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Title: Cathodal transcranial direct current stimulation of the extrastriate visual cortex modulates implicit anti-fat bias in male, but not female, participants

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Abstract

Explicit negative attitudes towards obese individuals are well documented and seem to modulate the activity of perceptual areas, such as the Extrastriate Body Area (EBA) in the lateral occipito-temporal cortex, which is critical for body-shape perception. Nevertheless, it is still unclear whether EBA serves a role in implicit weight-stereotypical bias, thus reflecting stereotypical trait attribution on the basis of perceptual cues. Here, we used an Implicit Association Test (IAT) to investigate whether applying transcranial direct current stimulation (tDCS) over bilateral extrastriate visual cortex reduces pre-existing implicit weight stereotypical associations (i.e. “Bad” with Fat and “Good” with Slim, valence-IAT). Furthermore, an aesthetic-IAT, which focused on body-concepts related to aesthetic dimensions (i.e. “Ugly” and “Beautiful”), was developed as a control condition. Anodal, cathodal, or sham tDCS (2 mA, 10min) over the right and left lateral occipito-temporal (extrastriate visual) cortex was administered to 13 female and 12 male participants, before performing the IATs. Results showed that cathodal stimulation over the left extrastriate visual cortex reduced weight-bias for the general evaluative (Bad vs. Good) but not specific aesthetic (Ugly vs. Beautiful) dimensions as compared to sham stimulation over the same hemisphere. Furthermore, the effect was specific for the polarity and hemisphere of stimulation. Importantly, tDCS affected the responses only in male participants, who presented a reliable weight-bias during sham condition, but not in female participants, who did not show reliable weight-bias at sham condition. The present results suggest that negative attitudes towards obese individuals may reflect neural signals from the extrastriate visual cortex.

Keywords: anti-fat bias; Extrastriate visual cortex; tDCS; Implicit Association Test

Introduction

There is mounting research evidence that overweight and obese people experience social disadvantages in a multitude of social settings, such as interpersonal relationships, employment, education and healthcare (Puhl and Brownell, 2001; Schupp and Renner, 2011). Indeed, various explicit measures have revealed that being overweight or obese is usually associated with a range of negative features, such as being unattractive, weak-willed and sexually estranged (Crandall, 1994; Phillipsp and Hill, 1998; Todorov and Uleman, 2003; Todorov et al., 2008). Furthermore, those negative attitudes towards obese individuals (anti-fat bias) seem to develop in early childhood and they have been even observed in children as young as 3 years old, gradually increasing after that (Cramer and Steinwert, 1998).

More recently, anti-fat bias has been detected (Teachman et al., 2003; Ahern and Hetherington, 2006; Schwartz et al., 2006) by applying “implicit” measures, such as the Implicit Association Test (IAT; Greenwald, Nosek and Banaji, 2003), which can provide an index of the automatic association between the face and body of an obese or slim individual and an evaluative dimension (e.g., Good vs. Bad). Interestingly, participants have shown higher levels of implicit, as compared to self-report measures of bias, thus suggesting that the IAT can reveal levels of prejudice that may not be otherwise apparent (Wang, Brownell and Wadden, 2004). These implicit negative attitudes toward overweight and/or obese individuals can then trigger a range of discriminative, non-verbal behaviours, for example eye contact and spatial distance. Such immediate negative behaviours may take place in the absence of reflective thinking (Todorov and Uleman,

2003), thus providing a constant source of discrimination elicited by the mere sight of an obese person (Schupp and Renner, 2011).

Human beings naturally rely on fundamental cues, such as race, sex and age, in order to categorize others (Fiske, 1993); however these cues may elicit stereotypes about the groups they represent and, thus, yield person-perception processes (Kunda and Thagard, 1996; Macrae et al., 1994). As such, body shape is an important cue to form impressions of other people on the basis of basic perceptual processing. It is still unclear, however, to what extent body-weight negative stereotypes entail only the activity of high-level brain areas involved in evaluative processing or also modulate the activity of brain regions involved in processing visual information conveyed by body shape. In spite of many studies investigating the underlying neural basis of stereotypical attitudes by administering the IAT (e.g., Cattaneo et al., 2011; Crescentini et al., 2014, 2015; Gallate et al., 2011; Gladwin, den Uyl and Wiers, 2012; Chee et al., 2000), only very few studies have so far used neuroimaging and/or neurophysiological techniques to focus on the neural bases of implicit obesity stigma. A seminal fMRI study of Krendl and colleagues (2006) investigated the neural basis of forming either explicit (“Do you like or dislike this person?”) and implicit (“Is this a male or female?”) judgments of people having well-established stigmatized conditions, such as obesity. The authors of the study proposed the activation of an extensive neural network, including the amygdala, insula, anterior cingulate, and lateral prefrontal cortex that is involved in the processing of highly negative social stigmas. These brain areas have been shown before to be also involved in responding to aversive stimuli, as well as in modulating inhibition and cognitive control. More recently, Azevedo et al. (2014) reported decreased neural reactivity as a result of observing obese people’s pain in areas associated with the representation of sensory and

affective-motivational aspects of pain (i.e. bilateral insula, somatosensory cortices and thalamus), revealing diminished resonance with obese people's pain.

In a similar vein, Schupp and Renner (2011) investigated the neural bases of implicit anti-fat bias by means of event-related potential (ERP) recordings. In this study, schematic portraits of underweight, normal weight, and overweight body shapes, as well as pictures of tools, served as stimuli. During a first passive viewing task, participants were asked to simply observe the stimuli, while in a subsequent distraction condition participants were asked to detect a specific tool. The authors reported that observing overweight in comparison to normal-weight or underweight body shapes elicited a positive potential shift over fronto-central sites and a relative negative potential over occipito-temporal regions in a time window from ~190 to 250 msec. No modulation was reported at later time windows. These findings are in accordance with those showing that an early differential ERP activity may be associated with the emotional processing of pictures, faces and words (Wieser et al., 2010) and suggest that the perception of images of obese individuals can modulate early perceptual processing areas, reflecting the intrinsic significance of stimuli (Schupp and Renner; 2011; Wieser et al., 2010). In line with this view, a recent fMRI study of Quadflieg et al. (2011) investigated whether early perceptual aspects of person construal are sensitive to the individuals' stereotype-related status. The authors found that the presentation of targets that violated stereotypic beliefs (e.g., male hairdressers and female airline pilots) increased neural activity not only in areas dedicated to executive control (i.e., DLPFC), but also in extrastriate areas related to person perception. These findings suggest that stereotypic beliefs modulate the activity of extrastriate areas involved in person percept in the brain.

