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NO EVIDENCE FOR PREFRONTAL TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) AFFECTING THE CONE OF GAZE

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ABSTRACT

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Relative activity between the left and the right prefrontal cortex has been associated with approach and avoidance motivation. In previous studies, perceiving a direct gaze has been shown to induce approach-related relative left frontal activity, and perceiving an averted gaze has been shown to induce avoidance-related relative right frontal activity. The current study aimed to manipulate approach-avoidance related frontal cortical activity with transcranial direct current stimulation (tDCS) to investigate if the prefrontal areas associated with motivational direction are causally involved in whether we interpret another person to be looking at us. To this end, cone of gaze was measured (i.e. the range of gaze angles participants interpreted to be looking at them) while the participants were being stimulated with tDCS.

tDCS was applied to dorsolateral prefrontal cortex with the aim to increase either relative left-sided or right-sided frontal cortical activity. The study was sham-controlled and double-blind. Within-subjects design was used. The results provided no evidence for tDCS affecting the width of the gaze cone. The problems associated with the interpretation of null-results in tDCS studies are discussed. It is concluded, that the current study is inconclusive and that further study is needed.

Keywords: frontal asymmetry, gaze, cone of gaze, approach, avoidance, motivation, withdrawal, tDCS, transcranial direct current stimulation

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INTRODUCTION

Approach-avoidance motivation and frontal asymmetry

The division of the possible direction of motivation to approach and avoidance is one of the most fundamental categorizations that can be made in the study of affect and motivation (Elliot, 2008). Since the time of the ancient Greeks to modern neuroscience, approach and avoidance categories have been used in one form or another in philosophical and scientific explanations of behavior (Elliot, 2006, 2008). All animals must have at least some rudimentary mechanisms by which they avoid harmful stimuli and approach advantageous stimuli. In humans, the mechanisms that control whether to approach or to avoid certain stimuli and environments are naturally highly complex [1].

Approach and avoidance motivation are often defined as an energization of behavior towards or away from stimuli (Elliot, 2006, 2008). Thus, approach-avoidance motivation is not used only to describe behavior, but also a psychological movement towards or away from stimuli or the desired goal. This can mean keeping the stimulus, environment, physical or psychological state close to the organism (approach motivation) or away from the organism (avoidance motivation) (Elliot, 2008). Motivation prepares for action, but motivational urges will not always lead to overt behavior. Approach motivation has been specifically defined as "*the impulse to go toward*" (Harmon-Jones, Harmon-Jones, & Price, 2013, p. 291). Harmon-Jones and Gable (2018) illustrated this idea with a manic individual. A person having a manic episode is in a highly approach-motivated internal state. This internal state raises the probability that the person moves towards, irrespective of if she has a specific goal to move towards to. Thus, approach and avoidance motivation are best described as internal states of the organism, conceptually distinct from the organism's physical movement (behavior) and the properties of the environmental stimuli.

Approach and avoidance motivation are also tightly linked to theories of emotion (Elliot, Eder, & Harmon-Jones, 2013). According to Elliot et al. (2013), both discrete emotion theories and theories emphasizing the role of appraisals usually assume that different emotional states have different

[1] Several conceptually related terms, such as appetite-aversion and approach-withdrawal, have been used to describe the same (or highly related) phenomenon as approach-avoidance motivation, each term arguably having different emphasis and context in which they are used (Elliot, 2008). Especially, approach-withdrawal has been widely used in studies cited by current thesis (e.g. Davidson, 2004; Harmon-Jones & Gable, 2017). However, when describing the research in question approach-avoidance has been used in place of approach-withdrawal (e.g. Kelley et al., 2017). For consistency with previous studies conducted in our laboratory (e.g. Hietanen et al., 2008), this paper will use the term avoidance even when the original articles have used the term withdrawal.

behavioral intentions of approach and avoidance associated with them. Typically, positive emotions are associated with approach motivation and negative emotions with avoidance motivation. Anger seems to be an exception, usually associated with negative subjective feelings but, in many situations, with approach tendencies (Harmon-Jones, 2003).

A large literature now shows, that there is a link between approach-avoidance related affective and motivational processes and asymmetrical frontal cortical activity (Coan & Allen, 2004; Harmon-Jones & Gable, 2018). There is a long history of interest in the possible lateralization of emotion and motivation (recently summarized by Harmon-Jones & Gable, 2018). Varying theories of lateralization of emotion have been proposed during the last hundred years with ideas arising both from clinical findings and basic research (Gainotti, 2018). For example, right frontal cortical lesions were found to led to euphoric symptoms (e.g. uncontrollable laughing) more often than left hemisphere lesions, whereas patients with left hemisphere lesions were noted to more likely suffer from depressive reactions (e.g. uncontrollable crying) (Sackeim et al., 1982). A methodological breakthrough in this line of research came in the late 1970s when Richard Davidson showed that electroencephalograph (EEG) can be used to study the lateralization of emotion and motivation (Allen, Keune, Schönenberg, & Nusslock, 2018). From early on in Davidson's and his colleagues' research, positive emotions and approach behavior was linked with relatively greater left frontal activity, and negative emotions and avoidance behavior linked to relatively greater right frontal activity (Davidson, 1992).

The asymmetrical EEG activity associated with emotion and motivation has since become known as the frontal (EEG) asymmetry (Allen et al., 2018). Typically, frontal asymmetry is measured between the left and the right dorsolateral prefrontal cortex (DLPFC), between the electrodes F3/F4 in the 10/20 EEG system (Allen et al., 2018; Davidson, 2004; Harmon-Jones & Gable, 2018). It is noteworthy, that the frontal asymmetry is the relative strength of activity between the hemispheres, that is, the asymmetry scores represent how much more the other DLPFC was active than the other. Frontal asymmetry is calculated from the EEG as a difference in alpha power, that is assumed to be inversely related to cortical activity (Coan & Allen, 2004). Many studies have measured alpha power also from other electrode pairs (e.g. parietal) as a control, showing that the asymmetrical activity related to affect is associated only with frontal regions (e.g. Davidson, Ekman, Saron, Senulis, & Friesen, 1990; Davidson & Fox, 1982; Harmon-Jones & Allen, 1998).

Frontal asymmetry can be studied both as a baseline measure and as a state-depended variable in response to affective stimuli or change in participants affective/motivational state (Coan & Allen, 2004). Typically, in studies using frontal asymmetry as a state-depended variable, changes in the EEG signal are measured in relation to experimental manipulation of participants emotional or motivational state (Coan & Allen, 2004). For example, in an early study by Davidson and Fox (1982), EEG was measured from infants who were shown videos of happy and sad faces. Results showed that when watching happy faces there was stronger relative left frontal activation than when watching sad faces. Frontal asymmetry has also been heavily investigated as a trait-like variable with baseline measures. Differences in relative left vs. right cortical activity at rest (i.e. resting frontal asymmetry) have been linked to, for example, in the risk of depression and anxiety disorders (Thibodeau, Jorgensen, & Kim, 2006), although it should be noted, that a recent meta-analysis showed evidence against the association between depression and baseline frontal asymmetry (van der Vinne, Vollebregt, van Putten, & Arns, 2017).

Harmon-Jones (2003) has referred to the different theories proposed to explain frontal asymmetry's association with affect and motivation as the valence model, the motivational direction model, and the valenced motivational model. These models differ in whether the frontal asymmetry is related only to the valence of the emotion (valence model), only to the motivational direction (motivational direction model) or both (valenced motivational model). Of these, the motivational direction model has gathered arguably the most support, mainly from the study of anger (see, Harmon-Jones & Gable, 2018). As said, positive and negative emotions are usually associated with approach-motivation and avoidance-motivation, respectively. According to Harmon-Jones (2003), most of the frontal asymmetry studies prior to research on anger had the valence of the elicited emotion confounded with motivational direction. Thus, from these prior studies, it was impossible to say whether frontal asymmetry was related to affective state or motivational direction. Anger, as an approach-motivated but negatively valenced emotion, was a natural object of study in frontal asymmetry research to disentangle the direction of the motivation from the valence of the emotion.

