial Direct Current Stimulation* (tDCS) (Nitsche et al., 2008; Nitsche, Liebetanz, Antal, et al., 2003; Poreisz, Boros, Antal, & Paulus, 2007). In the most traditional set-up, tDCS consists of placing two electrodes (the "target" and the "reference") on the scalp, and delivering a small current (\approx 1-2 mA) through them (Nitsche, Liebetanz, Lang, et al., 2003). TDCS alters cortical excitability via subthreshold depolarisation or hyperpolarisation of resting state membrane potentials (Bindman, Lippold, & Redfearn, 1964; Creutzfeldt, Fromm, & Kapp, 1962; Radman, Ramos, Brumberg, & Bikson, 2009). A few minutes of stimulation can induce after-effects, which reflect calcium (Ca⁺)- dependent plastic changes mediated by the N-methyl-D-aspartate receptor (NMDA-R), thus resembling long-term-potentiation (LTP)- and long-term-depression (LTD)- like plasticity (Liebetanz, Nitsche, Tergau, & Paulus, 2002; Nitsche, Fricke, et al., 2003; Nitsche et al., 2004). Depolarisation is typically achieved via "*anodal*" stimulation, whereas

hyperpolarisation typically follows "*cathodal*" stimulation (Fregni et al., 2015). In the context of tDCS, "polarity" refers to the polarity of the electrode positioned over the target region.

Human studies have demonstrated that anodal tDCS (a-tDCS) can enhance motor and cognitive skills. In typical subjects, a-tDCS has been shown to enhance motor learning when applied over the motor cortex (Nitsche, Schauenburg, et al., 2003), modulate attention when administered to the parietal cortex (Roy, Sparing, Fink, & Hesse, 2015), and boost working-memory performance when applied over the dorso-lateral-prefrontal-cortex (DLPFC) (Fregni et al., 2005). In addition, a-tDCS over the DLPFC has recently been adopted in psychiatric settings and shown to be effective in decreasing depressive symptoms in patients with chronic depression (Dell'Osso et al., 2012) and in boosting working-memory performance of patients with schizophrenia (Hoy, Arnold, Emonson, Daskalakis, & Fitzgerald, 2014) (see Shin, Foerster, & Nitsche, 2015 for a review).

Despite its reported efficacy in neurological, cognitive and clinical domains, only very little tDCS research has been conducted in the domain of face processing. There is cognitive (Bruce & Young, 1986), neural (Haxby et al., 2001) and clinical (Palermo et al., 2011) evidence indicating that face processing relies on parallel (and largely independent) systems mediating the recognition of facial identity and facial expression (i.e., emotion) recognition. Albeit recent evidence demonstrated that facial expression recognition can be boosted in healthy volunteers when delivering a-tDCS over the orbitofrontal-cortex (OFC) (Willis, Murphy, Ridley, & Vercammen, 2015), no study to date has examined the role of a-tDCS in enhancing face identification skills in typical human subjects. Additionally, no study has ascertained whether a-tDCS applied over visual areas relevant for face perception modulates the perception of multiple categories of visual stimuli (e.g., faces and objects). The only study that focused on the neuromodulator effects of face-identification abilities in healthy individuals utilized transcranial Random Noise Stimulation (tRNS), a technique that induces

low-intensity alternate currents at random frequencies (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008). Results showed that individuals who received bilateral occipito-temporal tRNS demonstrated affected (i.e., enhanced) face-perception abilities, but not face-trustworthiness perception (Romanska, Rezlescu, Susilo, Duchaine, & Banissy, 2015).

Although these findings show promise that neuromodulation can specifically affect face-perception, there are important theoretical, methodological and clinical aspects that still need to be addressed. For instance, it is still unknown whether occipito-temporal neuromodulation is face-specific, or if it could implicate different categories of visual stimuli. In fact, since brain stimulation with Transcranial Magnetic Stimulation (TMS) over different neighbouring sections of the lateral occipital cortex (especially in the right hemisphere) (i.e., occipital face area; extrastriate body area; lateral occipital complex) can modulate (i.e., impair) the perception of different categories of visual stimuli such as faces, objects, bodies and scenes (Dilks, Julian, Paunov, & Kanwisher, 2013; Pitcher, Walsh, Yovel, & Duchaine, 2007), it would be important for clinical applications to discover methodologies (e.g., a-tDCS) that can show an opposite effect, thus leading to perceptual enhancement of multiple categories of visual stimuli.

In addition, since our ability to learn and recognise faces relies heavily on memory, it will be relevant to ascertain whether neuromodulation in the typical population is limited to face-perception (as shown in Romanska et al., 2015), or can also affect memory for faces. In line with Dalrymple et al. (2014), face-perception skills allow for representations of the properties of a face with minimal memory demand, whereas face-memory skills involve the successful storage, retention, and retrieval of face identity information. Since face-perception and face-memory skills can be dissociated in clinical populations (Barton, 2008; Dalrymple et al., 2014), it would be important to investigate the neurophysiological mechanisms that can specifically lead to their enhancement. Finally, though tRNS and tDCS sometimes show

similar outcomes at the behavioural level (Terney et al., 2008) that can be mediated by common plasticity effects (Fertonani, Pirulli, & Miniussi, 2011), the specific neurophysiological effects of tRNS are not very well known, thus making results harder to interpret (Antal, Nitsche, & Paulus, in press). As such, in the current study we tested whether a-tDCS over the right occipito-temporal cortex of healthy participants can enhance face-perception and face-memory performance. To test the potential category-specificity of the effect, we also assessed object-perception and object-memory.

