



Obesity, subliminal perception and inhibition: Neuromodulation of the prefrontal cortex



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ABSTRACT

The prefrontal cortex (PFC) plays a central role in food choice, and may be partly dysfunctional in obesity – a condition linked to altered attention and inhibition processes, particularly in response to food-related stimuli. We investigated the role of the PFC in subliminal visual processing and response inhibition to food pictures using anodal, cathodal, or sham transcranial direct current stimulation (tDCS) in a sample of 53 normal weight, overweight, or obese participants. Subliminal processing was measured with a breaking continuous flash suppression task (bCFS), and inhibition with a Go/No-Go task. BMI was included in the analyses as a continuous predictor. Higher BMI was associated with prolonged subliminal processing for both food and nonfood pictures in the bCFS task, and with longer RTs in food Go trials in the Go/No-Go task. Therefore, higher BMI was associated with an attentional bias for food images during supraliminal, but not subliminal visual processing. Moreover, anodal tDCS resulted in shorter detection times in the bCFS task, especially in participants with higher BMI. We conclude that anodal tDCS affects subliminal perception and attentional processes, and speculate that these effects may explain previous reports of reduced craving and food intake after anodal tDCS.

1. Introduction

Obesity is a debilitating condition, and a major risk factor for cardiovascular diseases, diabetes, musculoskeletal disorders such as osteoarthritis, and some cancers (World Health Organization, 2018). Today, over a third of the world's population is either obese or overweight (Hruby & Hu, 2015). According to the World Health Organization, the worldwide prevalence of obesity has nearly tripled in the last forty years (World Health Organization, 2018). Therefore, it is important to understand the mechanisms underlying overeating behaviors. From a neurocognitive perspective, this has led to a significant number of studies exploring how altered cognitive functions and brain mechanisms may be involved in obesity.

In particular, obesity has been linked to impaired performance on attention allocation and impulsivity control tasks (Cook et al., 2017). Obese individuals, compared with normal-weight participants, have been reported to exhibit increased attentional biases for food cues (Hendrikse et al., 2015). For instance, obese individuals show longer fixation times for food compared to non-food items (Castellanos et al., 2009), response facilitation towards targets replacing food probes (Kemps, Tiggemann, & Hollitt, 2016), impaired inhibition of responses

to food pictures (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016; Kulendran, Vlaev, Gamboa, & Darzi, 2017, but see; Loeber et al., 2012), and altered implicit attitudes towards food (Craeynest et al., 2005; Roefs & Jansen, 2002). This attentional bias towards food seems to be already present at an automatic, implicit phase of stimulus processing (Cserjesi, Vos, & Deroost, 2016; Nijs, Franken, & Muris, 2010), and has been suggested to have a strong influence on appetitive behavior (Finlayson, King, & Blundell, 2008; Forman et al., 2018; Takada et al., 2018).

The presence of an attentional bias for food in obese individuals is in line with the view that obesity is characterized by an imbalance between cognitive control and reward sensitivity. Specifically, poor inhibitory control in obesity may favor attention towards food and promote, in turn, hedonic eating (Ziauddeen, Alonso-Alonso, Hill, Kelley, & Khan, 2015). Cognitive control is implemented by several regions, in particular the dorsolateral prefrontal cortex (dlPFC) (Alonso-Alonso et al., 2015). This region is also involved in controlling food choices, and has a top-down cognitive influence on satiation (Gluck, Viswanath, & Stinson, 2017). Interestingly, lateral sectors of the prefrontal cortex are active when participants think about the benefits of not eating a food item, or are asked to voluntarily suppress hunger (Alonso-Alonso

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et al., 2015). Moreover, obese and overweight individuals show decreased activity of this region (Dong, Jackson, Wang, & Chen, 2015; Gluck et al., 2017). Numerous studies have investigated the role of PFC areas for cognitive control and inhibition by applying neuromodulatory techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) (for a review, see Forcano, Mata, de la Torre, & Verdejo-Garcia, 2018). Transcranial DCS neuromodulation is implemented by applying a direct, weak electric current through electrodes placed on the scalp. The current facilitates or inhibits spontaneous neuronal activity of the brain areas directly below the electrodes (Nitsche et al., 2008). Specifically, anodal tDCS has been shown to increase cortical excitability, whereas cathodal tDCS decreases it (Nitsche & Paulus, 2001). Applying anodal tDCS could benefit attention, learning, and memory (Coffman, Clark, & Parasuraman, 2014).

Importantly, tDCS of the dlPFC may effectively reduce food cravings and overeating (Fregni et al., 2008; Gluck et al., 2015; Heinitz et al., 2017; Kekic et al., 2014; Ljubisavljevic, Maxood, Bjekic, Oommen, & Nagelkerke, 2016; Ray et al., 2017; Sauvaget et al., 2015), and can ameliorate symptoms in eating disorders such as bulimia and binge eating disorders (Burgess et al., 2016; Kekic et al., 2017; Khedr, Elfetoh, Ali, & Noamany, 2014). The common interpretation of these findings is that enhancing dlPFC activity may alter the reward-cognition balance, possibly facilitating cognitive control and suppressing reward-related mechanisms, although the specific cognitive processes being affected remain largely unknown (Val-Laillet et al., 2015).