In recent years, the converging evidence that supports the motivational direction model has been thoroughly reviewed (e.g. Harmon-Jones, 2003; Harmon-Jones & Gable, 2018; Kelley, Hortensius, Schutter, & Harmon-Jones, 2017). The conclusion from these reviews is that anger, negatively valenced approach-oriented emotion, is associated with relatively greater left frontal cortical activity, thus giving support for the motivational direction model. For example, greater left-sided than right-sided frontal cortical activity has been linked to anger as a trait and to induced anger in situations where the participants believe that they will later engage in approach-oriented behaviors (Harmon-Jones & Allen, 1998; Harmon-Jones, Lueck, Fearn, & Harmon-Jones, 2006). In a fMRI study by Berkman and Lieberman (2010), the left DLPFC was found to be more active during approach-oriented actions than the right, and critically, in this study the activity in DLPFC did not differ in relation to stimulus valence (positive or negative). Studies employing repetitive transcranial magnetic stimulation (rTMS) offer a more causal line of evidence. In rTMS studies, left prefrontal stimulation as compared to the right prefrontal stimulation has been shown to decrease the processing of anger in an attentional task and in a memory task (d'Alfonso, van Honk, Hermans, Postma, & de Haan, 2000; van Honk & Schutter, 2006). As these studies used frequencies of rTMS that aim to cause inhibition of cortical excitability, these findings were interpreted by the authors to favor the motivational direction model.

tDCS and frontal asymmetry

Transcranial direct current stimulation (tDCS) is a noninvasive neuromodulatory technique that modifies cortical excitability by applying a weak electrical current through the scalp (Nitsche et al., 2008). For decades, centuries even, the direct electrical current has been known to affect the central nervous system (Priori, 2003). However, it is only relatively recently that weak electrical currents have been systematically used to influence the human brain in neuroscience research. In its modern form, the use of weak electrical currents to modulate brain activity in humans was introduced by Nitsche and Paulus now almost two decades ago (Nitsche & Paulus, 2000). They showed, using TMS-induced motor-evoked potentials, that transcranially applied weak direct electrical current (current intensities 0.2—1.0 mA) can modify motor cortex excitability. Since then, tDCS has been increasingly gaining popularity as it is considered safe, easy to use and relatively cheap technique (Fregni et al., 2015). As opposed to the more well-known neurostimulation technique transcranial magnetic stimulation (TMS), tDCS is subthreshold neuromodulation as the current densities are not strong enough to induce action potentials by themselves (Nitsche et al., 2008; Stagg & Nitsche, 2011).

Conventional tDCS uses two electrodes. During stimulation, current flows from the cathode to the anode, that is, from the negatively charged electrode towards the positively charged electrode (Nitsche et al., 2008). This current flow is thought to lead to changes in the resting membrane potentials of the underlying neuronal populations (Nitsche et al., 2008). Ideally, the stimulation brings the neurons closer to or away from their threshold potential, depending on the stimulation polarity: under the anode the cortical neurons (or more precisely, their somas) are slightly depolarized and under the cathode slightly hyperpolarized (Stagg & Nitsche, 2011). However, the effects of the stimulation can be highly complex and a multitude of factors, such as the cell orientation, current density, and the stimulation duration, can modulate the response to the stimulation (Filmer, Dux, & Mattingley, 2014; Sellaro, Nitsche, & Colzato, 2016). In addition, several other variables (such cranial anatomy, genetic variability, and baseline neurophysiological state) might be additional modulating factors, although some of these have been little directly investigated (Li, Uehara, & Hanakawa, 2015). Despite these complexities, tDCS is considered useful and promising technique (Nitsche et al., 2008; Sellaro et al., 2016). Like TMS, tDCS allows the opportunity to study causal relationships of brain regions and cognitive functions (Filmer et al., 2014). To this end, there has been increased use of tDCS in social and affective neuroscience during the last few years (Sellaro et al., 2016).

Typical duration of the stimulation in tDCS experiments is 5–20 minutes with a current intensity between 1–2 mA (Filmer et al., 2014; Nitsche et al., 2008). During stimulation, the electrodes are placed in sponges (typically 25 cm^2 – 35 cm^2) that are usually soaked in NaCl solution to enhance conductivity and to minimize discomfort (Dundas, Thickbroom, & Mastaglia, 2007; Nitsche et al., 2008). Commonly, participants feel slight tingling or itching under the electrodes at the start of the stimulation. Placebo-stimulation or sham-stimulation, as it is called in tDCS-research, is achieved with actively stimulating for a brief time (usually 30 seconds), and then turning the stimulation off (Nitsche et al., 2008). This creates the typical skin sensations without significantly affecting neural activity (Nitsche et al., 2008). The tDCS protocol is referred to as either online or offline, depending on whether the stimulation is or is not applied during a task (Filmer et al., 2014). Although most of the published experiments have used the traditional two electrode tDCS, a more focal form of stimulation (HD-tDCS) has been developed where 4 cathode electrodes surround one anode electrode or vice versa (Edwards et al., 2013).

As said, tDCS has been increasingly used in last few years in social and affective neuroscience, and in a few studies, it has also been used with the intention to influence asymmetrical frontal cortical activity related to approach and avoidance motivation (see, Kelley et al., 2017). Typically, these studies employ bilateral montages (i.e. one electrode placed on the left and one on the right hemisphere) with electrodes placed over the left and the right prefrontal cortex (F3 and F4 in 10-20 EEG system) (Kelley et al., 2017). The aim of this montage is to influence asymmetrical frontal cortical activity by simultaneously increasing the activity in the other hemisphere with anodal stimulation and inhibiting the activity in the other hemisphere with cathodal stimulation (Kelley et al., 2017; Sellaro et al., 2016). Important confounder with bilateral montages is that it is not possible to know if the stimulation of only one hemisphere would be sufficient to produce the possible effects (Sellaro, et al., 2016). However, if committing to the theory that it is the relative activity of the prefrontal areas that contribute to approach-avoidance motivation, this may not be as serious confounder that it is in most experiments using bilateral montages.

Studies using tDCS to stimulate the DLPFC with an objective to influence asymmetrical frontal cortical activity linked to approach-avoidance motivation typically make their hypotheses based on previous EEG research on frontal asymmetry. For example, Hortensius, Schutter, and Harmon-Jones (2012) were interested in the role of frontal asymmetry in anger and aggression. Based on previous EEG research, they hypothesized that increasing relative left cortical activity with tDCS should lead to increased aggression when the participants are angry. In the study, participants received 15 minutes of stimulation to dorsolateral prefrontal areas (F3 anodal/F4 cathodal, F3 cathodal/F4 anodal, or sham). After the participants received the stimulation, they were intentionally insulted to induce anger. Then, aggression was measured as a volume and duration of noise blasts participants gave during a computer game to the person who they thought had insulted them (a modified version of Taylor Aggression Paradigm). The result showed that only in the left anodal/right cathodal group did the increased anger correlate positively with aggression (anger was measured with self-reports before and after the insult). The results were interpreted to support the motivational direction model.

One study stimulated prefrontal areas (F3 anodal/F4 cathodal, F3 cathodal/F4 anodal, or sham) during a version of the computer-based social exclusion task aimed to induce jealousy (Kelley, Eastwick, Harmon-Jones, & Schmeichel, 2015). As the authors hypothesized based on previous EEG study linking jealousy with left frontal activity (Harmon-Jones, Peterson, & Harris, 2009), self-reported jealousy among socially excluded was higher in the group who received stimulation that was aimed to increase left-sided frontal activity. Another study used the same anger inducing design as Hortensius et al. (2012) (Kelley, Hortensius, & Harmon-Jones, 2013). However, in this study, after the insult self-ruminative thoughts and state rumination, not aggression, was measured. The results showed that in the group that received left cathodal/right anodal stimulation had higher levels of rumination in both self-measures compared to the other stimulation conditions (left anodal/right cathodal and sham).