Another aspect we considered was the "timing of stimulation" with respect to task performance. Previous research show mixed results - for instance, a-tDCS over the motor cortex delivered during motor learning was found to be more effective than if the stimulation was applied before training (Kuo et al., 2008; Nitsche, Schauenburg, et al., 2003; Stagg et al., 2011). On the other hand, a-tDCS over the primary visual cortex (V1) delivered before an orientation discrimination task yielded stronger behavioural effects than when applied during task execution (Pirulli, Fertonani, & Miniussi, 2013). Given its potential relevance in clinical settings, the current experiment also examined the effects of timing of a-tDCS (i.e., online vs. offline) on behavioural performance.

We hypothesized the following effects: since face and object processing are mediated by nearby areas in the occipito-temporal cortex (especially in the right hemisphere) (Grill-Spector, Kourtzi, & Kanwisher, 2001; Malach et al., 1995; Rivolta, Woolgar, et al., 2014; Rossion, 2014), we expected the effect of tDCS to act upon both categories of visual stimuli. Moreover, since right occipital lesions can affect various aspects of face and object processing (James, Culham, Humphrey, Milner, & Goodale, 2003; Rossion et al., 2003), we predicted an effect of tDCS on both perceptual and memory systems. With respect to timing effects of a-tDCS on behaviour, we had no clear predictions given the mixed findings in the existing literature.

CCEPTED MANUSCR

2. Materials and Methods

2.1 Participants

Forty-eight participants (15 males) without any recorded history of psychiatric or neurological disorders and with a mean age of 27 years (range 20 - 47) participated in this single-blind, sham controlled study. All participants had normal or correct-to-normal vision and did not report everyday life problems with face and object perception. The study was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and approved by the ethical committees of University of East London (UEL). After giving a complete description of the study to the participants, written informed consent was obtained. Participants were asked to sign an informed consent form and were provided with written information about the study and the procedure. 2 10

2.2 Experimental design

Participants were assigned to one of three groups (N = 16 in each group). Group-1 ("sham") received sham stimulation, Group-2 ("tDCS ON") received anodal tDCS stimulation while completing the tasks (i.e., online) and "Group-3" ("tDCS PRE") received anodal tDCS stimulation for 20 minutes before completing the tasks (i.e., offline). The three groups did not differ in age (F(2,45) = 1.68, p = .20) and had the same M/F ratio (i.e., 5 M per group). Given that it has been indicated that females show similar cortical excitability to males only during the follicular phase of the menstrual cycle (i.e., progesterone levels are low and estrogen levels are high) (Inghilleri et al., 2004), we tested female participants only during the follicular phase of their menstrual cycle (see Fertonani et al., 2011 for a similar approach).

Participants from all three groups performed four tasks: the face perception task (FP), the object perception task (OP), the Cambridge Face Memory Task (CFMT) and the Cambridge Car Memory Task (CCMT). Both the perception and the memory tasks had identical structures for face and object presentation. All tasks run on Windows and were administered on a DELL desktop computer with a 17-inch monitor with a resolution of 1152 x 864 pixels. In the Face Perception Task (FP) (adapted from Barense, Henson, & Graham, 2011) three grayscale images of unfamiliar human faces were presented on each trial. Two of the images were of the same face taken from different angles, whereas the third one belonged to a different face (Figure 1, left). Participants were required to select the face that was different from the other two by pressing a key. A total of 81 trials were presented. For each trial, participants had a time limit of 4 seconds to press the button; if the button press happened after 4 sec., the trial was considered incorrect. Accuracy and reaction times (RTs) were recorded. The Object Perception task (OP) (adapted from Barense et al., 2011) had the same structure of the FP but objects, rather than faces, were shown (see Figure 1, right). Both the FP and OP were run using E-prime software (Psychology Software Tools, Pittsburgh, PA). The presentation order of the four tasks was counterbalanced across participants.

The *Cambridge Memory Face task* (CFMT; Duchaine & Nakayama, 2006) is a memory task for unfamiliar faces which requires the learning of six faces to be recognised in three different viewing conditions: recognition of the same face images; recognition of the same faces in different images (different viewpoint and/or lighting), and recognition of the same faces in different images covered with heavy visual noise. The task is comprised of 72 trials and accuracy (% correct) was recorded. The *Cambridge Car Memory task* (CCMT; Dennett et al., 2011) is identical in structure to the CFMT, but uses cars rather than faces as stimuli.

To check for unexpected between-group differences, participants completed the Cambridge Face Perception Test *before* the tDCS setup (CFPT; Duchaine, Germine, &

Nakayama, 2007). The CFPT involves arranging a set of six faces from the most similar to the least similar relative to a target face. Performance (i.e., number of deviations from the correct sequence) was recorded as a baseline measure of face processing.

