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Reducing proactive aggression through non-invasive brain stimulation

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Aggressive behavior poses a threat to human collaboration and social safety. It is of utmost importance to identify the functional mechanisms underlying aggression and to develop potential interventions capable of reducing dysfunctional aggressive behavior already at a brain level. We here experimentally shifted fronto-cortical asymmetry to manipulate the underlying motivational emotional states in both male and female participants while assessing the behavioral effects on proactive and reactive aggression. Thirty-two healthy volunteers received either anodal transcranial direct current stimulation to increase neural activity within right dorsolateral prefrontal cortex, or sham stimulation. Aggressive behavior was measured with the Taylor Aggression Paradigm. We revealed a general gender effect, showing that men displayed more behavioral aggression than women. After the induction of right fronto-hemispheric dominance, proactive aggression was reduced in men. This study demonstrates that non-invasive brain stimulation can reduce aggression in men. This is a relevant and promising step to better understand how cortical brain states connect to impulsive actions and to examine the causal role of the prefrontal cortex in aggression. Ultimately, such findings could help to examine whether the brain can be a direct target for potential supportive interventions in clinical settings dealing with overly aggressive patients and/or violent offenders.

Keywords: tDCS; dorsolateral prefrontal cortex; aggression; impulsivity; Taylor aggression paradigm; inter-hemispheric asymmetry

INTRODUCTION

Aggression is a behavior that intentionally causes physical or psychological harm to another being (Anderson and Bushman, 2002). It has a wide range of possible expressions and has been categorized into different subtypes based on distinct motivations: while reactive aggression refers to aggressive behavior in reaction to provocation, proactive aggression refers to using aggression in an instrumental way (Poulin and Boivin, 2000; Raine *et al.*, 2006). Aggression poses a threat to human collaboration and social safety. Aggressive reactions can lead to severe criminal acts putting potential victims at risk, but also destroying the lives of offenders and posing enormous costs to society. It is, therefore, crucial to understand the societal, cognitive and neurobiological mechanisms underlying aggression. This knowledge can lead to the development of interventions that can reduce overly aggressive behavior. In this study, we used non-invasive brain stimulation to attempt to reduce aggression.

Research has repeatedly tackled the question of why some individuals are highly aggressive, whereas others are not. The General Aggression Model (Anderson and Bushman, 2002) states that aggressive behavior results from an interplay between personal and situational variables and is mediated by cognitive, affective and arousal-related processes within an individual. One of the cognitive mechanisms playing a role in aggressive behavior is the processing of social cues such as, for instance, social situation, social counterpart or social

content of communication (Crick and Dodge, 1994). Social cue processing is biased in aggressive individuals (Crick and Dodge, 1996). In this context, proactive and reactive aggression could consistently be dissociated as two distinct types of aggression. For instance, behavioral research showed that a hostile interpretation style and an attentional bias toward angry faces was related to reactive aggression, whereas a stronger self-aggression association was shown to be related to proactive aggression (Lobbetael *et al.*, 2013; Brugman *et al.*, 2014).

More recently, neuroscientific research has identified potential neural substrates underlying aggression as one form of (anti)social behavior. Brain researcher studies have investigated behavioral aggression in healthy adults (Krämer *et al.*, 2007, 2011; Lotze *et al.*, 2007), adolescents (White *et al.*, 2013) and psychopaths (Veit *et al.*, 2010): neural networks associated with aggression included various regions within prefrontal cortex, the insular cortex, the cingulate cortex, striatal areas and the amygdala (Krämer *et al.*, 2007, 2011; Lotze *et al.*, 2007; Veit *et al.*, 2010; White *et al.*, 2013). Subsequently, attempts have been made to relate these brain networks to other executive networks. For instance, overlapping areas activated during aggressive behavior and failed motor inhibition could be located in prefrontal cortex (more specifically anterior insula) and thalamus (Dambacher *et al.*, 2014). Specifically, prefrontal cortex has repeatedly been associated with cognitive control (Miller, 2000; Koechlin *et al.*, 2003). Dual-path theories emphasize the role of prefrontal cortex as a mediator for subcortical communication (Ledoux and Phelps, 2008). An example of the prefrontal cortex as a mediator can be found in the communication between thalamus and amygdala. They can communicate via a direct pathway and this communication leads to rapid responses following emotional stimuli, but the responses are very unspecific. When signals from one subcortical region to the other are, however, directed through the prefrontal cortex, responses become more elaborate, though slower. Within the prefrontal cortex, inter-hemispheric balance determines the affective motivational state: motivational direction is the basic psychological domain related to hemispheric asymmetry (van Honk and Schutter, 2006). Although

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avoidance or withdrawal motivation is mainly associated with right fronto-cortical brain activity, approach motivation is related to the activity in the left prefrontal cortex (Davidson, 1992; Harmon-Jones and Allen, 1998; Harmon-Jones and Sigelman, 2001; Harmon-Jones, 2004). In the context of aggression, anger-related (thus approach-related) brain states have also been allocated to the left prefrontal cortex (Carver and Harmon-Jones, 2009). Based on this concept of fronto-cortical asymmetry, it has been demonstrated that through contractions of the right hand, greater left-hemispheric frontal activity compared with right-hemispheric frontal activity (measured by electroencephalogram) was induced, which led to increased aggression after provocation (Peterson *et al.*, 2008).