Together the above studies suggest that tDCS can be potentially used to influence asymmetrical frontal cortical activity, thus allowing a stronger test of causal relationships between variables previously found to be associated in EEG studies. Also, the above tDCS studies suggest that approach-avoidance motivation states can be induced by directly manipulating approach-avoidance related frontal areas. However, it is worth noting that in these studies approach-avoidance motivation has not been directly measured and the actual change in relative left or right frontal cortical activity has not been directly verified with EEG or other methods.

Eye gaze, approach-avoidance motivation and the cone of gaze

The eye gaze of a conspecific is undoubtedly a signal of special importance to us humans' whatever viewpoint one considers it from. Eyes and gaze carry a great amount of emotionally and socially crucial information (Itier & Barry, 2009), eyes playing a role in many of the most important forms of social communication to us, such as expressing intimacy (Kleinke, 1986). Humans have an automatic tendency to direct their attention towards what other people are looking at (Langton, Watt, & Bruce, 2000) and eye contact with another person appears to be inherently affective (Hietanen, 2018). From a neuroscientific perspective, for over thirty years has gaze processing been associated with anterior superior temporal sulcus (Perrett et al., 1985; Perrett, Hietanen, Oram, & Benson, 1992). Today, widespread networks in temporal, parietal and frontal lobes are considered to be involved with gaze processing (see reviews, Itier & Batty, 2009; Nummenmaa & Calder, 2009). Even morphologically the human eye is unique, and its features—discernible dark iris and a white sclera greatly paler than the facial skin surrounding it—might have been especially evolved to facilitate the detection of another person's gaze direction (Kobayashi & Kohshima, 1997).

Considering the importance of gaze direction as a social signal, it is reasonable to assume that gaze direction could also be used to interpret the approach-avoidance intentions of other people. There is some empirical evidence supporting this view. For example, gaze direction seems to affect the processing of facial emotions that are associated with different motivational tendencies (Adams & Kleck, 2003). Adams and Kleck (2003) hypothesized that the perception of an emotion should be enhanced if the approach-avoidance intention associated with the emotion matches the approach-avoidance intention associated with the gaze direction (approach motivation is associated with direct gaze, anger, and joy, and avoidance motivation is associated with averted gaze, fear, and sadness). In the study, approach-oriented facial emotions were recognized faster when the faces had direct gaze whereas avoidance-oriented facial emotions were recognized faster when the faces had averted gaze. A further study corroborated these findings with three experiments (Adams & Kleck, 2005). For example, in one of the experiments, participants were asked to attribute approach-avoidance related emotions to neutral faces. Anger and joy (approach-oriented emotions) were more likely to be attributed to faces with direct gaze, whereas sadness and fear (avoidance-oriented emotions) were more likely to be attributed to faces with direct gaze.

Gaze direction seems to also have an effect to the approach-avoidance related frontal cortical activity as measured by EEG (Hietanen, Leppänen, Peltola, Linna-aho, & Ruuhiala, 2008; Pönkänen, Peltola, & Hietanen, 2011). In Hietanen et al.'s (2008) study, participants looked at a live model through an electronically controlled shutter while the models gaze was either directed towards them or averted away from them. Frontal asymmetry was measured with EEG, and the results showed that the model's direct gaze elicited in the observer greater relative left frontal activity and averted gaze greater relative right frontal activity. Interestingly, the effect of gaze direction on frontal asymmetry has been shown to differ in groups that could be predicted to have different motivational responses to eye contact. One study compared the reactions of typically developed children and children with autism spectrum disorder to pictures of faces with closed, open or exaggeratedly wide-open eyes (Kylliäinen et al., 2012). In the study, compared to the other faces, open-eyed faces elicited relative left frontal activity in the typically developed group, but not in the autism spectrum group. In another study, neuroticism was associated with increased right-sided frontal activity while viewing a live face of a stranger with a direct gaze (Uusberg, Allik, & Hietanen, 2015). Together, these studies could be interpreted to suggest that the frontal EEG asymmetry associated with gaze direction results from changes in the observer's internal motivational state.

When asked to judge the eye gaze of another person, people typically accept surprisingly large horizontal gaze angle deviations from a strictly direct gaze (0°) as still being directed at them or looking at them (Gamer & Hecht, 2007). Gamer and Hecht (2007) called this range of gaze directions the "cone of gaze", with the cone metaphor defined as "*... a sector in space whose origin is the interpupillary point*" (Gamer & Hecht, 2007, p. 706). Thus, the gaze cone is the range of another person's gaze directions that people interpret to be looking at them. A common way to measure the cone of gaze is to show participants faces with varying gaze angle deviations (for example, from 0° to 8°), and ask them if the person in the picture was looking at them (e.g. Ewbank, Jennings, & Calder, 2009; Lyyra, Wirth, & Hietanen, 2017). A typical width of the gaze cone is a few degrees to both left and right from a 0° gaze. For example, in the four original experiments by Gamer and Hecht (2007), the overall width of the gaze cone was found to be 7.17° to 9.34° from a viewing distance of one meter. Experimental manipulations and individual differences have been shown to influence the width of the gaze cone. For example, it has been shown that cone of gaze is wider for participants who have recently been socially excluded as compared to socially included participants (Lyyra et al., 2017). Also, social anxiety and social phobia have been shown to be associated with a wider gaze cone in both non-clinical and clinical samples (Chen, Nummenmaa, & Hietanen, 2017; Gamer, Hecht, Seipp, & Hiller, 2011).

As mentioned previously, different emotions have different behavioral and motivational intentions of approach and avoidance associated with them. Interestingly, emotional expressions associated with different approach-avoidance intentions have also been shown to modulate the width of the gaze cone. For example, in one study the width of the gaze cone was larger for angry (approach-oriented) faces than fearful (avoidance-oriented) faces or neutral faces (Ewbank et al., 2009). Another study showed highly similar results (Lobmaier, Tiddeman, & Perrett, 2008). In Lobmaier et al. (2008) study, participants were shown pictures of emotional facial expressions from different angles (0°–10°), and asked if the person in the picture was looking at them (the difference to the gaze cone studies were that in this study, the whole face, not just the eyes, was rotated). Happy faces were found to elicit the most looking-at-me answers, followed by angry faces. Fearful and neutral expressions were the least likely to be interpreted as looking at the participants. A further study with concordant results suggested that this effect might be explained with a more general "self-referential positivity bias", because in the study, the participants were shown the same facial emotions but with the eyes covered (Lobmaier & Perrett, 2011).

Thus, gaze direction is in many ways associated with approach-avoidance motivation. Perceiving another person's gaze direction seems to be linked to the approach-avoidance intentions of that person (Adams & Kleck, 2003, 2005) and people interpret faces with approach-oriented emotions more easily to be looking at them (Ewbank et al., 2009). Moreover, in the observer of the gaze, another person's gaze direction modulates the frontal cortical brain activity (frontal asymmetry) associated with approach-avoidance motivation (Hietanen et al., 2008; Pönkänen et al., 2011). Based on these findings, it could be assumed that ambiguous gaze directions are more easily interpreted as eye contact when the observer herself is in a higher approach-oriented motivational state. The current study aimed to test, with tDCS, if stimulation of the brain areas that are associated with approach-avoidance motivation would influence the interpretation of another person's gaze direction. To the best of the author's knowledge, previous studies have not yet investigated the causal role of asymmetrical frontal cortical activity in the interpretation of eye gaze direction.

Current study

In the current experiment, prefrontal areas associated with approach-avoidance motivation were stimulated with tDCS. The aim was to manipulate asymmetrical frontal cortical activity associated with perception of gaze direction in previous studies, to investigate if this asymmetrical activity is causally linked with perception of eye gaze.

The study was conducted as a double-blind within-subject design. In the experiment, the width of the gaze cone was measured while participants received tDCS to prefrontal regions (F3/F4). There were three stimulation conditions, left anodal/right cathodal, left cathodal/right anodal, and sham.