2.2.2 tDCS

TDCS was delivered by a battery driven, constant current stimulator (Neuroelectrics®, Barcelona, Spain) via a pair of surface sponge electrodes (25 cm²), soaked in a saline solution (0.9% NaCl), and applied to the scalp at the target areas of stimulation. Electrodes delivered a constant current of 1.5 mA (current density: 0.080 mA/cm²); the choice of the intensity is in line with previous studies showing visual-perception enhancement (e.g., Willis et al., 2015). In the sham condition participants wore the tDCS cap during task performance; here, stimulation was maintained for only the first and last 10 seconds to evoke the sensation of being stimulated, without causing neurophysiological changes that may influence performance. Group-2 and Group-3 received the actual constant current stimulation, but differed in the time when the current was delivered with respect to tasks completion. Group 2 (tDCS ON) received the stimulation *during* task execution (the stimulation started 3 minutes before the beginning of the first task and finished as soon as the fourth task ended). Overall, participants in this group were stimulated for approximately 24.6 minutes (SD = 3.9). Group 3 (tDCS PRE) received the stimulation for 20 minutes *before* any task execution (Figure 2). The timing of offline stimulation (i.e., 20 minutes) was chosen to be consistent with recent studies demonstrating an enhancement effect of face identification and expression recognition after transcranial electric stimulation (Romanska et al., 2015; Willis et al., 2015). During these 20 minutes participants were comfortably placed on a chair without talking to the experimenter.

We adopted a bilateral bipolar-non balanced montage (Nasseri, Nitsche, & Ekhtiari, 2015). The sites of stimulation were identified using the Electroencephalography 10-20 system, with one of the electrodes (anode / target) placed over PO8 and the other (cathode / reference) over FP1. The choice of the electrode target site over PO8 was based on prior work which showed that, when using electroencephalography (EEG), the PO8 site ideally records the N170, a well-known neurophysiological component which strongly reflects face neural activity within the ventral visual cortex (Navajas, Ahmadi, & Quian Quiroga, 2013; Prieto, Caharel, Henson, & Rossion, 2011). Furthermore, PO8 lies above face- and objectsensitive regions in the right lateral occipital cortex (Gauthier et al., 2000; Malach et al., 1995; Pitcher, Charles, Devlin, Walsh, & Duchaine, 2009). Overall, the right hemisphere has been chosen as a site of stimulation since there is consistent evidence suggesting its dominant role in face processing (Kanwisher, 2010; Rivolta, Woolgar, et al., 2014; Rossion, 2014). The FP1 region was selected as the reference point in order to maximise the anodal-cathodal stimulation distance, which decreases the current shunted through the scalp, while increasing the current density in depth (Rockstroh, Elbert, Canavan, Lutzenberger, & Birbaumer, 1989). In addition, no specific face/object-relevant neurophysiological activity is typically recorded under FP1, making it an optimal site to use as reference.

2.2.3 Statistical analysis

All analyses were conducted using SPSS Statistics software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). A one-way ANOVA was conducted to test for potential baseline (i.e., CFPT) effects. Two separate 3x4 mixed analyses of variances (ANOVAs) were performed on both accuracy and reaction times (RTs) with the factors condition (sham, tDCS_ON, tDCS_PRE) as between-group factor, and task

(FP, OP, CFMT, CCMT) as a within group factor (see Romanska et al., 2015 for a similar approach). Post-hoc comparisons (Bonferroni-corrected) were performed in order to explore statistically significant main effects and interactions. Non-parametric Mann-Whitney (U) test was conducted to assess the order effect in the tDCS_ON condition (see results below).

3. Results

Participants did not report any discomfort during the three sessions. In addition, participants across the three groups did not differ in their performance on the CFPT [F(2, 47) = 1.23, p = .29, $\eta^2_{P} = .05$], thus suggesting an absence of baseline differences across groups.

Results showed a main effect of condition $[F(2, 45) = 5.67, p = .006, \eta^2_P = .20]$ and a main effect of task $[F(3, 135) = 14.26, p < .001, \eta^2_P = .24]$. There was no condition x task interaction $[F(6, 135) = 0.26, p = .95, \eta^2_P = .01]$. Post-hoc comparisons showed that tDCS_PRE (mean = 78.84%, SEM = 1.71) was, overall, characterised by higher accuracy than both the sham (mean = 71.83%, SEM = 1.71) (p = .017) and the tDCS_ON (mean = 71.74%, SEM = 1.71) (p = .016) conditions.

RTs analysis revealed no significant main effect of condition [F(2, 45) = 1.05, p = .36, $\eta^2_P = .05$], no significant main effect of task [F(1, 45) = 0.00, p = .98, $\eta^2_P = .01$], and no condition x task interaction [F(2, 45) = 0.19, p = .82, $\eta^2_P = .01$].

Since the tDCS_ON condition lasted on average 5 minutes longer than the tDCS-PRE condition we aimed to exclude the presence of effects due to time of stimulation. An order effect within the tDCS_ON condition would be present if performance increases or decreases during time, and thus would depend in a non-linear fashion on stimulation duration. Thus, we compared performance of each of the four tasks in the tDCS_ON condition when it was presented as first or second (i.e., within the first half), or as third or fourth (i.e., within the

second half). Non-parametric Mann-Whitney (U) test showed that there was no order effect in the performance of FP (first half: 75.1%, SD: 9.3; second half: 75.0%, SD: 10.0; p = .959), OP (first half: 64.4%, SD: 13.5; second half: 73.4%, SD: 8.1; p = .252), CFMT (first half: 81.3%, SD: 10.9; second half: 71.6%, SD: 13.0; p = .114) and CCMT (first half: 63.2%, SD: 13.9; second half: 66.9%, SD: 14.9; p = .681), thus indicating that the extra time of stimulation should have not affected our results.