Although tDCS over the prefrontal cortex reduces attentional bias towards food (e.g. Fregni et al., 2008), this has not been investigated in obese individuals specifically, nor has it been tested at a subliminal level of processing. The improvement of current, and the development of new clinical strategies, requires a comprehensive understanding of the cognitive processes and neural bases underlying attentional biases in obese individuals. Therefore, the aim of this study was to investigate the effects of right dlPFC modulation through tDCS on subliminal and inhibitory processing of food stimuli in obesity. To measure subliminal processing, we used Continuous Flash Suppression (CFS) to temporarily suppress stimuli from visual awareness (Tsuchiya & Koch, 2005). During CFS, a stimulus is shown to one eye, while a stream of distracters is presented to the other eye in the same field of view. Because participants' awareness is restricted to one image at a time in a given field of view (due to interocular suppression), and because stimuli are shown with less salient visual features compared to flashing distracters, awareness of the stimulus can be suppressed for up to several seconds. In the breaking CFS (bCFS) variant, presentation times of several seconds are used with the intention of capturing the moment in which participants become aware of the stimulus' position, which they indicate through button press. In bCFS stimulus perception is thus subliminal (preattentive or automatic) until suppression "breaks", and stimulus awareness occurs. Previous research has shown that the length of time during which participants remain unaware of the stimulus, i.e. the suppression time, depends on the characteristics of the stimulus and on its subjective salience. More salient and familiar stimuli, such as upright faces and recognizable words, tend to break suppression faster (Jiang, Costello, & He, 2007). Therefore, shorter reaction times (RTs) in a bCFS task are typically interpreted as reflecting a processing advantage (and longer RTs as reflecting a processing disadvantage).

Previous studies using CFS to investigate subliminal processing of salient stimuli in clinical populations have reported contradictory findings. Some studies have reported a processing advantage in clinical populations. For example, young violent offenders with low levels of unemotional traits were found to have shorter suppression times for fearful faces, suggesting a processing advantage for fear in this population (Jusyte, Mayer, Künzel, Hautzinger, & Schönenberg, 2015). Similarly, shorter suppression times for spider images were found in individuals with spider phobia, suggesting a processing advantage for these disorder-specific stimuli (Schmack, Burk, Haynes, & Sterzer,

2016). However, other studies have not found a advantage for the processing of disorder-relevant stimuli, and some have even found a processing disadvantage. For example, Yang and colleagues (Z. Yang et al., 2011) tested depressed patients and healthy controls with a task in which pairs of happy and sad faces were masked with CFS for 800 ms, and followed by an unmasked Gabor patch of which participants indicated the direction. While healthy control participants showed greater accuracy when the Gabor patch replaced sad faces, depressed patients had equal accuracy in all types of trials, suggesting that depression is associated with the absence of an attentional bias towards negative emotions. Similarly, using a bCFS task it was found that children with psychopathic traits lack the processing advantage for fearful and (to a lesser degree) disgusted faces, which is typically found in healthy individuals (Sylvers, Brennan, & Lilienfeld, 2011).

The (b)CFS literature has thus revealed differences of subliminal processing between clinical populations and healthy controls. However, the direction of these differences varies between studies. We therefore expected that in the bCFS task individuals with higher BMI, compared to individuals with lower BMI, would either have significantly shorter suppression times for food images, as a reflection of stimulus salience, or on the contrary have longer suppression times for food images, reflecting a processing disadvantage of a problematic stimulus.

In addition to the bCFS task, we administered a Go/No-go task to measure inhibitory mechanisms. According to previous findings (Kulendran et al., 2017), we expected a higher BMI to lead to slower RTs and lower accuracy in the Go/No-Go task, especially for food stimuli. The combined use of the bCFS and Go/No-Go tasks allowed us to investigate the effect of tDCS from subliminal to supraliminal stages of food stimulus processing. Underweight, healthy, and obese participants completed a bCFS task during sham, anodal or cathodal stimulation of the right dlPFC, in a within-subjects design. The Go/No-Go task was completed immediately following these stimulations. As mentioned above, higher BMI was expected to be associated with altered performance in the bCFS task, with either longer or shorter suppression times, and poorer performance in the Go/No-Go task, with slower RTs and lower accuracy, especially on food trials. Anodal stimulation was expected to reduce this association, and cathodal stimulation to strengthen it. Sham stimulation provided the control condition.

2. Methods

2.1. Participants

Fifty-three participants (11 males; 12 left-handed, one ambidextrous) took part in the study. Participants were recruited through online advertisement and notice boards from May to November 2017. They were enrolled with the aim of including in the experimental sample a wide distribution of BMIs, ranging from underweight (BMI < 18.5) to obese (BMI > 30, as per indications of the World Health Organization). Exclusion criteria were epilepsy, migraines, and the presence of metal parts in the upper part of the body, as well as strabismus and daltonism, i.e. the inability to distinguish between certain colors. Due to exclusion of two participants because of technical failure during testing, the final sample included fifty-one participants (11 males; demographical and clinical data are presented in Table 1). The study was approved by SISSA's Ethics Committee (protocol number

Table 1
Participants' demographic and clinical data.