The width of the gaze cone was measured with a computer task where the participants were shown frontal view pictures of virtual faces with varying gaze angles, and the participants were asked to decide if the person in the picture was looking at them or not.

The main hypothesis of the current study was that asymmetrical frontal cortical activity has a causal role in the interpretation of whether another person appears to be looking at us or not. Further, it was hypothesized that this would be due to changes in the participants' approach-avoidance motivational state. Thus, it was predicted that the left anodal/right cathodal stimulation widens the cone of gaze relative to sham stimulation, and that the left cathodal/right anodal stimulation narrows the cone of gaze relative to sham stimulation.

It is worth noting that if the predictions above would be correct, it would not directly follow that these effects were due to changes in the participants' motivational state. To partially rule out alternative explanations, a control task was included in the study with non-social stimuli (arrows). It was assumed that answers to the non-social stimuli would be unaffected by the changes in the participants' approach-avoidance motivational state. Thus, the control task was added to gain support for the hypothesis that the changes in the width of the gaze cone would be due to changes in participants' motivational state and not due to changes, for example, in discrimination accuracy of the direction of the stimuli. Accordingly, it was predicted that the stimulation does not affect how the participants will answer to the non-social stimuli.

A questionnaire surveying positive and negative affect (PANAS) was included in the study (Watson, Clark, & Tellegen, 1988). According to the motivational direction model, the relative activity in the left vs right prefrontal cortex is not related to the valence of the current affective state. Although some studies have found positive and negative affectivity to be related to frontal asymmetry (e.g. Tomarken, Davidson, Wheeler, & Doss, 1992), as the current study was based on the motivational direction model, it was hypothesized that the stimulation would not influence the participants' positive or negative affective state. Finally, as social phobia and anxiety has been previously shown to be associated with increased width of the gaze cone (e.g. Chen et al., 2017; Gamer et al., 2011) participant's social phobia was also measured (Social Phobia Scale, SPS; Mattick & Clarke, 1998). Accordingly, the hypothesis was that SPS scores would positively correlate with the width of the gaze cone.

METHOD

Participants

24 right-handed adults participated in the study, all with normal or corrected-to-normal vision. One participant's data was removed from all the analyses due to a psychiatric diagnosis about which the participant in question only informed the experimenter after the data collection. Thus, the final sample size was 23 (19 females, mean age = 23.22 ± 3.67 SD). For the analysis of the main hypotheses considering the width of the gaze cone, the final sample size was 20 (for details, see section 2.5. Data analysis).

Participants were students recruited from the email lists of the University of Tampere and the Facebook page of the Voionmaa Institute (folk high school). For each session participants received one movie ticket or a partial course credit. The exclusion criteria for this study were left-handedness, psychiatric and neurological diagnoses, damaged skin tissue in the scalp area and cardiac heart problems. All participants gave written informed consent and the study was approved by the Ethics Committee of the Tampere Region. The study was conducted in adherence to the Declaration of Helsinki.

Figure 1. Illustration of the face stimuli. Here are shown examples of 6°,4°,2°, and 0° gaze directions. The size of the face stimuli on the screen was approximately 18.5 cm (width) and 26 cm (height) (the size of the faces differed slightly).

Materials and questionnaires

19-inch LCD monitor was used for stimulus presentation (resolution 1280×1024). During the experimental task, the participants placed their head on a chin rest that was aligned with the center of the computer screen. The chin rest's distance was 63 cm from the screen. The height of the chin rest was set to a fixed position so that the participants' eye level was approximately aligned with the stimulus characters' eye level. The stimuli were presented with E-Prime software (version 2.0).

The stimuli were images of faces and arrows. The face stimuli were four male and four female characters with frontal head orientation, made using 3D animation software (Digital Art Zone 3D Studio). There were 9 different stimuli of each face: one with a direct gaze (0°) shown twice during the experimental task, and one of gaze angles 2°, 4°, 6°, 8° averted towards both left and right, each of these shown once during the experimental task. The characters had a mildly friendly expression (see, Figure 1). The face stimuli in the gaze cone task were the same as used in a previous study by Lyyra et al. (2017).

The arrow stimuli were made especially for the current study using Blender 3D modeling software (version 2.77a). 8 different arrow "characters" were used. Four of the arrow characters were in different shades of blue and four in different shades of red (see, Figure 2). Nine different angles were used for each arrow: 0° (direct) and 1°, 2°, 3°, 4° pointed towards both left and right. These arrow angles were chosen based on a pilot experiment (n = 12) where the participants were shown arrows in sets of deviations of 0°, 1°, 2°, 3°, 4° or deviations of 0°, 2°, 4°, 6°, 8°. In the pilot task, we asked the participants if they felt like the arrows were pointing them or not (the same task as in the current study). The answers to the set of 0°, 1°, 2°, 3°, 4° arrows resulted in a more similar data to our laboratory's previous gaze cone data as compared to the set of 0°, 2°, 4°, 6°, 8° arrows, and was thus chosen to be used in the present study (see, Figure 3).

The participants' current mood state was measured using Positive and Negative Affective Schedules (PANAS). PANAS is a 20-item inventory of positive and negative affect dimensions (Watson et al., 1988). Positive affect dimension consists of 10 items such as *attentive, enthusiastic and excited* and negative affect of 10 items such as *upset, irritable and nervous*. The items are rated on a five-point scale, based on how much the participant is feeling the emotion at the present moment (1 = very slightly or not at all, 2 = a little, 3 = moderately, 4 = quite a bit, 5 = extremely). Social phobia was measured with the Social Phobia Scale (SPS; Mattick & Clarke, 1998). SPS consists of 20 statements about social situations (e.g. "*I get nervous that people are staring at me as I walk down* *the street".*) that are rated from 1 (not at all characteristic of me) to 5 (extremely characteristic of me). All questionnaires were Finnish translation.

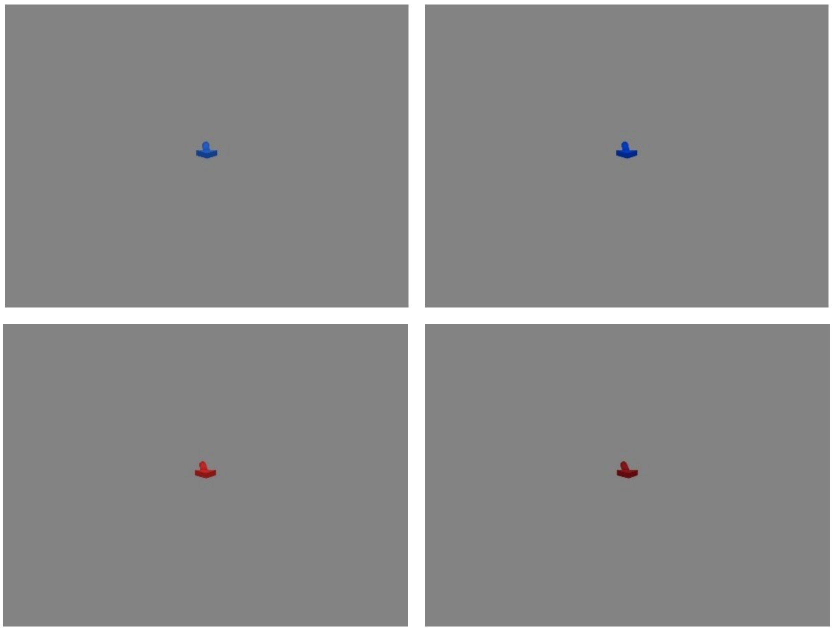

Figure 2. Illustration of the arrow stimuli. Here are shown examples of 0°, 1°, 2°, 3° arrow directions. The size of the arrow stimuli on the screen was 2 cm (width) and 2.2 cm (height).