4. Control condition: Rationale, Method and Results

To ascertain whether the *offline* a-tDCS behavioural enhancement was site specific (i.e., it was specifically due to right occipital stimulation and not to an unspecific stimulation effect), and to exclude potential behavioural effects due to testing time (i.e., participants in the sham and tDCS_ON conditions spent seventeen minutes less sitting on a chair than participants in the tDCS_PRE condition – see Methods section above), we collected data of extra sixteen healthy volunteers and compared their performance to the sham. The new sample (5 males; Age range: 20-40) was matched to the previous three groups and constituted our "tDCS_control" condition. The methodology adopted in the tDCS_control condition was identical to the one adopted in the tDCS_PRE (*offline*) condition; the only difference was in the location of the "active" electrode, which was now placed over the sensory-motor cortex (Cz) rather than over the right occipital cortex (P08).

Results showed no statistically significant difference between sham (Mean = 40; SEM = 3.0) and tDCS_control (Mean = 50; SEM = 6.9) on the CFPT [t(30) = 1.3, p = .19, d = .48], thus excluding baseline differences. In addition, a 2x4 mixed analyses of variances (ANOVAs) on accuracy was performed with condition (sham, control) as between-group factor, and task (FP, OP, CFMT, CCMT) as a within group factor. Results showed a main

effect of task [F(3, 90) = 5.98, p = .001, $\eta^2_P = .167$], but no main effect of condition [F(1, 30) = 1.44, p = .24, $\eta^2_{P} = .05$] and no task by condition interaction [F(1, 30) = 1.62, p = .21, $\eta^2_{P} = .21$.05]. Thus, our data indicate that, overall, sham (Mean = 71.8%; SEM = 2.1) and tDCS control (Mean = 68.3%; SEM = 2.1) conditions do not differ.

Overall, these results demonstrate that the effect of offline a-tDCS was site specific (i.e., right occipital) and was not due the effect of experimental time. In addition, this result excludes the contribution of the "return current" over left frontal regions in the reported offline a-tDCS effects (i.e., tDCS PRE). Scri

5. Discussion

In the present study, we demonstrate for the first time that a single session of offline a-tDCS targeted at the right lateral occipital cortex (PO8) can causally boost face-perception and face-memory. The effect of a-tDCS was not face-specific since it also improved general object-perception and object-memory. However, the effect of a-tDCS was site-specific, that is, stimulation of the sensory-motor cortex (Cz) did not lead to behavioural changes. Furthermore, a-tDCS applied online did not cause the effects seen in the offline condition.

The lateral occipital cortex is causally involved in visual cognition

Human face recognition relies on a network of cortical and subcortical brain regions (Haxby, Hoffman, & Gobbini, 2000). Over the last decade non-invasive brain stimulation techniques such as TMS (Pitcher et al., 2007) and tRNS (Romanska et al., 2015) demonstrated the causal involvement of the human lateral occipital cortex in face-perception skills. In line with this evidence, our findings show that a single session of a-tDCS causally boosts face-processing

skills in healthy individuals. Furthermore, our results extend previous findings by showing that face-memory, and not just face-perception skills, can be enhanced by a-tDCS. This is in line with human lesion data showing that right occipital lesions can lead to serious face-perception and face-memory difficulties (Barton, 2008; Davies-Thompson, Pancaroglu, & Barton, 2014).

Another novel aspect of our data is that the effect of a-tDCS is not process-specific (i.e., not limited to face perception) since it also affects object-perception and object-memory. Human neuroimaging studies have shown that face- and object- sensitive regions lie within the lateral occipital cortex (Dilks et al., 2013; Grill-Spector et al., 2001; Pitcher et al., 2009; Rivolta, Palermo, Schmalzl, & Williams, 2012). As such, it is not surprising that a-tDCS, which delivers a broad electrical stimulation, likely affects regions that process these two categories, thus causing behavioural enhancements on tasks that involve both faces and objects.

Overall, we demonstrated that offline a-tDCS can be safely applied over the human occipital cortex to improve face- and object- processing. This behavioural boost is likely driven by excitability after-effects, which enhance learning and perceptual processing (Antal et al., in press).

The relevance of timing in visual cognition

Our data also show that behavioural changes caused by a-tDCS are stronger when administered *offline* (i.e., neurostimulation before task execution), rather than *online* (i.e., neurostimulation during task execution). This finding is consistent with recent data in the cognitive domain; for instance, a-tDCS applied before task execution enhanced performance of a behavioural inhibition task (Ditye, Jacobson, Walsh, & Lavidor, 2012), and orientation

discrimination task (Pirulli et al., 2013). Particularly relevant to our results, Pirulli et al. (2013) showed that, when compared to the sham condition, *offline* a-tDCS over V1 has a bigger behavioural effect on an orientation discrimination task compared to *online* a-tDCS. Our finding are, however, in disagreement with the motor literature showing effective-*online*, (Boggio et al., 2006; Galea & Celnik, 2009; Nitsche, Schauenburg, et al., 2003; Reis et al., 2009), and ineffective/detrimental-*offline* (Kuo & Nitsche, 2012; Kuo et al., 2008; Stagg et al., 2011) a-tDCS. These differences in a-tDCS efficacy as a function of timing in the motor vs. cognitive domain may be due to neurophysiological differences between the motor and associative regions of the cortex, such as cyto- and myelo- architectonic diversities (e.g., differences in neuronal diameters may lead to different current propagations) (Spruston, 2008). Other sources of differences may include more technical aspects such as the electrodes size, current density, montage, and duration of stimulation (Stagg & Nitsche, 2011).