Interestingly, neuroimaging evidence shows that perceptual signals in the ventral visual stream are linked with person-knowledge processing in the Theory-of-Mind network (Greven et al., 2016; Greven & Ramsey, 2017). Specifically, Greven and Ramsey (2017) have recently demonstrated that parts of the extrastriate cortex (EBA), which is involved in the processing of body shape and posture (Urgesi et al., 2004; Downing and Peelen, 2011), exchange signals with areas involved in mentalising and making inferences about others' thoughts and traits (i.e., temporal pole). These findings supports the notion that brain areas that represent aspects of another person's physical appearance (person perception), such as body shape and posture, are coupled to brain circuits that respond when reasoning about another person's trait-based character (person knowledge) (Greven et al., 2016). However, the functional significance of the contribution of person-perception areas to high level representations of other people's traits is still unclear. In particular, previous studies have not provided evidence on how modulation of activity in person-perception areas contributes to the formation and reshaping of social biases.

To address this issue, we applied transcranial direct current stimulation (tDCS), a non-invasive brain-stimulation technique that can interfere with cerebral cortex processes by means of a weak electric current passed between two electrodes (anodal and cathodal) on the scalp. This way, decreased (cathodal) or enhanced (anodal) cortical excitability can be induced. We used tDCS to directly manipulate the cortical excitability of the extrastriate visual cortex, including the extrastriate body area (EBA), which has been shown to respond selectively to photorealistic depictions of whole human bodies or body parts, still images of human bodies or body parts extending to 'stick figures' and silhouettes, in

preference to human faces, images of objects parts and scenes (Downing et al., 2001; Candidi et al., 2008; Peelen and Downing, 2007; Urgesi et al., 2007a).

In two separated sessions, we applied anodal- (a-), cathodal (c-), or sham-tDCS over the extrastriate visual cortex in the right and left hemispheres of male and female participants with the aim of investigating its role in **mediating implicit negative weight stereotypical associations (i.e. “bad” with overweight and “good” with slim) as measured with a weight-related valence-IAT (v-IAT)**. Furthermore, an ad-hoc IAT, which focused on perceptual dimensions related to body aesthetics (i.e. ‘ugly’ with overweight and ‘beautiful’ with slim), was developed as a control task (aesthetic-IAT, ae-IAT). Importantly, while the v-IAT aimed at measuring general evaluative attitudes towards overweight individuals, the a-IAT referred to a more specific stereotype of ‘FAT-ugly’, which is more related to a perceptual rather than conceptual dimension. In particular, in these weight-related IATs, participants were required to classify the body of obese and thin people as Fat and Slim, respectively. In parallel, they were required to classify a series of adjectives along two dimensions (general evaluative, Good vs. Bad, or aesthetic, Beautiful vs. Ugly). In one (congruent) block, bodies and adjectives were randomly presented, while Slim categorization responses were mapped onto the same response key of Good (or Beautiful) categorization responses, whereas Fat and Bad (or Ugly) shared the same response key. In another (incongruent) block, response mapping was inverted, so that the Fat categorizations were mapped with the Good (or Beautiful) ones and the Thin with the Bad (or Ugly) categorizations. In keeping with previous studies (Teachman et al., 2003; Ahern and Hetherington, 2006; Schwartz et al., 2006), we expected participants to be

faster to respond in the first pattern than in the second one, which is taken as evidence of ‘anti-fat bias’.

In line with Greven, Downing, and Ramsey (2016), Greven and Ramsey (2017) and Quadflieg et al. (2015), we expected that neural activity in extrastriate visual cortex (and particularly in EBA) should provide information about bodily appearance to person knowledge areas (Gobbini and Haxby, 2007; Weiner and Grill-Spector, 2010 and Greven et al., 2016), thus selectively modulating the associations between implicit personality judgments and weight-bias. Conversely, the effects of EBA stimulation are expected to be more limited on the association between two perceptual dimensions of body appearance, namely thinness and beauty, which do not require access to person-specific processing. Predictions regarding the direction of the after-effects of c- and a-tDCS on occipito-temporal areas should be cautious, as they appear to be task-dependent and are still controversial (Antal, Nitsche, and Paulus, 2006). However, based on the results of Quadflieg et al. (2011), showing increased activity of EBA for stereotype-incongruent depictions of human bodies, we expected that inhibiting excitability of extrastriate visual cortex with c-tDCS should reduce implicit anti-fat bias, whereas facilitating excitability of extrastriate visual cortex with tDCS should increase it. Furthermore, comparing the effects obtained for the two weight-related IATs may allow us to verify whether the role of the extrastriate visual cortex is merely related to the perception of body weight (i.e., with comparable effects of tDCS for the v- and ae-IAT) or reflects higher-level involvement in associating specific evaluative dimensions to body forms (i.e., with selective effects for one IAT). Finally, tDCS effects should be influenced by the interindividual differences in implicit and explicit weight-related stereotypes that are expected between men and women

(Lieberman, Tybur and Latner, 2012), with men reporting more negative general attitudes toward obese individuals than women and, consequentially, specific reduction or increase of implicit anti-fat bias after c- or a- tDCS, respectively.