	Mean (SD)	range
Age	24.5 (3.7)	19–41
Body Mass Index (BMI)	22.9 (3.8)	16.7–34.3
Eating Attitudes Test-26 (EAT-26)	7.2 (6.7)	0–33
Binge Eating Scale (BES)	10.1 (6.0)	0–24

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2.2. Procedure and experimental tasks

Participants completed an online survey to determine whether they fulfilled the inclusion criteria, and to assess a series of variables, such as height and weight. Symptoms pertaining to eating disorders (ED) were investigated through two questionnaires to serve as covariates in all analyses. The Eating Attitudes Test –26 (EAT-26) (Garner, Olmsted, Bohr, & Garfinkel, 1982) was used to evaluate the risk of anorexia and bulimia nervosa. It assesses how often the individual engages in specific behaviors such as worrying about food, dieting, and purging. The Binge Eating Scale (BES, Gormally, Black, Daston, & Rardin, 1982) measures difficulties in controlling eating behavior, such as eating too much, too quickly, or unrelatedly to the feeling of hunger. Each participant was tested on three separate sessions, which were at least 48 h apart, to ensure washout of previous stimulations. A Latin square design was used to randomize and counterbalance the order of stimulations across subjects. A consent form was signed on the first session. Participants were instructed not to eat for two hours before coming to the laboratory. Before testing, they reported their hunger level on a 7-point Likert scale. This was done to control for the effect of hunger, which could influence the salience of food stimuli (e.g. Loeber, Grosshans, Herpertz, Kiefer, & Herpertz, 2013). Participants then completed a training of the bCFS task, after which the experimenter applied the electrodes, and started tDCS. After a 30 s ramp-up period, participants completed the bCFS task, followed by the NoCFS task (detailed descriptions of these two tasks are reported in the bCFS section). The Go/No-Go task was completed at the end of the tDCS stimulation.

2.3. tDCS protocol

Anodal, cathodal or sham tDCS was administered with a battery-driven DC stimulator (Eldith, NeuroConn). One of the electrodes, with an area of 25 cm², was positioned over the right dlPFC, defined as the location 8 cm frontally and 6 cm laterally of the vertex. The other electrode, with an area of 70 cm², was placed on the upper right arm (Fig. 1). Electrode conductance was ensured through the use of a saline NaCl 0.9% solution and conductive gel. Previous studies reported the greatest benefit of tDCS stimulation for ED symptoms from stimulation of the PFC using the anode/right, cathode/left montage (Val-Laillet et al., 2015). Placing one electrode on the right dlPFC, and the other one extracephally on the right arm, enabled us to limit the stimulation to the dlPFC, and therefore to distinguish between the effects of

anodal and cathodal stimulation (see also Koenigs, Ukueberuwa, Campion, Grafman, & Wassermann, 2009; Martin et al., 2011; Mengotti, Aiello, Terenzi, Miniussi, & Rumiati, 2018). During stimulation the current intensity was of 1.5 mA (current density of 0.06 mA/cm²), with a ramping-up period of 30 s. The stimulation lasted 20 min, to comply with safety limits (Woods et al., 2016). However, the effects of tDCS stimulation have been reported to last for up to one hour (Nitsche & Paulus, 2001). During the sham session, the montage was the same as during the anodal stimulation, but the current was supplied only during the first 30 s – enough to elicit a tingling/itching sensation. At the end of each session, participants filled in a questionnaire about the sensations experienced during the stimulation (Fertonani, Ferrari, & Miniussi, 2015). A Chi-squared test was used to compare the frequency at which participants thought they were in each condition. This revealed no significant differences between the three stimulation sessions (anodal, cathodal, sham) [$\chi^2(6) = 6.38, p = 0.38$].

2.4. Breaking continuous flash suppression (bCFS)

Being a specific type of binocular rivalry, bCFS consists in showing two different streams of images to each eye, in the same field of view. While one eye is shown a stimulus, which is slowly increasing in contrast, the other eye perceives a series of continuously changing high-contrast geometric patterns (distractors). The incongruity between the two, and the attention-grabbing nature of the distractors, result in the suppression of the awareness of the stimulus of interest for up to a few seconds. As customary, stimuli and distractors were embedded in separate squared frames shown side by side on the screen. However, by looking through an individually calibrated mirror stereoscope (ScreenScope), participants' conscious perception, was that of a single superimposed and perfectly aligned square. The stimulus was displayed to one eye in one of the quadrants of the square, while the distractors were displayed to the other eye over the whole square. Participants were instructed to indicate the position of the stimulus relative to the central fixation cross by pressing the 'f' button on a QWERTY keyboard if the stimulus was on the left, or the 'j' button if it was on the right. Participants used their index fingers and were told to respond as fast and accurately as possible. A similar procedure was used in the first two experiments in Korb, Osimo, Suran, Goldstein, and Rumiati (2017). Order, position, and the side the stimuli were presented were randomized so that each participant saw each stimulus once in all four quadrants in a different order. Distractors were shown at 100% contrast and changed at a rate of 10 Hz, while the contrast of the stimuli increased linearly from 0% to 60% over the course of one second, and