A potential limitation of the current study involves the duration of stimulation. In fact, individuals in the *online* a-tDCS condition (tDCS_ON) received, on average, circa 5 minutes longer stimulation than those who received a-tDCS *offline* (tDCS_PRE). This was necessary to ensure that each of the four tasks was completed while a-tDCS was applied. Here it might be relevant to acknowledge that the effect of a-tDCS on physiology and cognition does not always follow a linear rule; that is, more-intense/longer stimulations do not necessarily lead to stronger behavioural effects (Hoy et al., 2013; Monte-Silva et al., 2013). Thus, it might be speculated that the stronger physiological effects generated via a-tDCS during task performance (i.e., *online*), which could be mediated by (i) longer stimulation, (ii) presence of neuroplastic and acute membrane polarization effects, and (iii) summation of task- and stimulation- induced cortical activity alterations, have resulted in homeostatic or conversion effects that limited performance improvement. Albeit further studies are needed to clarify the issue, our finding of the absence of an order effect in the tDCS_ON condition seems to

CCEPTED MANUSCR

exclude the effect of time on performance. Furthermore, in line with our results, previous research showed enhanced performance on a visual perception task after stimulating the visual cortex with a-tDCS for \approx 30 minutes before task completion (i.e., *offline*), but failed to report an enhancement when stimulating for ≈ 30 min during (i.e., *online*) task completion (Pirulli et al., 2013).

A further point to highlight is that albeit both face/object-perception and face/objectmemory improved after right-occipital a-tDCS, it is hard to tell whether the improvement is truly independent for the two processes or whether the boost in face/object-perception has led nusci to improved face/object-memory.

Conclusions and Future directions

In summary, the current findings demonstrate that a single offline session of a-tDCS over the right lateral occipital cortex causally enhances the perception and memory of both faces and objects. Our results have implications for cognitive neuroscience and for clinical/therapeutic settings, as they offer insights to the design of effective neuromodulation protocols, and add to the breadth of cognitive processing (perception / memory), and stimuli (faces / objects) that can be modulated by a-tDCS. The present study also serves as a foundation for future studies examining the neurophysiological mechanisms of the effects of a-tDCS. For instance, it would be interesting to combine tDCS and EEG to characterise the oscillatory mechanisms behind the behavioural effects found in this study and/or to localise anatomical regions involved during a-tDCS stimulation. In addition, the current study sets the ground for future investigations aimed at characterising the boundaries of a-tDCS effects in low- and higherlevel vision. To conclude, a better knowledge of the features that lead to effective tDCS in typical subjects can be extended and applied to clinical populations, such as in CP.

Acknowledgments

We wish to thank Diandra Brkic, Adeeba Khan, Alona Saveljeva, Milani Pathmanathan and Emma C. Chester for their help in data collection. We wish to thank Dr Morgan Barense for kindly providing stimuli adopted in the face perception task (FP) and in the object perception task (OP). We also wish to thank Dr Isabella Premoli and Sharon Noh for their insightful comments on early versions of the manuscript.



Figure legends

Figure 1. Examples of faces and objects adopted in the face-perception task (FP) (left) and object-perception task (OP) (right).

Figure 2. Methodology adopted in three conditions: Sham (top), tDCS_ON (middle) and tDCS_PRE (bottom). Dotted lines indicate the time when participants wore the cap. The blue color (dotted with a thunder) indicates when tDCS has been applied, whereas the (dotted) black color indicates that the cap was on without tDCS.

Figure 3. Single-subjects accuracy values as averaged across the four tasks (FP, OP, CFMT, CCMT) in the three experimental conditions (Sham, tDCS_ON, tDCS_PRE). Average and SEM are indicated in red (* p < .05).

Figure 4. Accuracy results on the four tasks (FP, OP, CFMT, CCMT) across the three experimental conditions (sham, tDCS_ON, tDCS_PRE). Error bars represent the SEM.

References

- Antal, A., Nitsche, M. A., & Paulus, W. (in press). Application of transcranial brain stimulation (tDCS, tACS, tRNS): From the MEP biomarker towards modulation of behaviour *European Psychologist*.
- Barense, M. D., Henson, R. N., & Graham, K. S. (2011). Perception and conception: temporal lobe activity during complex discriminations of familiar and novel faces and objects. *J Cogn Neurosci, 23*(10), 3052-3067. doi: 10.1162/jocn_a_00010
- Barton, J. J. (2008). Structure and function in acquired prosopagnosia: Lessons from a series of 10 patients with brain damage. *Journal of Neuropsychology*, *2*(1), 197-225.
- Behrmann, M., & Avidan, G. (2005). Congenital prosopagnosia: Face-blind from birth *Trends in Cognitive Neuroscience*, *9*, 180-187.
- Bindman, L. J., Lippold, O. C., & Redfearn, J. W. (1964). THE ACTION OF BRIEF
 POLARIZING CURRENTS ON THE CEREBRAL CORTEX OF THE RAT (1)
 DURING CURRENT FLOW AND (2) IN THE PRODUCTION OF LONGLASTING AFTER-EFFECTS. *J Physiol, 172*, 369-382.
- Boggio, P. S., Castro, L. O., Savagim, E. A., Braite, R., Cruz, V. C., Rocha, R. R., . . . Fregni,
 F. (2006). Enhancement of non-dominant hand motor function by anodal transcranial
 direct current stimulation. *Neurosci Lett, 404*(1-2), 232-236. doi:
 10.1016/j.neulet.2006.05.051
- Bruce, V., & Young, A. (1986). Understanding face recognition. British Journal of Psychology, 77, 305-327.
- Creutzfeldt, O. D., Fromm, G. H., & Kapp, H. (1962). Influence of transcortical d-c currents on cortical neuronal activity. *Exp Neurol*, *5*, 436-452.