Methods

Participants

A total of 25 students (13 women, range: 20-29 years old; 12 men, range: 20-28 years old) from the University of Udine, Italy, participated in the experiment in return for course credits. Participants were naïve as to the purpose of the study and information about the experimental hypothesis was provided only during the debrief period, after all the experimental tests were completed. All subjects, but one male and one female, were right-handed as identified by means of a Standard Handedness Inventory (Briggs and Nebes, 1975). They were all native Italian speakers of Caucasian race and they all reported heterosexual orientation. Finally, all participants reported normal or corrected to normal vision, they were in good health, free of psychotropic or any other medication, with no past history of psychiatric or neurological disease and with no contraindication to tDCS (Poreisz et al., 2007). At the end of the experiment, participants filled two questionnaires: 1) the Sociocultural Attitudes Toward Appearance Questionnaire-3 (SATAQ-3; 4 scales; Stefanile et al., 2011; Thompson et al., 2004) to measure multiple aspects of societal influence, such as the degree of mass media internalization of the models; 2) the Fat Phobia scale (short version from Bacon et al., 2001) in order to measure fat phobic attitudes. In particular, The Fat Phobia Scale – short form (Bacon et

al., 2001) assesses explicit negative attitudes and stereotyped perceptions of obese people. This scale consists of 14 pairs of adjectives that are sometimes used to describe obese individuals. For each pair, participants have to indicate, using a 5-point scale, the adjective that best describes their feelings and beliefs (e.g. 1 = Industrious/5 = Lazy). Higher scores reflect greater fat phobia. Furthermore, we estimated participants' BMI from self-report measures of weight (Kg) and height (cm). The participants' demographics and self-report questionnaire scores as a function of gender are reported in Table 1. Participants gave their written informed consent and all experimental procedures were previously approved by the ethics committee of the Scientific Institute (IRCCS) 'E. Medea' and were in accordance with the ethical standards of the Declaration of Helsinki (1964).

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Materials and Methods

Body Stimuli

All participants were shown a series of 6 virtual human models (3 females / 3 males) previously selected from a database of adult body stimuli created by means of Poser Pro 2010 (e-frontier, Santa Cruz, CA) (for details see Cazzato et al., 2012). Virtual models rather than “real” persons were used in order to limit confounds related to differences in attractiveness, clothing, attire, and familiarity (**Schupp and Renner, 2011**). The coloured virtual models were rendered in two different static daily poses (e.g., standing). The body

weight was gradually increased or decreased in order to create two body size extremes for each model (fat/slim). All pictures were taken with the models standing in frontal-view, against a grey background and wearing identical black clothing (underwear). Following that, photorealistic textures were applied and the images were rendered with global illumination. Finally, in order to avoid the influence of any facial features, the pictures were imported into Adobe Photoshop 7.0 (Adobe System Inc. CA; <http://www.adobe.com>) and a circle region around the face was scrambled.

IAT words

A pilot study was run to appropriately select words stimuli for the valence (good and bad) and aesthetic (beautiful and ugly) categories, which were used respectively in the v-IAT and ae-IAT. The entire corpus of evaluative- and aesthetics-related adjectives was selected among a larger sample of words contained in the COLFIS database (CoLFIS database: Corpus and Frequency Lexicon of Written Italian, Bambini and Trevisan, 2012). An independent group of 25 Italian subjects (9 males and 16 females; range: 18-36 years old), who did not take part in the tDCS experiment, rated each word (n=94) on a series of 7-point Likert scale by judging: 1) familiarity (subjective report about how frequently a word occurs in the life of a person); 2) imageability (ease and speed of a word in evoking a mental image or a sensory experience); 3) concreteness (reference to objects, living things, actions and materials that can be experienced through the senses); 4) valence (ability of a word to elicit in the speaker and listener positive or negative feelings) and 5) strength of association of each adjective with aesthetic and valence dimensions. Table 2 reports the mean values for each of the above-mentioned dimensions

for the four categories of stimulus words. A total of final forty-eight words (12 for each category) were selected as stimuli (see Table 3). A series of one-way ANOVAs on each dimension indicated that the categories were matched for familiarity [$F(3,44) = 2.130, p = 0.110, \eta p^2 = 0.127$], imageability [$F(3,44) = 2.540, p < 0.069, \eta p^2 = 0.148$], length of letters [$F(3,44) = 1.321, p = 0.280, \eta p^2 = 0.083$] and frequency of word use in Italian language (COLFIS database) [$F(3,44) = 1.145, p = 0.341, \eta p^2 = 0.072$], but not for concreteness [$F(3,44) = 13.954, p < 0.001, \eta p^2 = 0.488$]. Newman-Keuls post hoc tests for the concreteness measure showed that the words used in the aesthetic category (Beautiful and Ugly) were judged more concrete than the other two categories of words (Valence: Bad and Good) (all $p < 0.001$). Importantly, the analysis on valence ratings revealed a main effect of category [$F(3,44) = 326.896, p < 0.001, \eta p^2 = 0.957$], with Beautiful and Good words having more positive valence than the other two types of words (all $p < 0.001$). Finally, the analysis on the strength of association (difference between the association of each word with the aesthetic and valence dimensions) confirmed that Beautiful and Ugly words were more associated with the aesthetic than the valence dimension and that Good and Bad words were more associated with the valence than the aesthetic dimension [$F(3,44) = 42.393, p < 0.001, \eta p^2 = 0.743$; all $p < 0.001$]. Thus, the pilot experiment confirmed the validity of our measures of aesthetic and valence representations.

----- Please insert Table 2 around here -----

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Experimental Procedure

During the experiment, participants were seated in a dimly light room at a distance of approximately 57 cm away from a LCD monitor (19 inches, resolution of 1024*768 pixels, refresh frequency at 60 Hz). The experiment was designed and controlled with E-Prime software (version 2.0 Professional, Psychology Software Tools, Inc., Pittsburgh, PA). At the beginning participants had to complete their demographic details, followed by brief written instructions about the task and, then, by the v-IAT. Participants were instructed to respond as fast and accurate as possible immediately after the onset of the stimuli (i.e., single words or images presented one at a time at the centre of the screen), by pressing a left (E) or a right (I) key on the computer keyboard with the index finger of their left and right hand, respectively. Each IAT lasted approximately 8 minutes and was administered in seven blocks, each consisting of both congruent and incongruent condition blocks (blocks 3, 4, 6, and 7) and familiarization blocks (blocks 1, 2, and 5) (Greenwald, 2003; Cattaneo et al., 2011; Crescentini et al., 2014). Before the first running of each IAT, participants were shown a list with all the words belonging to the two relevant categories and they were asked to carefully study all the stimuli.