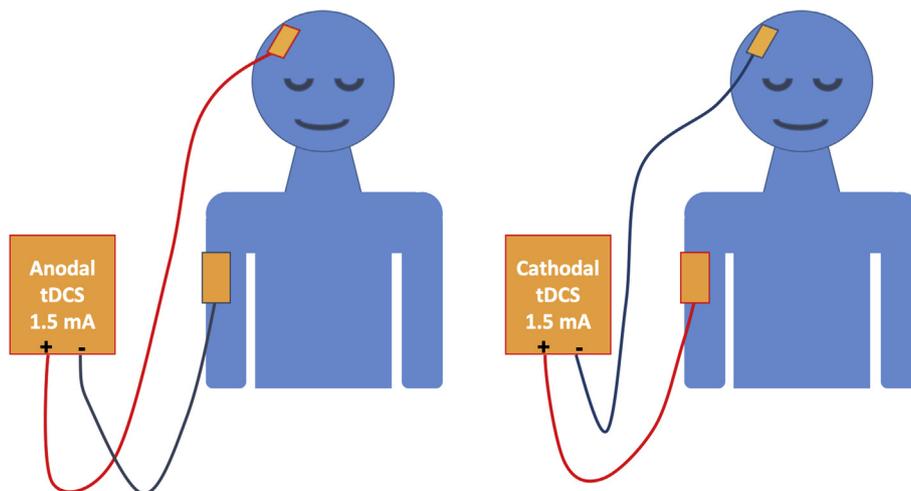


Fig. 1. Electrode placement for the cathodal (left) and anodal (right) tDCS stimulation. The sham stimulation had the same setup as the anodal stimulation, but after the ramping up period of 15 s the current between the electrodes stopped.

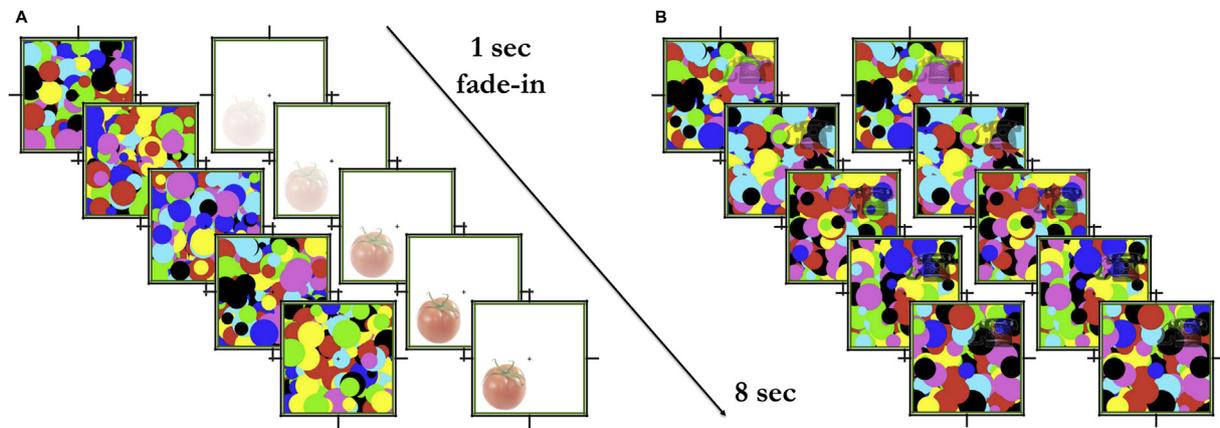


Fig. 2. An example trial of the bCFS task (A) and of the NoCFS task (B).

then stayed at 60% until response. If no response was given during eight seconds, the task moved automatically to the next trial. The bCFS task was preceded by a five-minutes training, consisting of 80 trials during which another set of stimuli was used. The bCFS task included 160 trials, and every 30 trials the task paused, and participants were allowed to rest. To ensure that the results of the bCFS task are due to processing during suppression, participants performed an equivalent task without suppression (hence NoCFS), in which the stimuli and the distractor were immediately perceived consciously. This task had the same instructions, number of trials, and stimuli as the bCFS task, but stimuli and distractors were superimposed and shown to both eyes simultaneously. Example trials of the bCFS and NoCFS tasks are shown in Fig. 2.

In both the bCFS and the NoCFS tasks, stimuli were displayed on a 17" LCD monitor with a resolution of 1280×1024 pixels and a refresh rate of 60 Hz, positioned 50 cm away from participants. A chin rest was used to minimize head movements. The two squares were 400×400 pixels, and stimuli were shown in a 190×190 pixel quadrant. The tasks were programmed in and presented with Python using the Psychopy 2 library (Peirce, 2007) running on a notebook computer with Windows XP.

2.5. Go/No-Go task

In the Go/No-Go task, the instructions were to respond as quickly as possible to Go stimuli, and to refrain from responding when a No-Go stimulus was presented. In half of the blocks, Go cues consisted of food images and No-Go cues of non-food images (kitchen utensils), while in the other half the assignment was reversed. There were four blocks of 40 trials each. In each block, 12 out of 40 trials (30%) were No-Go trials. The Go/No-Go task and the stimuli were the same as those used by Aiello and colleagues (Aiello, Eleopra, Foroni, Rinaldo, & Rumiati, 2017). The order of the blocks was semi-random (ABAB or BABA) and counterbalanced across sessions and across participants. The order of the stimuli within each block was randomized. Reaction times (RTs) and accuracy for each trial were recorded. Only RTs of correct Go trials were used in the analyses. The task was programmed using E-Prime software (Psychology Software Tools, Inc., 2012) and lasted approximately eight minutes. An example trial is depicted in Fig. 3.