 Dalrymple, K. A., Garrido, L., & Duchaine, B. (2014). Dissociation between face perception and face memory in adults, but not children, with developmental prosopagnosia. *Developmental Cognitive Neuroscience, 10*, 10-20. doi: 10.1016/j.dcn.2014.07.003

Davies-Thompson, J., Pancaroglu, R., & Barton, J. (2014). Acquired prosopagnosia: structural basis and processing impairments. *Front Biosci (Elite Ed)*, *6*, 159-174.

Dell'Osso, B., Zanoni, S., Ferrucci, R., Vergari, M., Castellano, F., D'Urso, N., . . . Altamura,
A. C. (2012). Transcranial direct current stimulation for the outpatient treatment of poor-responder depressed patients. *Eur Psychiatry*, 27(7), 513-517. doi: 10.1016/j.eurpsy.2011.02.008

Dennett, H. W., McKone, E., Tavashmi, R., Hall, A., Pidcock, M., Edwards, M., & Duchaine,
B. (2011). The Cambridge Car Memory Test: A task matched in format to the
Cambridge Face Memory Test, with norms, reliability, sex differences, dissociations
from face memory, and expertise effects. *Behavior Research Methods*.

- Dilks, D. D., Julian, J. B., Paunov, A. M., & Kanwisher, N. (2013). The occipital place area is causally and selectively involved in scene perception. *J Neurosci*, 33(4), 1331-1336a. doi: 10.1523/jneurosci.4081-12.2013
- Ditye, T., Jacobson, L., Walsh, V., & Lavidor, M. (2012). Modulating behavioral inhibition by tDCS combined with cognitive training. *Exp Brain Res*, 219(3), 363-368. doi: 10.1007/s00221-012-3098-4

Duchaine, B. (2000). Developmental prosopagnosia with normal configural processing. *Neuroreport*, *11*(1), 79-83.

Duchaine, B., Germine, L., & Nakayama, K. (2007). Family resemblance: Ten family members with prosopagnosia and within-class object agnosia. *Cogn Neuropsychol*, 24, 419-430.

- Duchaine, B., & Nakayama, K. (2006). The Cambridge Face Memory Test: Results for neurologically intact individuals and an investigation of its validity using inverted face stimuli and prosopagnosic participants. *Neuropsychologia*, 44(4), 576-585.
- Fertonani, A., Pirulli, C., & Miniussi, C. (2011). Random noise stimulation improves neuroplasticity in perceptual learning. *J Neurosci*, 31(43), 15416-15423. doi: 10.1523/JNEUROSCI.2002-11.2011
- Fregni, F., Boggio, P. S., Nitsche, M., Bermpohl, F., Antal, A., Feredoes, E., . . . Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Exp Brain Res, 166*(1), 23-30. doi: 10.1007/s00221-005-2334-6
- Fregni, F., Nitsche, M. A., Loo, C. K., Brunoni, A. R., Marangolo, P., Leite, J., ... Bikson, M. (2015). Regulatory Considerations for the Clinical and Research Use of Transcranial Direct Current Stimulation (tDCS): review and recommendations from an expert panel. *Clin Res Regul Aff, 32*(1), 22-35. doi: 10.3109/10601333.2015.980944
- Galea, J. M., & Celnik, P. (2009). Brain polarization enhances the formation and retention of motor memories. *J Neurophysiol*, 102(1), 294-301. doi: 10.1152/jn.00184.2009
- Gauthier, I., Tarr, M. J., Moylan, J., Skudlarski, P., Gore, J. C., & Anderson, A. W. (2000). The fusiform "face area" is part of a network that processes faces at the individual level. *J Cogn Neurosci*, *12*, 495-504.
- Grill-Spector, K., Kourtzi, Z., & Kanwisher, N. (2001). The lateral occipital complex and its role in object recognition. *Vision Research*, *41*, 1409-1422.
- Haxby, J. V., Gobbini, M. I., Furey, M. L., Ishai, A., Schouten, J., & Pietrini, P. (2001).Distributed and overlapping representations of faces and objects in ventral temporal cortex. *Science*, 293, 2425-2430.

- Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends Cogn Sci*, *4*(6), 223-233.
- Hoy, K. E., Arnold, S. L., Emonson, M. R., Daskalakis, Z. J., & Fitzgerald, P. B. (2014). An investigation into the effects of tDCS dose on cognitive performance over time in patients with schizophrenia. *Schizophr Res*, 155(1-3), 96-100. doi: 10.1016/j.schres.2014.03.006
- Hoy, K. E., Emonson, M. R., Arnold, S. L., Thomson, R. H., Daskalakis, Z. J., & Fitzgerald,
 P. B. (2013). Testing the limits: Investigating the effect of tDCS dose on working memory enhancement in healthy controls. *Neuropsychologia*, *51*(9), 1777-1784. doi: 10.1016/j.neuropsychologia.2013.05.018
- Inghilleri, M., Conte, A., Curra, A., Frasca, V., Lorenzano, C., & Berardelli, A. (2004). Ovarian hormones and cortical excitability. An rTMS study in humans. *Clin Neurophysiol*, 115(5), 1063-1068. doi: 10.1016/j.clinph.2003.12.003
- James, T. W., Culham, J., Humphrey, G. K., Milner, A. D., & Goodale, M. A. (2003). Ventral occipital lesions impair object recognition but not object-directed grasping: an fMRI study. *Brain*, 126(Pt 11), 2463-2475. doi: 10.1093/brain/awg248
- Kanwisher, N. (2010). Functional specificity in the human brain: A window into the functional architecture of the mind. *Proceedings of the National Academy of Science* USA, 107(25), 11163-11170.
- Kuo, M. F., & Nitsche, M. A. (2012). Effects of transcranial electrical stimulation on cognition. *Clin EEG Neurosci*, 43(3), 192-199. doi: 10.1177/1550059412444975
- Kuo, M. F., Unger, M., Liebetanz, D., Lang, N., Tergau, F., Paulus, W., & Nitsche, M. A.
 (2008). Limited impact of homeostatic plasticity on motor learning in humans.
 Neuropsychologia, 46(8), 2122-2128. doi: 10.1016/j.neuropsychologia.2008.02.023