In the first block of v-IAT, 12 images of Fat and 12 images of Slim people were presented and had to be classified as being either Fat (left key) or Slim (right key). Each of the 12 images of the two categories was presented only once for a total of 24 trials. The second block also consisted of 24 trials, in which Bad-related (requiring a left-key response) and Good-related (requiring a right-key response) words were presented. In the third block (24 practice trials) and in the fourth block (48 test trials), both Fat and Slim bodies and Good and Bad words were randomly presented and participants were instructed to press the left key for Bad-related words and images of Fat people, and the

right key for Good-related words and images of Slim people (congruent-stereotype condition). In the fifth block (24 trials), response key assignments were reversed in relation to the categorization involving images of fat people (right key) and images of slim people (left key). Finally, in the sixth block (24 practice trials) and in the seventh block (48 test trials), both Fat and Slim bodies and Good and Bad words were randomly presented and participants were required to press the left key for images of Fat people and Good words and the right key for images of Slim people and Bad words (incongruent-stereotype condition) (see Table 3). Typically, participants are faster and more accurate in the congruent- than in the incongruent-stereotype blocks, thus demonstrating an automatic association between Fat and Bad categories and Slim and Good categories (Greenwald, Banaji and Nosek, 2003).

With regards to the control ae-IAT, the procedure was exactly the same as the v-IAT, with the exception that aesthetics-related words were presented and participants were instructed to classify the words as being related to Beautiful or Ugly categories (see Table 3). The 12 images of fat and slim people presented during the v-IAT were also used in the ae-IAT. Stimuli within each block were presented in random order. Each stimulus (word/image) persisted on the computer screen until the participant gave a correct response. If participants made an error, then a red “X” appeared below the word stimulus in order to prompt them to correct the mistake and press the correct key. Following the response, the next stimulus appeared after 500 msec, during which only the category labels were visible on the screen. **In two separate days (one per each hemisphere), the two IATs were presented to each participant in three blocks, one for each of the stimulation type (sham, a- and c-tDCS). Each block lasted for about 20 min (tDCS stimulation + task duration). Moreover, half of the participants performed first the**

v-IAT and then the ae-IAT; the opposite order was used for the other half. Finally, after the tDCS experiment, participants were required to provide information about their weight and height (for calculating BMI) and to complete the SATAQ-3 and Fat Phobia Questionnaires.

----- Please insert Table 3 around here -----

tDCS

Anodal, cathodal or sham-tDCS (2 mA) was delivered by means of a battery-driven, constant-current stimulator (BrainStim, EMS, Bologna, Italy) through a pair of saline-soaked sponge electrodes (5×5 cm, 25 cm^2).

The electrodes were first firmly attached by elastic bands and saline solution was applied under the electrodes in order to reduce contact impedance before the montage. To comply with current safety regulations (Poreisz et al., 2007), a constant current of 2 mA intensity was applied. Specifically, the stimulating current was ramped up during a 10-sec fade-in phase, then held constant at 2 mA for 10 min, and then ramped down during a 10-sec fade-out phase. We chose this specific duration of the tDCS stimulation on the basis of previously reported experimental protocols, which have described effects on cortical excitability, sufficiently enduring to cover the duration of the experimental task (Nitsche and Paulus, 2001; Mancini et al., 2012). The experimental task was initiated exactly in the last 2 min of tDCS. In each daily session, the participants received a-, c-, and s-tDCS on the same hemisphere in three separate blocks. **The order of the hemisphere daily sessions and of the stimulation-condition blocks was counterbalanced across**

subjects. An interval of 3-5 days was allowed between the two daily sessions and of at least 90 min between the three stimulation-condition blocks in order to avoid carryover effects and to guarantee a sufficient washout of the effects of the previous session (e.g., Mancini et al., 2012; Bolognini, et al., 2010; 2011). During the 90 minutes of break, participants were free to leave the laboratory and take some rest. During the three different experimental blocks, the location of the active electrode was identified by means of the 10–20 system for EEG electrode placement. In keeping with previous studies targeting the lateral occipito-temporal cortex with tDCS (Mancini et al., 2012), the active electrode was placed between O2 and PO8 to stimulate the extrastriate visual cortex, including visual body-specific regions (Mancini et al., 2012; Downing et al., 2001). The reference electrode was always fixed on the vertex (Cz). Moreover, as in previous studies, for the sham condition, the electrodes were placed over the target sites (see Fig. 1), with the same parameters of a- and c-tDCS, but the stimulator was turned off after 30 sec (Nitsche and Paulus, 2000; Mancini et al., 2012). This ensured that participants could initially feel the itching sensation at the beginning of the tDCS protocol, but no effective modulation of cortical excitability could be elicited (Gandiga, Hummel and Cohen, 2006). Finally, in-house software switched the tDCS on and off without intervention from the participants or experimenters, allowing for successful blinding.

----- Please insert Fig. 1 around here -----

Data Handling

Statistical analyses were performed on the mean D-scores, which measure the IAT effects by combining both accuracy and speed aspects of responses and were computed following the improved algorithm procedure described by Greenwald et al. (2003) and Cattaneo et al. (2011). In particular, we first checked that there were no trials with latencies greater than 10,000 msec and no participants responded faster than 300 msec in more than 10% of all the experimental trials. Then, for computing the mean reaction times (RTs), RTs of error trials were removed and replaced with the mean RTs of correct trials in the corresponding block plus an addition of 600 msec. To compute D-scores, the mean RTs of block 3 were subtracted from the mean RTs of block 6 and the difference was divided by the pooled SD of all trials in blocks 3 and 6; similarly, the mean RTs of block 4 were subtracted from the mean RTs of block 7 and the difference was divided by the pooled SD of all trials in blocks 4 and 7. Finally, the two quotients obtained in the previous two steps were averaged (Cattaneo et al., 2011). For the sake of clarity, error rates and RTs of correct responses are reported in Table 4, respectively for each IAT.