2.6. Stimuli

In the bCFS and NoCFS tasks, stimuli consisted of 20 images of food and 20 images of non-food items (e.g. animals, man-made objects etc.), selected from the FoodCast research image database (FRIDA; Foroni, Pergola, Argiris, & Rumiati, 2013). Food pictures were comprised of 10 high-calorie food pictures (caloric density > 100 Kcal per 100 g) and 10 low-calorie food pictures, in order to represent a wide variety of food

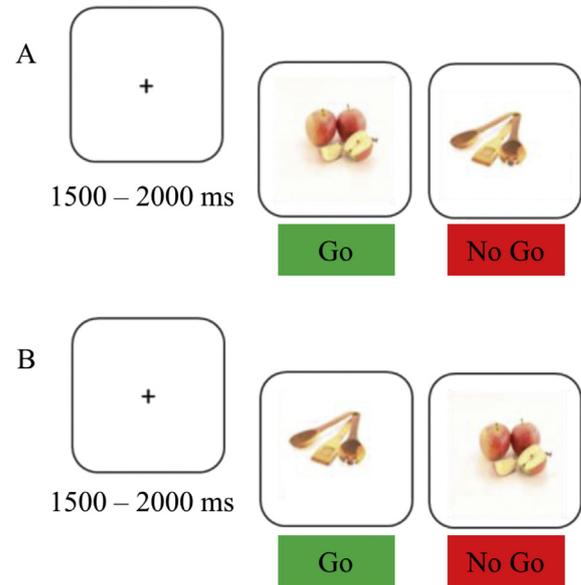


Fig. 3. Example trial in the Go/No-Go task in a block using food images as Go cues (above) and in a block using non-food pictures as Go cues (below). This picture is adapted from [43].

stimuli. Food and non-food items were matched for brightness [$p = 0.82$] and spatial frequency [$p = 0.09$], since low-level visual features can influence suppression times (Gayet, Van der Stigchel, & Paffen, 2014; Gray, Adams, Hedger, Newton, & Garner, 2013; E.; Yang & Blake, 2012). Moreover, food and non-food items did not differ in valence, familiarity, typicality or arousal [$ps > 0.15$]. The distractor images consisted of a set of 100 pictures with colorful oval shapes of different sizes creating random patterns.

2.7. Analyses

RTs in the bCFS, NoCFS and Go/No-Go tasks, as well as accuracy in the Go/No-Go task, were analyzed with linear mixed-effects models (LMMs) using the lmer function (lme4 package) in the software R (version 3.4.3; www.r-project.org). In the bCFS and NoCFS tasks, data were cleaned by removing trials with no responses, i.e. trials in which the stimuli did not break suppression during the course of the eight second trial (6.59% across all participants), trials with wrong responses (1.44%), trials with RTs below 500 ms, as these responses are unlikely to represent stimulus awareness (0.16%), and trials with RTs that were more than 2.5 SD from the mean of each subject (0.01%). In addition, six participants were excluded as they failed to respond to two thirds of

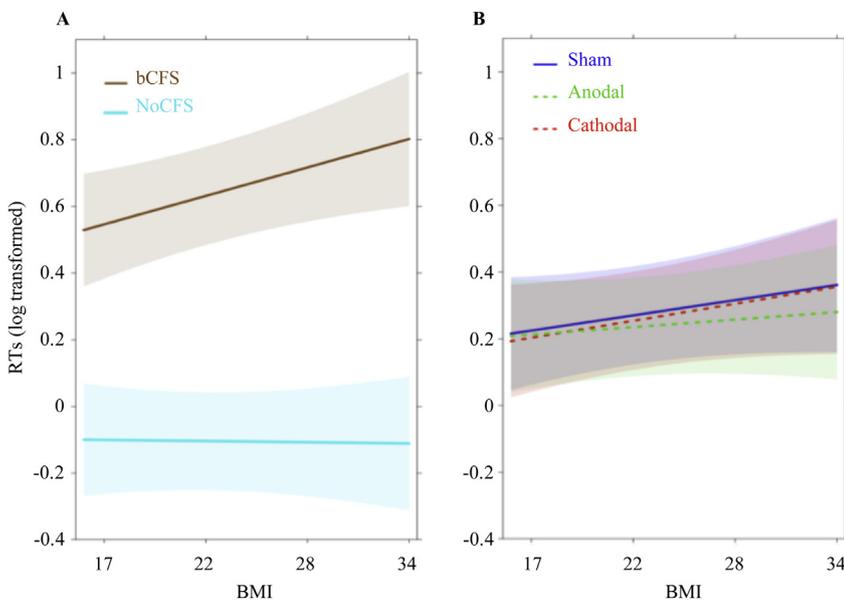


Fig. 4. Fit lines of the model addressing the effect of the stimulation on RTs of the bCFS and NoCFS tasks. A) Task by BMI effect. A higher BMI significantly predicted longer suppression times in the bCFS task, but not in the NoCFS task. B) Stimulation by BMI effect. Anodal stimulation shortened RTs both in high and low BMIs, with a greater effect on high BMIs. Cathodal stimulation does not differ from Sham stimulation.