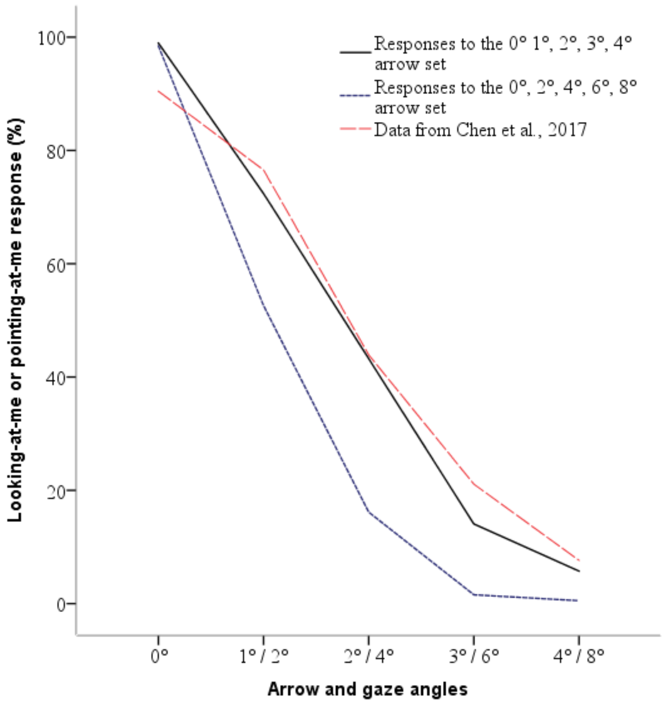

Figure 3. Visual comparison of the responses in the pilot study and in Chen et al. (2017) as a function of arrow and gaze direction. On the right of the deviation sign is shown the arrow angles from the pilot study's arrow set of 0°, 2°, 4°, 6°, 8° arrows and the gaze angles from the Chen et al. (2017) study.

tDCS

tDCS was applied with battery-driven Magstim DC stimulator (HDCkit, TheMagstim Company Ltd., Carmarthenshire, UK). Two 5 cm x 5 cm rubber electrodes placed in saline-soaked sponges were used. Stimulation lasted for 17 minutes, with a current intensity of 1.5 mA. Thus, the current density was 0.06 mA/cm². Ramp-up and ramp-down times were 15 s. In the sham condition, the stimulation duration was 30 seconds with 15-second ramp-up and ramp-down times. Impedance was measured before the start of the stimulation and the electrodes were adjusted until the impedance was under 5 kΩ.

There were three stimulation conditions: left anodal/right cathodal, left cathodal/right anodal and sham. These are from now on simply referred to as left anodal, left cathodal and sham. In the left anodal stimulation condition, the anode was placed over the left dorsolateral prefrontal cortex and the cathode over the right dorsolateral prefrontal cortex (F3 and F4 according to the 10-20 EEG system). In the left cathodal stimulation condition, the electrode placement was reversed, with anode over the F4 and cathode over the F3. In the sham stimulation condition, half of the participants received sham stimulation with electrode placement in the left anodal position and half of the participants in the left cathodal position. The F3 and F4 were located using a method described by DaSilva, Volz, Bikson, and Fregni (2011).

The study used online-stimulation. The stimulation began 4 minutes and 15 seconds before the first trial of the experiment and lasted for 17 minutes. All the participants finished the experimental task before the end of the stimulation.

Experimental task

The computer screen instructed the participants to put their head onto the chin rest 30 seconds before the first trial began. All trials started with a fixation cross in the center of the screen (800 ms) which was followed by the target stimulus (150 ms.) shown against a gray background. After 500 ms break, the participants were asked if they felt like the stimulus person had looked at them or not (in face blocks) or if they felt like the arrow had been pointing at them or not (in arrow blocks). The participants had to give the response using numbers on the right side of a keyboard (1 = yes, 2 = no).

A new trial started 1000 ms after the response. The response time for a single trial was limited to 7 seconds.

The experiment consisted of eight blocks, each block containing either 20 consecutive face trials or 20 consecutive arrow trials. A face trial block was always followed by an arrow trial block and vice versa until every stimulus had been shown. A total of 160 different stimuli (80 faces and 80 arrows) were used in the present study. In half of the experiments, the task begun with a face block and in half of the experiments with an arrow block. The starting order was counterbalanced between different tDCS conditions and between participants. In each block, two different stimuli of every possible stimulus angle were shown in random order. This means that in face blocks, two 0° stimuli and one 2°, 4°, 6°, 8° stimuli towards both left and right directions were shown, and that in arrow blocks, two 0° stimuli and one 1°, 2°, 3°, 4° stimuli towards both left and right directions were shown. After 80 trials, there was a break of one minute. The participants were instructed (on the computer screen) to continue the task by pressing any button.

Procedure

A sham-controlled, double-blind, within-subject design was used. All participants participated in three separate sessions, receiving one of the three stimulation conditions (left anodal, left cathodal or sham) in each session. Order of the conditions was fully counterbalanced across participants. We tried to arrange the three different tDCS sessions of each participant in consecutive weeks, on the same weekday and approximately during the same time of the day. With most participants (19/23), this arrangement succeeded. With participants who were unable to participate at the same weekday, there was a minimum break of one week between the sessions. All participants participated in three separate sessions. However, due to technical failure of the tDCS stimulation device, one participant's session was rerun in another day. Thus, one participant took part in 4 experimental sessions.

At the start of each session, participants were seated in front of a computer and the experimental task was briefly explained to the participants. The purpose of the experiment was not revealed. The participants were informed that they would receive active stimulation in two of the three sessions and sham stimulation in one of the three sessions. In addition, the participants were told that the stimulation condition was controlled by a separate investigator who would later come to connect the electrode cables, and so neither the participant nor the experimenter would know in which one of the three sessions they would receive the sham stimulation. The participants were told, that the tDCS device is battery-driven and that the stimulation has no known serious adverse effects, but they might feel a slight tingling sensation when the stimulation would start. After the briefing, participants were instructed to carefully read the exclusion criteria for the study and to sign the informed consent form. After this, the tDCS electrodes were fixed onto the participants' head.

Next, the participants filled the Positive and Negative Affective Schedules (PANAS) measuring their current mood. After this, they were given detailed instructions on how to perform the experimental task. Participants were instructed to sit comfortably during the whole experiment and always follow the instructions on the computer screen. Although the stimuli were virtual characters, the participants were asked to imagine that the character is a real person. After the instructions, participants started a practice task. The practice task consisted of 10 trials, one stimulus from each possible gaze direction (0° and 2°, 4°, 6°, 8° either left or right) and one stimulus from each different arrow direction (0° and 1°, 2°, 3°, 4° either left or right).

After the practice task, a separate investigator came to the laboratory to connect the electrode cables. Electrode cables were connected in a way that ensured that the experimenter could not know if the participant would be given stimulation in anodal or cathodal electrode positioning. During this procedure, the participants looked at the computer screen while the investigator connected the cables. The investigator did not speak to the participants and did not see the participants faces (or vice versa). After the cables were connected, the other investigator left the laboratory and the experimenter started the stimulation. During the task, the experimenter sat behind a curtain in a separate area of the laboratory.

Immediately after they completed the task, the participants filled the Positive and Negative Affective Schedules (PANAS) again. The tDCS stimulation was not interrupted between the task and PANAS. Once the stimulation had ended and the PANAS had been filled, the electrodes were removed, and the participants were asked to fill a questionnaire surveying any possible side effects that they had experienced. At the end of the final third session, all participants filled the Social Phobia Scale (SPS). Also, at the end of the third session, the participants were debriefed about the purpose of the experiment. No other independent or depended variables than the ones discussed in this methods section were measured.

Data analysis

Trials with no response (response time was limited to 7 seconds) were removed before the data analysis (0.001% of the face trials and 0.0005% of the arrow trials). The responses to equal size stimulus (separately for gaze and arrows) were pooled together before further analysis, as has been done in previous studies (e.g. Lyyra et al., 2017; Uono & Hietanen, 2015). This produced five different directions for both faces (0°, 2°, 4°, 6°, 8°) and arrows (0°, 1°, 2°, 3°, 4°).