First, we tested whether male and female participants presented with significant weight bias in the two IATs at the baseline (sham) condition by comparing the corresponding mean D-scores to zero (where zero refers to the absence of any response bias). Then, to test the effects of tDCS on the implicit association of weight to good/bad attributes and to control beautiful/ugly attributes, the D-score data were entered into two separated mixed-model Analyses of Variance (ANOVAs), one for each IAT, with gender group (male, female participants) as between-subjects factor and tDCS stimulation (anodal, cathodal, sham) and Hemisphere (left, right) as within-subject variables. Significant three-way interactions were followed up by separate 2-way ANOVAs in each gender group, while

the source of significant two-way interactions was analysed using the Newman-Keuls post-hoc test.

Finally, we calculated, for each condition, a measure of the change of v-IAT D-scores as the difference between the individual values after c- and a-tDCS and the corresponding values in the sham-tDCS condition [active-tDCS – sham-tDCS]. The change indexes were correlated, using Pearson correlations, with BMI and individual scores at the Fat Phobia Scale and SATAQ questionnaire.

All statistical analyses were performed with STATISTICA 8.0 (StatSoft Inc, Tulsa, Oklahoma). Effect sizes were estimated using the partial eta square variable (η_p^2). All data are reported as Mean (M) and Standard Error of the Mean (s.e.m.). A significance threshold of $p < 0.05$ was set for all effects.

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Results

Valence-IAT

One sample t-tests comparing the mean D-scores to zero showed that male participants showed a significant stereotypical anti-fat bias in both sham-tDCS conditions, indicating that they were more prone to associate fat people to the bad-related category and slim people to the good-related category than vice versa [$t(11) = 3.56, p = 0.004$ for right sham-tDCS and $t(11) = 5.04, p < 0.001$ for left sham-tDCS]. Conversely, the analysis of the female participants' mean D-scores revealed absence of the anti-fat bias in both sham-

tDCS conditions, namely for right [$t(12) = 1.15, p = 0.271$] and for left sham-tDCS [$t(12) = 1.61, p = 0.134$].

The 3-way ANOVA on the v-IAT revealed a significant 3-way interaction of hemisphere \times tDCS stimulations \times gender [$F_{(2,46)} = 3.356; p = 0.044; \eta_p^2 = 0.127$]. The follow-up 2×3 ANOVA on the mean D-scores for male participants revealed a significant 2-way interaction of hemisphere \times tDCS stimulations [$F_{(2,22)} = 7.522; p = 0.003; \eta_p^2 = 0.406$], but no main effects of hemisphere [$F = 0.794, p = 0.392; \eta_p^2 = 0.067$] or stimulation [$F = 0.924, p = 0.412; \eta_p^2 = 0.077$]. Newman-Keuls post-hoc comparisons showed that c-tDCS over left extrastriate visual cortex reduced the weight-bias for the v-IAT, as compared to sham [0.13 ± 0.7 vs. $0.44 \pm 0.09, p = 0.007$]. The effect was specific for the polarity and hemisphere of stimulation, since the weight-bias after c-tDCS over the left extrastriate visual cortex was significantly lower than that after c-tDCS over the right extrastriate visual cortex [0.13 ± 0.7 vs. $0.37 \pm 0.06; p = 0.035$; see Fig. 2A]. Crucially, the difference between the two sham conditions in the right and left hemisphere stimulation sessions was not statistically significant [0.26 ± 0.07 vs. $0.44 \pm 0.09; p = 0.126$]. Furthermore, the difference between a-tDCS over extrastriate visual cortex as compared to the relative sham condition was not statistically different for both right [0.30 ± 0.06 vs. $0.26 \pm 0.07, p = 0.568$] and left [0.23 ± 0.08 vs. $0.44 \pm 0.09, p = 0.096$] hemispheres. Finally, non-significant difference was observed between right and left a-tDCS conditions [$p = 0.637$].

----- Please insert Fig. 2 around here -----

The 2 × 3 ANOVA on the mean D-scores of female participants revealed non-significant main effects of hemisphere and stimulation and non-significant interaction [all $F_s < 1.367$, all $p_s > 0.274$; all $\eta_p^2 < 0.102$] (See Fig. 2B).

Aesthetic-IAT

At baseline, male participants showed a significant stereotypical anti-fat bias in both sham-tDCS conditions, indicating that they were more prone to associate fat people to the ugly-related category and slim people to the beautiful-related category than vice versa [$t(11) = 0.29$, $p = 0.007$ for right sham-tDCS and $t(11) = 0.40$, $p < 0.001$ for left sham-tDCS]. The analysis of the female participants' mean D-scores revealed a significant anti-fat bias in both sham-tDCS conditions, namely for right [$t(12) = 0.3$, $p = 0.015$] and for left sham-tDCS [$t(12) = 0.34$, $p = 0.010$]. Thus, the aesthetic anti-fat bias was apparent in both gender groups.

However, the 3-way ANOVA on the ae-IAT D-scores (Fig. 3) revealed non-significant main effects or interactions [all $F_s < 0.724$; all $p_s > 0.404$; $\eta_p^2 < 0.031$]. In particular, the non-significant 3-way interaction between gender group, hemisphere, and stimulation [$F_{(2,46)} = 0.199$; $p = 0.821$; $\eta_p^2 = 0.009$] suggests that the gender- and hemisphere- specific modulation of the weight-bias in the valence dimension was not reflected in the aesthetic dimension.