trials. The final analyses therefore included 44 participants (demographic data of the final sample is reported in Table S1). RTs of the bCFS, NoCFS and Go/No-Go tasks were log transformed, and fixed factors were mean centered. EAT26 and BES scores were used as covariates to control for symptoms related to eating disorders. Intercepts for the random effects of Participant, Session, Stimulus and Stimulus Location were included in all models. After initial inclusion, these predictors were removed one by one, and the resulting model was compared to the initial more complicated one by using the anova function (lmerTest package) and the AIC criterion – a reduction of which suggests better model fit (Bolker et al., 2009). When the AIC of two models did not differ significantly, the model with fewer factors was chosen. In addition, once non-significant factors had been removed, non-significant high-level interactions were pruned. In order not to split the sample in two groups when evaluating the relative weight of higher and lower BMIs in higher-order interactions, all post-hoc interactions that included continuous factors were conducted according to Aiken and West (1991). The LMMs were therefore re-run after adding or subtracting one standard deviation from each participant's BMI, in order to weigh the relative strength of higher and lower BMIs in influencing the interaction. As the distribution of participants was not equal between females and males, a random intercept for Sex was included in each model. As this intercept did not improve any of the models' fit (all p s = n.s.), it was removed from all analyses.

The final model investigating the effect of stimulation on bCFS and NoCFS included Task (bCFS, NoCFS), Stimulation (Anodal, Cathodal and Sham) and BMI, entered as a continuous variable, as factors. In the analyses of the Go/No-Go task, the final model investigating the effect of stimulation on RTs included Stimulus Category (Food, Non-Food) and BMI, entered as a continuous variable, as factors; the model on accuracy included the factors Trial Type (Go, NoGo) and Stimulation. All comparisons between initial and final models are reported in Table S2.

3. Results

To ensure that eventual RT differences were not caused by learning effects, the RTs from the three training sessions of the bCFS task were compared. No difference between RTs in the training sessions emerged [$F(2) = 0.40$, $p = 0.67$]. Moreover, participants' hunger levels did not differ between sessions [$F(2) = 0.58$, $p = 0.56$].

3.1. bCFS and NoCFS tasks

Results showed a main effect of Task [$F(1, 40344) = 43764$, $p < 0.001$], indicating longer RTs in bCFS compared to NoCFS, confirming that suppression did occur during the bCFS task (for an overview of RTs during bCFS and NoCFS tasks, see Fig. S1). We also found a main effect of Stimulation [$F(2, 40343) = 34$, $p < 0.001$], reflecting shorter reaction times during anodal stimulation compared to sham [$t(40343) = 8.23$, $p < 0.001$] and to cathodal stimulation [$t(40343) = 4.38$, $p < 0.001$], and a reduction of RTs in cathodal compared to sham stimulation [$t(40343) = 3.83$, $p = 0.001$].

In addition, a significant Task \times Stimulation interaction was found [$F(2, 40343) = 9$, $p < 0.001$]. Post-hoc tests showed shorter RTs in the bCFS task, during both the anodal [$t(40343) = 8.49$, $p < 0.001$] and the cathodal [$t(40343) = 4.96$, $p < 0.001$] stimulation, with a stronger effect of the anodal compared to the cathodal stimulation [$t(40343) = 3.54$, $p < 0.001$]. Conversely, in the NoCFS task only the anodal stimulation caused significant shorter RTs compared both to the sham [$t(40343) = 3.08$, $p = 0.002$] and the cathodal stimulation [$t(40343) = 2.67$, $p = 0.008$], and RTs during cathodal stimulation did not significantly differ from sham [$t(40343) = 0.20$, $p = 0.67$].

A significant Task \times BMI interaction was also observed [$F(1, 40344) = 363$, $p < 0.001$]. Post-hoc analyses revealed that higher BMI led to longer RTs in the bCFS task [$t(43) = 2.4$, $p = 0.02$] but not in the NoCFS task [$t(43) = -0.12$, $p = 0.91$]. Moreover, although a significant difference between bCFS and NoCFS was present in both lower and higher BMIs, post-hoc tests showed that this difference was greater in participants with a higher BMI [lower BMIs $t = 134.67$, $p < 0.001$; higher BMIs $t = 161.45$, $p < 0.001$, see Fig. 4 Panel A]. Interestingly, we found a significant Stimulation \times BMI interaction [$F(2, 40347) = 14$, $p < 0.001$]. Post-hoc tests showed that BMI's effect was stronger during anodal stimulation than during either sham or cathodal stimulations [all $t > 3.9$, all $p < 0.001$]. Further exploring this effect, we found that anodal stimulation significantly shortened RTs for both lower BMIs and higher BMIs compared to sham stimulation, but this effect was greater in higher BMIs [lower BMIs $t = 2.97$, $p = 0.003$; higher BMIs $t = 8.47$, $p < 0.001$]. See Fig. 4 Panel B and Table S3.

In summary, especially in individuals with higher BMI, anodal tDCS of the right dlPFC resulted in faster awareness in the bCFS task. This finding was not, however, specific to food-related images.