The width of the gaze cone was analyzed by calculating the point of subjective equality (PSE) separately for each participant. The PSE was calculated with a binary logistic regression model. PSE is a gaze deviation degree calculated from the logistic regression model for which there is an equal probability of being judged as being looked at and not being looked at. To calculate the width of the gaze cone, the PSE-values are multiplied by two (for example, Chen et al., 2017; Uono & Hietanen, 2015). This way both the left and the right sides are covered. From the answers to the control stimuli, "arrow-PSE" value for each participant was similarly calculated with a binary logistic regression model. As in the gaze cone analysis, the arrow-PSE value can be interpreted as the angle of the arrow in which there is a 50% probability that the arrow is being judged as pointing toward the participant.

The PSE-values were analyzed with 2 x 3 repeated measures analysis of variance (rm-ANOVA) with stimuli (faces, arrows) and stimulation condition (anodal, sham, cathodal) as within-subject factors. From this analysis, two participants were excluded because the width of their gaze cone had an uninterpretable negative value in one or more of the three sessions (due to a low number of yes-responses). Additionally, one participant was excluded because the participants' arrow-PSE value could not be calculated in one of the stimulation conditions (the participant responded "yes" to every single trial). Thus, the final sample size for the analysis of PSE-values was 20. The PSE-values were normalized with log10 -transformation to meet the normally distributed error terms assumption of rm-ANOVA. In the results section, untransformed PSE-values are reported. There were no outliers in the data after the log10 -transformation.

From the PANAS values, a change score was calculated separately for positive and negative affect by subtracting the pre-task values from the post-task values. These scores were entered into an rm-ANOVA with stimulus condition (anodal, sham, cathodal) as a within-subject factor. However, the change values for negative affect violated the normally distributed residuals assumptions of rm-ANOVA and were thus analyzed with a nonparametric Friedman test. All the 23 participants were included in the analysis of the PANAS-values. The possible effect of the degree of social phobia on the width of the gaze cone was analyzed with Pearson correlation. Anonymized versions of the responses to the questionnaire surveying side effects was given to an independent research group for database purposes and were not analyzed in the current study.

The statistical analyses were performed in SPSS version 25. Alpha-level was set for 0.05 for all statistical analysis.

RESULTS

PSE-values

Stimulus category (faces vs. arrows) had a significant main effect on PSE-values ($F(1,19) = 27.002$, $p < 0.000$ $\eta_p^2 = 0.587$). The PSE-values were higher in responses to faces (M = 3.34, SE = 0.23) than to arrows (M = 2.10, SE = 0.21, p < 0.000, Pairwise comparison Bonferroni corrected). The main effect of the stimulation was not significant ($F(2,38) = 1.615$, $p = 0.212$, $\eta_p^2 = 0.078$). Most importantly, the interaction between stimulation condition and stimulus category was not significant ($F(2,38) = 1.952$, $p = 0.156$, $\eta_p^2 = 0.093$). Thus, no evidence for the influence of tDCS on the width of the gaze cone was found. The untransformed cone of gaze and "cone of arrow" values are presented in Figure 4.

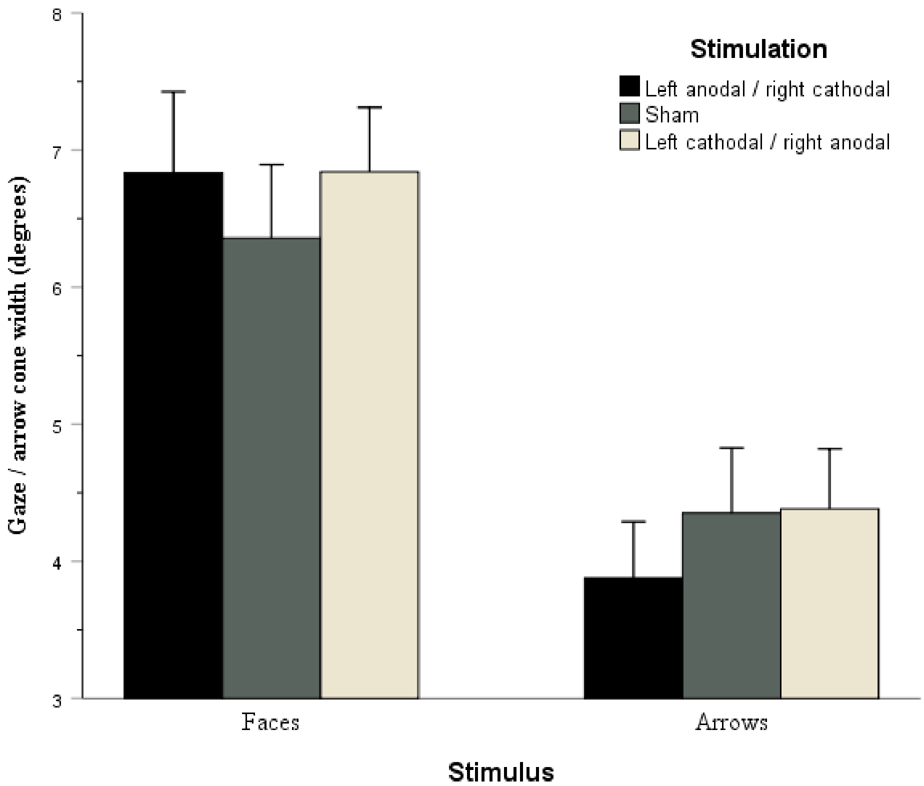

Figure 4: Mean width of the gaze cone and mean width of the "arrow cone" from the 20 participants included in the rm-ANOVA. Error Bars represent +1 SE

Positive and negative affect and social phobia

As expected, the pre-stimulation to post-stimulation change in the PANAS scores between the stimulation conditions was not significant for positive affect ($F(2,44) = 0.155$, $p = 0.857$, $\eta_p^2 = 0.007$) or negative affect ($\chi^2(2) = 2.113$, $p = 0.348$). Degree of social phobia was not associated with the width of the gaze cone, as the correlation between the SPS scores and PSE-values was not significant either when the PSE-values were averaged across conditions ($r = -0.073$, $p = 0.754$) or within each condition separately (left anodal: $r = 0.091$, $p = 0.695$, sham: $r = -0.178$, $p = 0.441$, left cathodal: $r = -0.128$, $p = 0.581$). The pre- and post-stimulation PANAS values are shown in Table 1.

Table 1. Means and standard deviations of the PANAS values for each stimulation condition (n = 23)

	Left anodal/right cathodal		Sham		Left cathodal/right anodal	
	Pre-stimulation	Post-stimulation	Pre-stimulation	Post-stimulation	Pre-stimulation	Post-stimulation
PANAS Positive	24.52 (5.88)	22.35 (5.72)	24.30 (5.70)	21,65 (6.21)	24,04 (5.06)	21.48 (6.26)
PANAS Negative	12.26 (2.60)	12.17 (2.53)	11.57 (2.27)	11,74 (2.58)	12,83 (2.96)	12.22 (2.73)

DISCUSSION

The current study investigated the causal role of frontal cortical activity in the interpretation of gaze direction. The range of gaze directions participants interpreted to be looking at them (i.e. the cone of gaze) was measured, while the participants received tDCS. There were three stimulation conditions: a sham condition, and two active conditions aimed to increase either relative left-sided or right-sided frontal cortical activity. A within-subject design was used, thus, all the participants participated in all three stimulation conditions above. The cone of gaze was measured with a computer task, where the participants were shown pictures of faces with varying gaze angles (0°—8°) and asked if the person in the picture was looking at them or not. A similar task with arrows as stimuli was used as a control task. The prediction was that the left anodal/right cathodal stimulation would widen the cone of gaze whereas the left cathodal/right anodal stimulation would narrow the cone of gaze (both as compared to sham-stimulation). However, no evidence for the prefrontal tDCS affecting the cone of gaze was found. As expected, there were no significant differences in the pre-task to post-task changes in participants' positive and negative affectivity between the stimulation conditions.