----- Please insert Fig. 3 around here -----

Self-reported questionnaires

As shown in Table 1, independent sample t-tests indicated that male and female participants were matched for both age and BMI. The analysis of the SATAQ-3 data revealed that, compared to women, men had higher scores on the internalization-athlete SATAQ-3 subscale, thus indicating that they might have a stronger internalization of media influences related to the achievement of an athletic physique (Internalization-Athlete); conversely, the two gender groups did not differ on the thin-ideal internalization score (Internalization-General), the perceived feelings of pressure to conform to the Western ideals exhibited by the media (Pressures) and the recognition of the social importance of the media's messages about Western beauty ideals information (Information). Furthermore, no differences were found between men and women in the explicit phobic attitude towards fat people. Finally, no significant correlations were found between the tDCS change indexes and the BMI, Fat Phobia, and SATAQ subscales for both male and female participants ($-0.612 < \text{all } r_s < 0.433$).

Discussion

This study applied tDCS to examine whether non-invasive brain stimulation can modulate anti-fat bias, and we demonstrated that stimulation over the left, but not right, extrastriate visual cortex, where EBA has been previously located (Sadeh et al., 2011; Taylor et al., 2010), decreased negative attitude towards fat people. Importantly, we also developed a control ae-IAT, which focused on body-concepts related to aesthetic representations (i.e. “ugly” and “beauty”) and we found that inhibiting neural excitability in the left occipital cortex by applying c-tDCS diminished the anti-fat bias only for the v-

IAT but not for the ae-IAT. Conversely, enhancing cortical excitability through a-tDCS did not exert any effects in either hemisphere. Interestingly, the effects of tDCS for the v-IAT were found only in male participants, who displayed a significant anti-fat bias, but not in female participants, who did not show a reliable anti-fat bias. To the best of our knowledge this is the first study showing a causative role of the lateral occipito-temporal cortex in the anti-fat bias.

In keeping with the results of previous behavioral studies (Puhl, Luedicke, and Heuer, 2011; Musher-Eizenman, and Carels, 2009), our brain stimulation study found dominant implicit representations of obese individuals as dishonest, villain and immoral when sham stimulation was applied. The weight v-IAT effect, however, was only significant in male but not in female participants, suggesting a lack of implicit anti-fat bias in women even if no differences were found between men and women in their explicit fat phobic attitudes. Nevertheless, the absence of a significant implicit weight bias in female participants allowed for an indirect control for general effects of tDCS on the IAT performance in the absence of any reliable weight bias. Importantly, this result seems to be in agreement with previous experimental evidence suggesting a strong prevalence of negative attitudes towards overweight individuals and, in general, of social stigma in men as compared to women (Lewis, Cash and Bubb-Lewis, 1997). Most importantly, gender differences in obesity stigma may reflect different conceptions and attitudes toward obesity in the two genders: women usually report significantly greater fear of becoming fat than men do; in contrast, men are significantly more likely to attribute obesity to a lack of willpower and to report greater dislike of obese individuals as compared to women. This is true even after controlling for BMI (Lieberman, Tybur, and Latner,

2012). Hence, future studies should take into consideration specific subtypes of anti-obesity attitudes that may show systematic sex differences, as this is particularly important for future intervention implications (Kelly, Jorm and Wright, 2007).

Importantly, after c-tDCS over left extrastriate visual cortex, the men's negative bias for stereotype-congruent stimuli was reduced, revealing that the anti-fat bias involves the contribution of this brain area. That the inhibition of left extrastriate cortex induced a reduction of the weight-bias is in line with previous evidence about implicit processing of emotional faces (Cecere, Bertini and Ladavas, 2013). This study showed that presenting congruent/emotional vs. incongruent/neutral masked faces facilitated responses to emotional faces. However, inhibiting with c-tDCS the activity in the left occipital cortex suppressed this facilitation. This documents the crucial role of the left occipital cortex in mediating high-order implicit visual processes, such as the emotion congruency effects (Cecere, Bertini and Ladavas, 2013).

It has been previously shown that the extrastriate visual cortex and the functional localized EBA is causatively involved in mapping morphological features of human bodies (Downing et al., 2001; Candidi et al., 2008; Urgesi et al., 2007a). This process can prove critical for maintaining constant the identity of others, even when body configurations change drastically during action sequences. Thus, the role of EBA may be fundamental for the identification of actors, particularly when facial cues are unavailable or ambiguous. Indeed, several studies have shown that EBA is sensitive to subtle variations of human body size and shape (Aleong and Paus, 2010) in healthy individuals and its neuro-functional alteration is associated with body image disturbance, such as

body size overestimation and negative evaluation of one's own body, in patients with Eating Disorders (ED) (Uher et al., 2005). The present study shows that neural activity in the extrastriate visual cortex, and possibly EBA, may play a role in contributing to implicit weight-stereotypical bias. This may reflect top-down modulation due, for example, to increased attention towards fat as compared to thin bodies. Hence, our results extended previous knowledge (e.g., Quadflieg et al., 2011) on the role of perceptual processing areas in social biases by showing that artificially modulating the neural excitability of extrastriate visual areas implicated in the evaluation of body shape (Urgesi et al., 2007b; Downing et al., 2001) can change prejudice towards fat people.

It is worth noting that, while EBA c-tDCS significantly modulated the association between a specific perceptual dimension of the body (i.e., thinness) and general conceptual attributes of a person (i.e., honest, kind etc.), no effects were found on the association between the same perceptual dimension and an evaluative dimension (i.e., aesthetics) related to body perception, but not involving person-specific processing. Thus, EBA c-tDCS did not alter how thin or round bodies appeared or how beautiful they were judged. Its effects were rather specific when body perception involved forming representations about high-level traits of a person. Previous studies (Calvo-Merino et al., 2010; Cazzato et al., 2014a, 2016a) have shown that magnetic stimulation of EBA alters the judgements of how much an observer likes other people's bodies. These judgements require using basic perceptual aspects, either static (i.e., thinness) or dynamic (Cazzato et al., 2012), to express a general evaluation about the appeal of an unfamiliar individual. Thus, these findings are in keeping with the suggestion (Greven et al., 2016; Greven and Ramsey, 2017; Quadflieg et al., 2015) that body perception processing in EBA (and

other body specific areas in the occipito-temporal cortex) is functionally coupled with person knowledge processing in the theory-of-mind network to form an integrated representation of other people.