- Liebetanz, D., Nitsche, M. A., Tergau, F., & Paulus, W. (2002). Pharmacological approach to the mechanisms of transcranial DC-stimulation-induced after-effects of human motor cortex excitability. *Brain*, 125(Pt 10), 2238-2247.
- Malach, R., Reppas, J. B., Benson, R. R., Kwong, K. K., Jiang, H., Kennedy, W., . . . Tootell,
 R. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proceedings of the National Academy of Sciences (PNAS)*, US, 92, 8135-8139.
- Monte-Silva, K., Kuo, M. F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2013). Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. *Brain Stimul, 6*(3), 424-432. doi: 10.1016/j.brs.2012.04.011
- Nasseri, P., Nitsche, M. A., & Ekhtiari, H. (2015). A framework for categorizing electrode montages in transcranial direct current stimulation. *Front Hum Neurosci*, 9, 54. doi: 10.3389/fnhum.2015.00054
- Navajas, J., Ahmadi, M., & Quian Quiroga, R. (2013). Uncovering the mechanisms of conscious face perception: a single-trial study of the n170 responses. *J Neurosci*, 33(4), 1337-1343. doi: 10.1523/jneurosci.1226-12.2013
- Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., . . .
 Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimul*, 1(3), 206-223. doi: 10.1016/j.brs.2008.06.004
- Nitsche, M. A., Fricke, K., Henschke, U., Schlitterlau, A., Liebetanz, D., Lang, N., . . .
 Paulus, W. (2003). Pharmacological modulation of cortical excitability shifts induced by transcranial direct current stimulation in humans. *J Physiol*, *553*(Pt 1), 293-301. doi: 10.1113/jphysiol.2003.049916

Nitsche, M. A., Jaussi, W., Liebetanz, D., Lang, N., Tergau, F., & Paulus, W. (2004).
 Consolidation of human motor cortical neuroplasticity by D-cycloserine.
 Neuropsychopharmacology, 29(8), 1573-1578. doi: 10.1038/sj.npp.1300517

- Nitsche, M. A., Liebetanz, D., Antal, A., Lang, N., Tergau, F., & Paulus, W. (2003). Modulation of cortical excitability by weak direct current stimulation--technical, safety and functional aspects. *Suppl Clin Neurophysiol*, *56*, 255-276.
- Nitsche, M. A., Liebetanz, D., Lang, N., Antal, A., Tergau, F., & Paulus, W. (2003). Safety criteria for transcranial direct current stimulation (tDCS) in humans. *Clin Neurophysiol*, 114(11), 2220-2222; author reply 2222-2223.
- Nitsche, M. A., Schauenburg, A., Lang, N., Liebetanz, D., Exner, C., Paulus, W., & Tergau, F. (2003). Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. *J Cogn Neurosci, 15*(4), 619-626. doi: 10.1162/089892903321662994
- Palermo, R., Willis, M. L., Rivolta, D., McKone, E., Wilson, C. E., & Calder, A. J. (2011). Impaired holistic coding of facial expression and facial identity in congenital prosopagnosia. *Neuropsychologia*, 49, 1226-1235.
- Pirulli, C., Fertonani, A., & Miniussi, C. (2013). The role of timing in the induction of neuromodulation in perceptual learning by transcranial electric stimulation. *Brain Stimul*, 6(4), 683-689. doi: 10.1016/j.brs.2012.12.005
- Pitcher, D., Charles, L., Devlin, J. T., Walsh, V., & Duchaine, B. (2009). Triple dissociation of faces, bodies, and objects in extrastriate cortex. *Current Biology*, *19*, 319-324.
- Pitcher, D., Walsh, V., Yovel, G., & Duchaine, B. (2007). TMS evidence for the involvement of the right occipital face area in early face processing. *Curr Biol*, *17*(18), 1568-1573. doi: 10.1016/j.cub.2007.07.063