Previous studies using the same or highly similar stimulus set have found group means of the gaze cone ranging from 7° to 9.7°, depending on the experimental condition (Lyyra et al. 2017; Syrjämäki, Lyyra, & Hietanen, 2018). The current study showed comparable results (see Figure 4), thus suggesting, that cone of gaze was successfully measured by the current experimental task.

In the current study, all the statistical tests used to test the predicted effects were non-significant. Thus, no evidence for the main hypothesis was found. It is generally accepted, that failing to reject the null hypothesis is not evidence for the null hypothesis itself (e.g. Altman & Bland, 1995), although it is worth noting, that methods for showing support for the absence of effects have been developed (equivalence testing in frequentist tradition or the Bayes factor in Bayesian tradition, see, Lakens, McLatchie, Isager, & Scheel, 2018). Beyond just the logic of null-hypothesis significance testing, there are other important reasons why the achieved results do not provide strong evidence against the hypotheses of the current study.

When gathering experimental data and using the gathered data to test a hypothesis, any test of the hypothesis is concurrently also a test of associated auxiliary assumptions and the particulars of the experimental situation (e.g. Meehl, 1978). The current study relied on crucial auxiliary assumptions (e.g. approach-avoidance motivation is associated with the width of the gaze cone, approach-avoidance motivation is associated with asymmetrical frontal cortical activity) that, although justified, might potentially be problematic. It is also impossible to know in retrospect if the stimulation really did affect the frontal cortical activity in the way that was predicted. As a result of these features of the current study, it is hard to make strong conclusions about the main theoretical hypothesis of interest (i.e. is asymmetrical frontal cortical activity causally involved in interpretation of gaze direction).

Problems associated with the interpretation of tDCS effects

The design of the current study was based on the expectation that the anodal stimulation would increase the activity and the cathodal stimulation decrease the activity in the stimulated areas (the left and the right dorsolateral prefrontal cortex). The classical effects of anodal and cathodal stimulation to neuronal activity in humans are based on the Nitsche and Paulus (2000) study, where up to 1 mA anodal stimulation produced cortical excitation and cathodal stimulation cortical inhibition in the motor cortex. The assumption of these same effects underlies many tDCS studies: that the anodal stimulation will enhance neural activity (or facilitate behavior) and the cathodal stimulation will reduce neural activity (or hinder behavior). However, in many cases, this assumption will not hold, as the net effect of DC stimulation for the activity of any neural system can be complex and hard to predict (see Bestmann, de Berker, & Bonaiuto, 2015; Parkin, Ekhtiari, & Walsh, 2015).

There are many reasons for this. First, the effects of brain stimulation are dependent upon the initial state of the neurons being stimulated (Silvanto, Muggleton, & Walsh, 2008). This is called the principle of state-dependency and it has been argued to be one of the major factors explaining the unreliable results of tDCS studies in the cognitive domain (Horvath, Forte, & Carter, 2015; Tremblay et al. 2014). The assumption that the anodal stimulation will always increase, and cathodal stimulation will always decrease neuronal activity is demonstrably simplified. For example, the effect of stimulation intensity is non-linear: It has been shown that, in the motor cortex, 2 mA cathodal stimulation is excitatory in its effects, that is, the classical inhibitory response of the cathodal stimulation is reversed with 2 mA stimulation intensity (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013). All in all, 2 mA stimulation has been shown to be unreliable in its effects between individuals: In one study, 26% of the participants showed cortical inhibition after anodal stimulation (Wiethoff, Hamada, & Rothwell, 2014). Further complicating factor is that DC stimulation might have different effects on neural activity in gyri and sulci, and even different effects in a single gyrus, as the current can enter from one side of the gyrus creating effectively "anodal stimulation effect" and leave from the other side, creating effectively a "cathodal stimulation effect" (de Berker, Bikson,

& Bestmann, 2013; Rawji et al., 2018). Based on these and other results, it has been argued, that we should be careful with simplistic interpretations of study results that are based on the idea that anodal stimulation is always excitatory and cathodal stimulation always inhibitory in their effects (Bestmann et al., 2015; Parkin et al., 2015).

The interpretation of the null results is further complicated by the fact that the dorsolateral prefrontal cortex is likely only a small part of the complex circuitry involved in affect and motivation and its precise function in these phenomena is by no means clear (Davidson, 2004). That is, it is not well-established what component of affect and motivation the asymmetrical activity of the dorsolateral prefrontal cortices represents. Most of the frontal asymmetry studies find some affective and motivational state or trait to be correlated with asymmetrical activity, but beyond just association, more mechanistically informed explanations (let alone computational models) are rarely explicitly discussed or investigated.

There have been few theories of varying levels of specificity discussed in the literature. Proponents of the motivational direction model have suggested, that the lateralization of motivation might be due to the need to inhibit competing behavioral responses (e.g. Kelley et al., 2017). In each situation, one hemisphere will be dominant over the other which will affect the tendency of the organism to approach or to avoid in that situation. One neurobiological hypothesis that has been put forward, is that the dominance is achieved by inhibiting connections via corpus callosum between the dorsolateral prefrontal cortices (Harmon-Jones & Gable, 2018; Schutter & Harmon-Jones, 2013). However, it is noteworthy, that there have also been rival interpretations of what the frontal EEG asymmetry is signal of altogether. By one account, the relative left frontal cortical activity is associated with behavioral activation and the relative right frontal cortical activity with behavioral inhibition, and thus not with affect or the direction of motivation (Wacker, Chavanon, Leue, & Stemmler, 2008). According to Craig's (2005) homeostatic model, the lateralization of motivation and affect arise partly from the divergent representations of parasympathetic and sympathetic activity in the left and the right hemisphere, respectively.

A comprehensive review of the strength and weaknesses of competing theories of DLPFC (in affect and motivation) is outside the scope of this discussion section. The general point I am making is that the motivational direction model is neurobiologically and cognitively (i.e. what subprocesses of motivation the asymmetrical frontal activity represents) rather vague, and not universally accepted. We know much more about the function of the motor cortex, but even predicting what effects DC stimulation has on the excitability of this region is not always straightforward (e.g. Wiethoff et al., 2014). Added to the uncertainty of how tDCS affected frontal cortical activity in the current study, the complexity of the neurophysiological effects of the stimulation renders the null result of the current study inconclusive. As Davidson (2004) argued, frontal asymmetry research should try to integrate more with basic neuroscience research studying prefrontal cortex. This is also necessary if we want to make more well-founded predictions of the behavioral effects of DC stimulation aimed to influence asymmetrical frontal cortical activity.

It is also noteworthy, that the dorsolateral prefrontal cortex is a relatively common area of stimulation in tDCS studies. Tremblay et al. (2014) reviewed studies that stimulated areas F3 and F4 (10-20 EEG system), the same areas as targeted in the current study. The range of cognitive processes that DLPFC stimulation has been shown to modulate include, among other things, risk-taking, working memory, verbal memory, fear memory, attention, and pain perception, and it was not uncommon that different studies showed effects in opposite directions (Tremblay et al., 2014). Tremblay et al. (2014) concluded that prefrontal stimulation likely affects many cognitive processes simultaneously and because the neurophysiological effects of tDCS are complex, interpretation of the results is difficult. The same argument can be applied to the current study.

Thus, it is hard to state with confidence, that the stimulation in the current study achieved the aimed biological response (change in the asymmetrical frontal cortical activity) or the aimed psychological response (change in the approach-avoidance motivational state).

Further discussion and limitations

The current study used pictures of animated faces as stimuli (see Figure 1). In recent years, there has been interest in increasing the ecological validity of the experiments in social neuroscience, as highly-controlled laboratory studies with simple stimuli might be inherently limited in their capability to unravel the neural basis of social perception and cognition (e.g., Adolphs, Nummenmaa, Todorov, & Haxby, 2016; Hari & Kujala, 2009). One possible explanation for the current results is that as the faces were not realistic, they might have not been motivationally engaging enough for the participants. A natural suggestion for further studies is to consider using pictures of real faces. Also, it might be possible to implement the cone of gaze task with trained live actors as stimuli by using a similar electrically controlled shutter that was used in Hietanen et al. (2008) study. This would undoubtedly reduce experimental control but would also significantly increase the ecological validity of the stimuli and possibly activate the neural systems associated with approach-avoidance systems more reliably. Already in the studies that showed the modulating effect of gaze direction on frontal asymmetry, the effect was only found when the participants were watching live faces of real people, not when they were watching pictures (Hietanen et al., 2008; Pönkänen, et al., 2011).