In spite of the reliable effects of EBA c-TDCS, a-tDCS of the extrastriate visual cortex did not modulate the anti-fat bias. Anodal-tDCS has been shown to enhance perceptual (Falcone et al., 2007) and motor (Nitsche et al., 2003) learning, social ability (Santiesteban et al., 2012), and visual analgesia (Mancini et al., 2012). However, studies using tDCS in animal models (Bindman et al., 1964; Creutzfeldt, Fromm and Kapp, 1962) have shown that the effect of cathodal stimulation may be stronger than the effect of anodal stimulation if identical stimulation parameters are used. This is in line with the general observation of asymmetric neuroplastic effects in the central nervous system, with excitability reductions being easier to elicit than excitability increases, as shown in animals in vivo (Froc et al., 2000; see Antal et al. 2006 for a review on tDCS effects on visual cortex). Part of the explanation of this asymmetry may reside in the fact that in some experiments the visual system is probably already optimally tuned in healthy subjects and, thus, an excitatory enhancement induced by a-tDCS cannot further improve the perception of visual stimuli (Antal et al., 2006). **However, evidence with regards to the effectiveness of cathodal vs. anodal tDCS is still inconclusive and further experimental manipulations are deemed as necessary to further investigate the potential roles of these factors with respect to the absence of a-tDCS effects over occipital brain areas.**

Overall, these findings support the notion that additional factors, such as the orientation of the electric field (e.g., Nitsche and Paulus, 2000) and the background level of activity in the system when tDCS is applied, might have affected our results. Hence, some

features of the task-related activation may interact with the physiological state of the cortex and polarity of tDCS stimulation (Vallar and Bolognini, 2011; Antal and Paulus, 2008; Antal et al., 2004).

A further result of the present study is that, despite differences between the two gender groups, no relation was observed between the changes of weight bias after c-tDCS and the individual level of explicit phobic attitude and internalization of Western ideals and BMI. This might be due to the fact that the range of observers' BMI and self-report measures within our female and male samples was not large enough to disclose any relevant effects of interindividual differences. This finding, however, is in keeping with a study of Teachman and Brownell (2001) and Teachman et al. (2003), who found no evidence of statistically significant relation between the Fat Phobia Scale and implicit bias as detected with a bad/good weight-IAT that was similar to our task. Such dissociation between implicit and explicit measures of anti-fat bias might result from considering social undesirable the labelling of obese individuals as 'bad' (Teachman and Brownell, 2001).

The possible mediating role of perceived attractiveness of the body stimuli used during both IATs needs to be considered. Indeed, some researchers have claimed that anti-fat prejudice may stem from the perception of overweight individuals as unattractive or aesthetically displeasing (e.g., Morrison and O'Connor, 1999). However, we found gender differences in the v-IAT during sham stimulation, but both male and female participants showed reliable implicit weight-bias in the association of fat or slim bodies to the beautiful-ugly dimension in the ae-IAT. Furthermore, tDCS affected men's v-IAT, but no specific tDCS modulation was found for the ae-IAT, suggesting that valence and aesthetic evaluations may be two independent judgement categories during person

perception and might be underpinned by different neural circuitry. Furthermore, during the IAT procedure, participants are explicitly required to classify stimuli according to their body weight. **Thus, it is unclear whether body-related perceptual areas are similarly involved when anti-fat bias is prompted by the mere sight of an obese body independently from explicit focus on the weight dimension (Moors and De Houwer, 2006; Schupp and Renner, 2011; see also Quadflieg et al., 2011).**

The present findings might have clinical relevance for the understanding and treatment of body schema disturbances in Eating Disorders (EDs). Although, there is currently large evidence to suggest that neuromodulation has potential for altering disordered eating behaviours, food intake and body weight, evidence of using tDCS (and/or TMS) on broader brain network responsible in sustaining ED symptomatology, are still scanty. In fact, much of the research on neuromodulation and eating behaviour has targeted the dorsomedial and dorsolateral prefrontal cortex (Brass and Haggard, 2007; Campbell-Meiklejohn et al., 2008; Khedr, Elfetoh, Ali, and Noamany, 2014; Ljubisavljevic, Maxood, Bjekic, Oommen, & Nagelkerke, 2016; see also McClelland et al., 2013 and Hall & Vincent, 2017 for a recent review on non-invasive brain stimulation for food cravings, consumption, and disorders of eating), which have a key role in self-regulatory control mechanisms (Ochsner & Gross, 2008).

While the prefrontal cortex is very theoretically meaningful as a modulation target for food-related outcomes (Miller and Cohen, 2001), little attention has been paid to cortical areas that are involved in human visual body processing. Indeed, recent studies have shown that perceptual adaptation to model bodies may alter weight-related body preferences in healthy individuals and patients with EDs

(Winkler and Rhodes, 2005; Glauert et al., 2009; Mele et al., 2013, 2016; Cazzato et al., 2016b).

Importantly, several studies have shown that EBA is active when subjects are engaged in viewing images of bodies through interconnections with other brain regions, also involved with body image (e.g., ventral premotor cortex; Kitada, Johnsrude, Kochiyama, & Lederman, 2009). Furthermore, Suchan and colleagues (2013), using an fMRI task that showed body images in contrast with images of chairs, found a reduced connectivity between middle occipital gyrus and fusiform body area (FBA) and between FBA and EBA in patients with AN. Some studies have shown that EBA is also activated by the selective display of images of bodies that express emotions (anger, disgust, happiness, fear), supporting a close correlation between extrastriate visual areas and the amygdala, which is involved in processing emotional information (Myers & Sowden, 2008). Furthermore, modulating neural activity of EBA with repetitive transcranial magnetic stimulation altered the hedonic value attributed to body figures by healthy individuals (Cazzato et al., 2014; 2016). In keeping with this view, our study documents the involvement of these areas in weight-related stereotypes about other individuals. Thus, brain stimulation studies targeting EBA and other relevant body image brain regions may open new horizons to understand the neural substrate of EDs and evaluate the therapeutic potential of tDCS for treating distortions of perception, conceptions and affects related to one's body weight or shape.