- Poreisz, C., Boros, K., Antal, A., & Paulus, W. (2007). Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Res Bull*, 72(4-6), 208-214. doi: 10.1016/j.brainresbull.2007.01.004
- Prieto, E. A., Caharel, S., Henson, R., & Rossion, B. (2011). Early (n170/m170) facesensitivity despite right lateral occipital brain damage in acquired prosopagnosia. *Front Hum Neurosci*, 5, 138. doi: 10.3389/fnhum.2011.00138
- Radman, T., Ramos, R. L., Brumberg, J. C., & Bikson, M. (2009). Role of cortical cell type and morphology in subthreshold and suprathreshold uniform electric field stimulation in vitro. *Brain Stimul*, 2(4), 215-228, 228.e211-213. doi: 10.1016/j.brs.2009.03.007
- Reis, J., Schambra, H. M., Cohen, L. G., Buch, E. R., Fritsch, B., Zarahn, E., . . . Krakauer, J. W. (2009). Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. *Proc Natl Acad Sci U S A*, 106(5), 1590-1595. doi: 10.1073/pnas.0805413106
- Rivolta, D., Castellanos, N. P., Stawowsky, C., Helbling, S., Wibral, M., Grutzner, C., ...
 Uhlhaas, P. J. (2014). Source-reconstruction of event-related fields reveals
 hyperfunction and hypofunction of cortical circuits in antipsychotic-naive, firstepisode schizophrenia patients during Mooney face processing. *J Neurosci, 34*(17), 5909-5917. doi: 10.1523/jneurosci.3752-13.2014
- Rivolta, D., Palermo, R., & Schmalzl, L. (2013). What is Overt and what is Covert in Congenital Prosopagnosia? *Neuropsychology Review*, 23(2), 111-116.
- Rivolta, D., Palermo, R., Schmalzl, L., & Coltheart, M. (2012). Covert face recognition in congenital prosopagnosia: A group study. *Cortex*, 48(3), 344-352.
- Rivolta, D., Palermo, R., Schmalzl, L., & Williams, M. A. (2012). Investigating the features of the M170 in congenital prosopagnosia. *Front Hum Neurosci, 6:45.*(doi:10.3389/fnhum.2012.00045).

- Rivolta, D., Woolgar, A., Palermo, R., Butko, M., Schmalzl, L., & Williams, M. A. (2014).
 Multi-voxel pattern analysis (MVPA) reveals abnormal fMRI activity in both the
 "core" and "extended" face network in congenital prosopagnosia. *Front Hum Neurosci, 8*, 925. doi: 10.3389/fnhum.2014.00925
- Rockstroh, B., Elbert, T., Canavan, A., Lutzenberger, W., & Birbaumer, N. (1989). *Slow Cortical Potentials and Behaviour*. Baltimore (MD): Urban & Scharrzenberg.
- Romanska, A., Rezlescu, C., Susilo, T., Duchaine, B., & Banissy, M. J. (2015). High-Frequency Transcranial Random Noise Stimulation Enhances Perception of Facial Identity. *Cereb Cortex*. doi: 10.1093/cercor/bhv016
- Rossion, B. (2014). Understanding face perception by means of human electrophysiology. *Trends Cogn Sci, 18*(6), 310-318. doi: 10.1016/j.tics.2014.02.013
- Rossion, B., Caldara, R., Seghier, M., Schuller, A. M., Lazeyras, F., & Mayer, E. (2003). A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. *Brain, 126*(Pt 11), 2381-2395. doi: 10.1093/brain/awg241
- Roy, L. B., Sparing, R., Fink, G. R., & Hesse, M. D. (2015). Modulation of attention functions by anodal tDCS on right PPC. *Neuropsychologia*, 74, 96-107. doi: 10.1016/j.neuropsychologia.2015.02.028
- Shin, Y. I., Foerster, A., & Nitsche, M. A. (2015). Transcranial direct current stimulation (tDCS) - application in neuropsychology. *Neuropsychologia*, 69, 154-175. doi: 10.1016/j.neuropsychologia.2015.02.002
- Spruston, N. (2008). Pyramidal neurons: dendritic structure and synaptic integration. *Nat Rev Neurosci, 9*(3), 206-221. doi: 10.1038/nrn2286
- Stagg, C. J., Jayaram, G., Pastor, D., Kincses, Z. T., Matthews, P. M., & Johansen-Berg, H.(2011). Polarity and timing-dependent effects of transcranial direct current stimulation

in explicit motor learning. *Neuropsychologia*, *49*(5), 800-804. doi: 10.1016/j.neuropsychologia.2011.02.009

Stagg, C. J., & Nitsche, M. A. (2011). Physiological basis of transcranial direct current stimulation. *Neuroscientist*, 17(1), 37-53. doi: 10.1177/1073858410386614

Tang, J., Falkmer, M., Horlin, C., Tan, T., Vaz, S., & Falkmer, T. (2015). Face Recognition and Visual Search Strategies in Autism Spectrum Disorders: Amending and Extending a Recent Review by Weigelt et al. *PLoS One, 10*(8), e0134439. doi: 10.1371/journal.pone.0134439

- Terney, D., Chaieb, L., Moliadze, V., Antal, A., & Paulus, W. (2008). Increasing human brain excitability by transcranial high-frequency random noise stimulation. J Neurosci, 28(52), 14147-14155. doi: 10.1523/jneurosci.4248-08.2008
- Willis, M. L., Murphy, J. M., Ridley, N. J., & Vercammen, A. (2015). Anodal tDCS targeting the right orbitofrontal cortex enhances facial expression recognition. Soc Cogn Affect Neurosci. doi: 10.1093/scan/nsv057

Highlights

- Anodal transcranial direct current stimulation (a-tDCS) was administered to healthy participants.
- *Sham, online* (during task execution) and *offline* (before tasks execution) right-occipital atDCS has been administered.
- Only offline a-tDCS enhanced face- and object- processing.











Figure2

$\left\{ \begin{array}{ccc} & & & & & & & & \\ & & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & &$

ACCEPTED MANUSCRIPT