In previous studies, social anxiety and social phobia have been found to be associated with increased width of the gaze cone (e.g. Chen et al., 2017; Gamer et al., 2011). The current study used the same questionnaire (SPS) as Chen et al. (2017) study and measured the cone of gaze with a similar task. Why did not the result replicate? One major difference to the Chen et al. (2017) study is that it used pictures of real faces. Thus, one possible explanation for the non-replication is the low ecological validity of the of the current stimuli, although, also at least one previous study that used pictures of real faces did not find an association between SPS scores and the cone of gaze (Uono & Hietanen, 2015). When considering non-significant effects, one must remember that null-findings are to be expected in a series of studies even if the studied effect is real. For example, if we consider five studies with all the studies having power of 0.8 (which is a hugely optimistic estimate of the real power in psychology and neuroscience, see Button et al., 2013; Szucs & Ioannidis, 2017), the probability that there is at least one nonsignificant result in the set of those five studies is 67% ($1 – 0.8^5 = 0.67232$). If the power in each of the five studies is, say, 0.4 the probability rises already to 99% ($1 – 0{,}4^5 = 0.98976$).

Finally, it is also possible that neither asymmetrical frontal cortical activity nor approach-avoidance motivation are associated with the width of the gaze cone. As I have argued, in terms of these statements, the current study is inconclusive. That we must arrive at this conclusion, can be considered a limitation of the current study design. That is, the current study was designed in a way that if null-results were to be observed (as they were), the achieved results would not be very informative. To be fair, this applies to most of the studies with null-results in psychology and neuroscience.

Replication crisis and reproducible science

There is an increasing concern in psychology and other sciences about the reliability of the published research literature (called the replication or reproducibility crisis, see Baker, 2016; Chambers, 2017), aptly captured by the titles of two highly-cited papers "*Why most published research findings are false*" (Ioannidis, 2005) and "*False-positive psychology*" (Simmons, Nelson, & Simonsohn, 2011). Especially in psychology, the concern for the reliability of the research literature has been fueled by recent largescale replication projects, where in a collaborative effort, direct replications of published studies have been performed with a very high statistical power (e.g. Klein et al., 2018; Open Science Collaboration, 2015). For example, the Open Science Collaboration (2015) performed 100 direct replications of studies in social and cognitive psychology. The overall results were not encouraging: the conductors of the replication project rated that only 39% of the studies were replicated. Although the replication projects have not employed a random sample of the published studies, these projects seem to indicate, that a large percentage of published research in psychology, at least in some subfields, can be called into question.

Several factors have been suggested to have contributed to the current crisis. These include biased incentive structures of the academia (e.g. Poldrack, 2019), underappreciation of direct replication studies (e.g. Chambers, 2017), publication bias (e.g. Munafò et al., 2017), widespread use of experimental designs with low statistical power (e.g. Button et al., 2013), hypothesizing after results are known (e.g. Munafò et al., 2017), p-hacking (e.g. Simonsohn, Nelson, & Simmons, 2014) and other researcher degrees of freedom in data analysis and interpretation (e.g. Gelman & Loken, 2014). To improve the replicability and reproducibility of psychological science, many suggestions for reforms have been put forward (e.g. Chambers, 2017; Munafò et al., 2017).

The current study could have been improved in several ways to adhere more to the best practices of reproducible and open science. For example, greater concern could have been paid to statistical power, as no a priori power analysis was performed. The data analyses of the current study could have been performed with an opensource software (e.g. R), and with providing the code used in the analysis, the ease of reproducing the statistical analyses would have been greatly increased. The current study could have also been preregistered, that is the hypotheses, study design, and data analytic decision could have been disclosed before the data collection, for example through an online service (Munafò et al., 2017). Even more powerful way than preregistration to combat many of the problems that have led to the current replication crisis is a new form of publishing called the registered report (RR), where the review process of a journal article is divided in to two stages: before and after the data collection (Munafò et al., 2017). In RR, the study can be accepted to be published before data collection if the study plan meets necessary requirements for methodological rigor. The current study would have been ideal for RR, as a relatively straightforward experiment with clear predictions about the direction of the effects and with no need for explorative data-driven analysis or computational modeling.

Strengths, further research, and practical applications

A major strength of this study was the use of within-subjects design. There are two reasons why the within-subjects design was a better choice for the current experiment. First, from a neurobiological standpoint, within-subjects designs reduce the problems associated with interindividual variability with the neurophysiological response to the tDCS (Li et al., 2015). Second, albeit related reason, statistical power in within-subjects designs is greater than in between-subjects designs with an equal number of observations (Greenwald, 1976). Another strength of the current study was the use of a double-blind design, which minimizes experimenter effects and demand characteristics.

The use of a control task can also be considered a strength of the current experiment. Many tDCS studies have failed to employ control tasks in their experimental designs. Arguably, the conclusions that can be made from these studies, at least regarding cognitive functions being associated with certain brain regions, are limited. Double dissociation is a basic principle of making strong associative claims, already used in classical neuropsychology. A double dissociation is found, when some task or cognitive function is associated with a brain region X but not with brain region Y (single dissociation), and some other task or cognitive function is associated with a brain region Y, but not with brain region X (double dissociation) (Dunn & Kirsner, 2003). With similar reasoning, a functionally independent control task has been argued to be a prerequisite for making conclusions about cognitive functions based on tDCS research (Parkin, et al., 2015). In this study, arrows were used as a control. Another possibility for a control task in future tDCS studies employing cone of gaze tasks would be to use inverted faces, as in Ewbank et al. (2009).

An important topic for further investigation is to examine the association between approach-avoidance motivation and the cone of gaze more carefully. This could be achieved by measuring the cone of gaze in tasks where the participants' approach-avoidance motivation is manipulated. For example, one possibility would be to use similar approach-motivation inducing procedures as have been used in the study of anger (e.g. Harmon-Jones et al., 2006; Hortensius et al., 2012), after which the cone of gaze could be measured. Also, further studies with similar designs should examine if the tDCS really changes the asymmetrical frontal cortical activity associated with approach-avoidance motivation. Techniques of applying tDCS with simultaneous recording of EEG are being developed that might offer the possibility to carry out these kinds of studies in the future (e.g. Schestatsky, Morales-Quezada, & Fregni, 2013).

This study is limited in its practical applications, especially because the statistical null finding in this study does not constitute strong evidence against the underlying theoretical hypothesis. Thus, generation of practical applications based on the current study would be gratuitous. This study represents basic research aimed at theory testing, and even with significant results could be argued to be limited with its potential practical applications. However, as meta-analyses have found evidence of publication bias in the tDCS literature (Mancuso, Ilieva, Hamilton, & Farah, 2016; Westwood & Romani, 2017), at this point, also null findings are important. Also, the left DLFPC is the targeted region of anodal stimulation in the clinical trials investigating the use of tDCS in treatment of depression (Shiozawa et al., 2014). Thus, basic research investigating what effects the stimulation of DLPFC has in different contexts is of utmost importance.

Conclusions

This experimental study investigated the effects of prefrontal tDCS on interpretation of gaze direction, i.e. on the cone of gaze. Within-subjects, sham-controlled, double-blind design was used. No effect of the stimulation on the cone of gaze was found. It is argued, that the current data are inconclusive, and as such, no suggestions for practical applications or strong theoretical arguments can be made based on this research. Further research is needed in order to make conclusions about asymmetrical frontal cortical activity being causally involved in whether we interpret another person’s gaze to be directed at us.

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