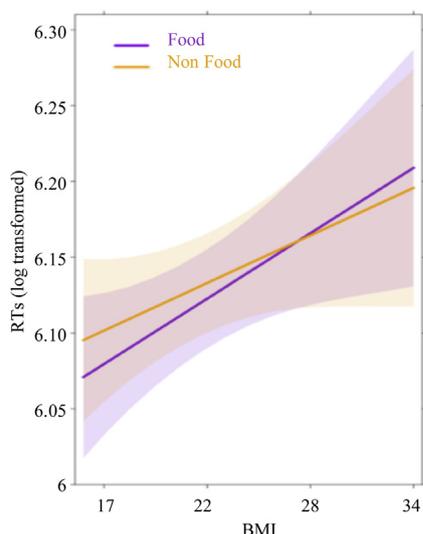


Fig. 5. Fit lines of the model on the effect of anodal stimulation on the Go trials of the Go/No-Go task. A higher BMI predicts slower RTs on food trials, but not in non food trials.

3.2. Go/No-Go

In the analysis of the RTs of Go trials, we observed a main effect of BMI [$F(1, 49) = 4.2, p = 0.046$], reflecting a correlation between higher BMI and longer RTs, and a significant interaction between Stimulus Category and BMI [$F(1, 16431.7) = 10.5, p = 0.001$] (Table S4). Participants' BMI significantly affected their reaction times to foods [$p = 0.02$] but not to non-foods [$p = 0.09$]. In particular, the difference between foods and non-foods was significant for lower BMIs [$p = 0.045$] but not for higher BMIs [$p = 0.88$]. See Fig. 5.

In the analysis on accuracy, we found a significant effect of Trial Type [$F(1, 9393.9) = 649.06, p < 0.001$] meaning higher accuracy for Go trial compared to NoGo trials. No other effect reached the significance level (Table S5).

4. Discussion and conclusions

The study investigated if different ranges of BMI are associated with changes in subliminal perception and inhibitory processes in response to food images, and how these processes are affected by the modulation of neural activity in the right dIPFC through tDCS. Longer suppression times were found in the bCFS task in individuals with a higher BMI. This result is in line with the hypothesis that a domain-general attentional deficit characterizes obese individuals (Cook et al., 2017; Prickett, Brennan, & Stolwyk, 2015). In addition, this result shows, for the first time, that this impairment may also affect subliminal perception. Interestingly, using a different methodology, such as visual masking, a higher threshold of perceptual awareness has been reported in multiple sclerosis and linked to white matter damage and altered connectivity between distant cortical areas (Reuter et al., 2007, 2009). Numerous studies have demonstrated white matter alterations in obese individuals, especially in the corpus callosum and fornix (see for instance Kullmann, Schweizer, Veit, Fritsche, & Preissl, 2015; Xu, Li, Lin, Sinha, & Potenza, 2013).

In relation to the processing of food-related cues, it is important to note that, in contrast to expectations, we did not observe a bias for food stimuli at the subliminal level. We propose several explanations for this results. First, it is possible that a bias for food stimuli does not occur at the subliminal level, but instead emerges only at a later processing stage, or it may appear only when the task requires explicit categorization of foods vs. non-foods. This possibility is corroborated by the fact that the current literature on food bias in obesity has mostly been

based on paradigms in which food stimuli were consciously perceived by participants (Kemps, Tiggemann, & Hollitt, 2014; Nijs & Franken, 2012). In the present study, a higher BMI predicted longer RTs on food Go trials in the Go/No-go task, which seems to support this explanation. Mogg et al. (1998) also report an attentional bias when food was perceived consciously, but not when it was presented subliminally. Secondly, two other factors might have had an impact on our results: hunger and eating disorders symptomatology (Nijs & Franken, 2012). Concerning the effect of hunger, Castellanos et al. (2009) only reported differences in attentional bias for foods between obese and normal-weight individuals after satiation and our participants fasted for two hours before testing. However, the presence of a food effect in the Go/No-Go task excludes the possibility that a lack of subliminal bias for foods can be ascribed to participants' satiation, as the tasks were performed at a similar time during the same session. Nijs and Franken (2012) have also proposed that enhanced attentional bias for food may only be present in obese individuals showing an eating disorder. Interestingly, in another study, we observed faster awareness of food stimuli in obese individuals with higher self-reported eating-disorder symptoms (Osimo et al., under review). One interpretation of these results is that a higher BMI predicts a bias toward food only at late attentive stages, or when categorizing stimuli as foods or non-foods. Alternatively, a high BMI only predicts a food bias at a subliminal level in individuals with eating disorders symptomatology. Finally, it is possible that the stimuli that we have used were not salient enough, as half of them depicted high calorie foods and the other half low calorie foods. Previous studies have shown that the calorie content of food pictures modulates the activation of brain areas related to reward processing (Frank et al., 2010; Killgore et al., 2003), and in particular, that individuals with a high BMI show a stronger bias for, and a stronger response towards high calorie foods (Graham, Hoover, Ceballos, & Komogortsev, 2011; Killgore & Yurgelun-Todd, 2005; Rothmund et al., 2007). It is therefore possible that a set of stimuli comprised of only highly caloric, palatable foods might elicit a subliminal processing bias that was not observed with this stimulus set.