Limitations

There are a few limitations to consider when interpreting the current findings. First of all, we need to consider that the spatial resolution of tDCS, due to using large sponge pads positioned on the skull, can be relatively diffuse. **Indeed, it has been previously reported that brain stimulation by means of tDCS protocols is unlikely to be constrained to the cortex underneath the electrodes (Datta et al., 2009; Bikson and Rahman, 2013; Bestmann, de Berker and Bonaiuto, 2015). In particular, a recent modelling study (DaSilva et al., 2015) estimated that, with a similar vertex-occipital cortex montage (with the anode over Cz and cathode over Oz), current flows mainly to the parietal and occipital lobes with the maximum electric field occurring in the primary and secondary visual cortices. However, current flow extended to the cingulate cortex, insula, central sulcus and thalamus. As such, we cannot rule out that that stimulation of extrastriate visual cortex might have affected nodes of a broader network involved in person perception and person knowledge. Indeed, it has been previously reported that the frontal cortex, anterior temporal lobes and the limbic system are key areas implicated in the forming of social prejudice. More specifically, the amygdala has been found to be critically involved in cognitive and affective learning, including implicit attitudes (Amodio and Devine, 2006; Dolan et al., 2000; Phelps, Cannistraci, and Cunningham, 2003; Stanley, Phelps, and Banaji, 2008). Furthermore, recent experimental evidence has proposed a critical involvement of the anterior temporal lobes in expressing prejudice by means of conceptual processing (Snyder, Bossomaier, and Mitchell, 2004; Gallate et al., 2011). Finally, a study of Cattaneo and colleagues (2011) demonstrated the causal role of the prefrontal cortex in controlling gender stereotypical beliefs in men. Interestingly, they found that non-invasive brain stimulation delivered at stimulus presentation over the prefrontal cortices**

led to an increased gender-stereotypical bias for the D-scores of male participants, as compared to a control condition. It therefore remains to be determined how specific the current results are to the stimulation site and, for example, whether interfering with the activity of the extrastriate visual cortex might have in turn interfered with key areas important for the control of automatic (negative) associations, such as the prefrontal cortices.

In a similar vein, we cannot rule out that tDCS may have affected top-down control mechanisms, such as the ability to regulate bias (Conrey et al., 2005) and task-switching abilities (Klauer et al., 2010), which are involved in performing an IAT. **Although the gender- and IAT-selectivity of the effects of c-tDCS over left extrastriate visual cortex would speak against general effects on IAT categorization performance, one may speculate that c-tDCS might have affected cognitive control abilities particularly in those individuals (i.e., men) who show higher anti-fat bias and, thus, need more cognitive control to moderate it.**

Although the order of testing was counterbalanced across participants, one potential limitation of this study could rely on the repetition of the same IAT task under different tDCS conditions (anodal, cathodal, sham) within the same day/week. Indeed, it has been shown that the magnitude of the effect tends to decline with repeated administrations (Nosek, Greenwald and Banaji, 2007). However, the absence of any repetition effects for the control ae-IAT points against this possibility.

Finally, it cannot be determined to what extent the selective decrease in the anti-fat bias after EBA c-tDCS observed in this study can be generalised to other specific subtypes of anti-obesity attitudes and/or social stigma in general. Further studies are

required to systematically examine the effects of tDCS on various negative attitudes against stigmatized social groups.

Conclusions

Overall, the present study may contribute to the growing social neuroscience literature on the neural underpinnings of person perception, thus extending previously reported work on explicit and implicit weight stigma as a function of first impression formation (e.g. facial attractiveness, trustworthiness, and competence). Previous neuroimaging studies (e.g., Quadflieg et al., 2011) have shown that early perceptual aspects of person construal are sensitive to the stereotype-related status of individuals. Here, we provided causative evidence that activity in body-selective occipito-temporal areas actively contributes to the formation and expression of implicit stigma based on body size. This pairing of functional responses between distinct brain circuits may indicate that person-perception and person-knowledge neural networks are not entirely encapsulated from other neural brain systems. **It has been proposed that the primary function of EBA is grounded on visually analysis of the bodies of conspecifics (Urgesi et al., 2004; Downing & Peelen, 2011). However, during this process EBA may exchange signals not only with other brain circuits that represent aspects of another person's physical appearance (person perception), such as body shape and posture (Cazzato et al., 2014), but also with brain areas (i.e., TPJ and temporal pole) that respond when reasoning about another person's trait-based characteristics (person knowledge) (Greven et al., 2017). In keeping with previous neuroimaging findings (Greven, Downing and Ramsey, 2016; Ewbank et al., 2011; Quadflieg et al., 2011;**

Zimmermann et al., 2013), the results of our brain stimulation study provide empirical support for this notion and enhance the belief that interactions between specific person perception and person knowledge neural systems underlie social perception abilities.

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Figures Legends:

Fig. 1: Schematic representation of tDCS electrodes montage over left and right Extrastriate visual cortex.

Fig. 2: Effects of cathodal (c-tDCS), anodal (a-tDCS) and sham-tDCS (s-tDCS) on D-scores as a function of gender (men, women) and t-DCS hemisphere (right EVC, left EVC) for the valence-IAT. A: male participants, B: female participants. *Error bars* indicate standard errors mean over participants * $p < 0.05$. Notes: tDCS. Transcranial direct current stimulation; EVC. Extrastriate Visual Cortex; IAT. Implicit association test.

Fig. 3: Effects of cathodal (c-tDCS), anodal (a-tDCS) and sham-tDCS (s-tDCS) on D-scores as a function of gender (men, women) and t-DCS hemisphere (right EVC, left EVC) for the aesthetic-IAT. A: male participants, B: female participants *Error bars* indicate standard errors mean over participants * $p < 0.05$. Notes: tDCS. Transcranial direct current stimulation; EVC. Extrastriate Visual Cortex; IAT. Implicit association test.