As for the effects of the tDCS stimulation on the bCFS and NoCFS tasks, we found that anodal stimulation significantly reduced RTs compared to sham and cathodal stimulation. This result accords well with studies showing benefits of anodal stimulation of the PFC on visual attention (Leite, Carvalho, Fregni, Boggio, & Gonçalves, 2013; Vierheilig, Mühlberger, Polak, & Herrmann, 2016) and cognitive performance (Coffman et al., 2014; Hussey, Ward, Christianson, & Kramer, 2015). Moreover, while anodal stimulation significantly reduced RTs in both tasks, we found that it had a stronger effect on the bCFS task, i.e. at a subliminal level. However, it should be noted that the stimulation protocol differed between the bCFS and the Go/No-Go tasks, as the former was performed during an online tDCS stimulation, while the latter at its end, i.e. offline. This difference in stimulation protocol may have affected the results, and thus limits the conclusions one can draw based on direct comparison of the two tasks. Interestingly, PFC lesions have shown to affect the threshold for conscious access, and the PFC has been suggested to contribute to conscious perception of masked stimuli (Del Cul, Dehaene, Reyes, Bravo, & Slachevsky, 2009). Finally, the greater effect of stimulation in participants with a higher BMI is consistent with the fact that these individuals show decreased activity in this area (Dong et al., 2015; Gluck et al., 2017), and might therefore be showing greater effects following anodal stimulation.

When considering the effect of the cathodal modulation on the bCFS and NoCFS tasks, contrary to our predictions, no inhibitory effect was found. Cathodal inhibition effects are usually found on motor tasks, but they are rarely observed on cognitive tasks (Fertonani, Rosini, Cotelli, Rossini, & Miniussi, 2010; Fregni et al., 2005; Kraft et al., 2010), which has been attributed to cognition relying on bilateral, rich brain networks, that can compensate contralaterally (Jacobson, Koslowsky, & Lavidor, 2012). In addition, cathodal stimulation unexpectedly shortened RTs in the bCFS task. Other studies have shown similar effects of

anodal and cathodal stimulation (see for instance Brückner & Kammer, 2017). Nonetheless, cathodal stimulation's effect did not interact with participants' BMI, suggesting that it does not have a specific effect on obesity-related cognitions and behaviors.

In the Go/No-Go task, we did not find any significant effects of stimulation. The lack of a strong influence of tDCS stimulation on the Go/No-Go task might be due to the fact that participants did not perform this task during the stimulation, but at its end. Indeed, even if tDCS effects can last for a certain period of time post stimulation (Horvath, Carter, & Forte, 2014; Nozari, Woodard, & Thompson-Schill, 2014), several studies did not find an effect of offline tDCS stimulation on Go/No-Go performance (Conley, Fulham, Marquez, Parsons, & Karayanidis, 2016; Cosmo et al., 2015; Filmer, Lyons, Mattingley, & Dux, 2017; McLaughlin, Conelea, Blanchette, Greenberg, & Mariano, 2017; Sallard, Mouthon, Pretto, & Spierer, 2018, but see; Boggio et al., 2007). Moreover, we did not observe an association between BMI and error rate in this task. Admittedly, not all studies are consistent with the idea that BMI *per se* is associated with increased inhibitory deficits (Aiello et al., 2018; Bartholdy et al., 2016).

Finally, we are aware that our study has several limitations. First, our sample does not represent males and females in the same number. Previous studies have shown that gender might play a role in attention towards food and in impulsivity (Hummel, Ehret, Zerweck, Winter, & Stroebele-Benschop, 2018; Mitchell & Potenza, 2015). While our analyses show that gender does not influence our results, future studies should address this limitation by enrolling an equal number of males and females.

Secondly, handedness was not controlled for, as previous bCFS studies include both right- and left-handed participants (Costello, Jiang, Baartman, McGlennen, & He, 2009; Jiang et al., 2007; Knotts, Lau, & Peters, 2018; Veto, Schütz, & Einhäuser, 2018; Yang et al., 2011). It is however possible that handedness might have influenced lateralization, which could have affected our results. Finally, the tDCS stimulation protocol differed between the bCFS and Go/No-Go tasks, being online during the former, and offline (right after stimulation) in the latter. Therefore, the extent to which one can compare the results from the two tasks is limited.

In conclusion, higher BMI is associated with longer suppression times in the bCFS task. This effect is not food-specific, and suggests that an elevated threshold for conscious perception may characterize obesity. This topic is open to future investigation, since visual information outside of awareness may influence conscious experience, decision-making and goal pursuit behavior (Finlayson et al., 2008; Forman et al., 2018; Takada et al., 2018). Conversely, a higher BMI is associated with an attentional food bias at a later stage of attentional processing, as observed in the Go/No-Go task, and inhibitory deficits (Bartholdy et al., 2016; Kulendran et al., 2017; Loeber et al., 2012). Anodal stimulation on the right PFC reduces RTs, probably due to its effects on cognitive control and attention. This effect was particularly strong in the bCFS task, suggesting an influence of anodal stimulation on subliminal processing, and in participants with a higher BMI.

As early processing of food has been shown to have a role in the unconscious regulation of appetite and food choice (Finlayson et al., 2008; Takada et al., 2018), one could speculate that the reported beneficial effects of anodal tDCS on craving and food intake (Kekic et al., 2014; Val-Laillet et al., 2015) may be mediated by its effects on cognitive control and attention (Gluck et al., 2015; Heinitz et al., 2017), starting at a subliminal level. Future research should investigate how subliminal perception may affect eating choices in obese individuals, and test the effects of anodal modulation on this process.

Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this chapter can be found online at <https://doi.org/10.1016/j.brat.2019.05.005>.

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