The experimental induction of either left or right fronto-cortical dominance seems promising to understand how cortical balance theories can translate to behavior. Non-invasive brain stimulation methods such as Transcranial Magnetic Brain Stimulation (TMS) or transcranial Direct Current Stimulation (tDCS) are mechanistic or causal techniques that are able to further clarify the role of the prefrontal cortex in mediating aggressive behavior. While TMS can enhance or disturb brain activity in a specific region by means of electromagnetic induction, tDCS induces low electric currents into brain tissue to either decrease or increase the excitability of the stimulated areas. Until hitherto, surprisingly few studies investigated the role of prefrontal cortex in aggression using non-invasive brain stimulation techniques: the induction of relative left fronto-cortical activation by means of tDCS was shown to increase aggressive behavior in a reaction time game (Hortensius *et al.*, 2012). Similar mechanisms were demonstrated in the attentional domain: increased left-to-right and simultaneously reduced right-to-left transcallosal inhibition (measured via motor-evoked potentials induced by TMS) was associated with a stronger attentional bias for angry faces (Hofman and Schutter, 2009). Furthermore, the disruption of right prefrontal cortex by means of repetitive TMS (and, thus, induction of relative left frontal brain activity) shifted selective attention toward angry faces (d'Alfonso *et al.*, 2000).

The described results from behavioral aggression research indicate that different aspects of aggressive behavior—that is, proactive vs reactive aggression—are dissociable. This suggests that the neural mechanisms underlying these different forms of aggression might also be different. The described neuroscientific findings indicate that shifting fronto-cortical balance can affect cognitive mechanisms underlying aggression (d'Alfonso *et al.*, 2000; Hofman and Schutter, 2009) and lead to more aggressive behavior (Hortensius *et al.*, 2012). Particularly, right-hemispheric fronto-cortical dominance was found to be related to avoidance- or withdrawal-related behavior. Increasing activity in this area should decrease aggressive behavior by increasing avoidance, as compared with approach, motivation. So far it has not been investigated if the induction of right fronto-cortical dominance can experimentally reduce different aspects of aggression in a controlled behavioral aggression paradigm. Reducing aggression under controlled experimental conditions in healthy volunteers is necessary to causally clarify the role of the right prefrontal cortex in mediating aggressive behavior. To directly provide this missing piece of evidence, we investigated whether shifting fronto-cortical balance by means of tDCS affects proactive and/or reactive aggression in healthy participants. We expected that the induction of right-hemispheric fronto-cortical dominance by applying tDCS over right dorsolateral prefrontal cortex should enhance avoidance motivation and, thereby, cause a significant reduction in aggressive behavior as compared with sham tDCS. Furthermore, we expected that this reduction would differentially affect proactive as compared with reactive aggression.

METHODS

Participants

Forty-three healthy university students ($N=20$ male, mean age in years = 22.14, *s.d.* = 2.00) took part in this study. All had no history of neurological or psychiatric disorders and gave their written informed consent before participating.

Paradigms and tools

Taylor Aggression Paradigm

To measure aggressive behavior, a standard controlled behavioral aggression paradigm was employed (Taylor, 1967): participants were made to believe that they played a competitive reaction time game against another participant sitting in the room next door. The amount of win and lose trials were pre-programmed and the players were made to believe that the winner of a trial could administer a loud noise to the loser as 'feedback'. Before each trial, the participants were asked to choose the duration and volume of this noise blast on a 10-point scale (volume: 0–100 dB, duration: 0–5 s). Thirty trials were played. The first provocation (first noise feedback not being zero) was given in the seventh trial. Three aggression scores could be calculated: a proactive aggression score was calculated by summing intensity score and duration score for the unprovoked (first seven) trials. A reactive aggression score was calculated by summing intensity score and duration score for the provoked (last 23) trials. A total aggression score was calculated by summing and averaging intensity score and duration score across all trials. The Taylor Aggression Paradigm (TAP) has previously demonstrated high validity (Bernstein *et al.*, 1987; Giancola and Zeichner, 1995; Anderson *et al.*, 1999; Giancola and Parrott, 2008).

Reactive Proactive Aggression Questionnaire

The Reactive Proactive Aggression Questionnaire (RPQ) (Raine *et al.*, 2006) was used to measure self-reported trait aggression. Twelve items measured proactive aggression (e.g. 'Used physical force to get others to do what you want'), while 11 items measured reactive aggression (e.g. 'Reacted angrily when provoked by others'). By taking all 23 items into account, an overall total aggression score could be calculated. High internal reliability has been shown for all scales ($\alpha=0.81$ for reactive aggression, $\alpha=0.84$ for proactive aggression, $\alpha=0.90$ for total aggression; Raine *et al.*, 2006).

Experimental design

To assure that behavior in the experiment was unaffected by social desirability, participants were told that they took part in a study investigating the effects of human feedback on reaction time performance. In every experimental session, two participants of the same gender took part simultaneously.

The tDCS setup was mounted on the participants' heads and they received instructions about the task. After the brain stimulation was initialized, participants performed the TAP. Immediately after completion of the experiment, participants had to answer some general questions about how they perceived the task in order to make sure that they were fully deceived by the experimental setup. Twenty-four hours after completing the experiment, participants had to fill in the RPQ.

After all the measurements had been finalized, the experiments' real purpose and motivation was disclosed to the participants. The study was approved by the local ethical committee and conformed to the Declaration of Helsinki.

Non-invasive brain stimulation

Three participants had to be excluded as they were suspicious about the real purpose of the investigation. Another eight participants had to

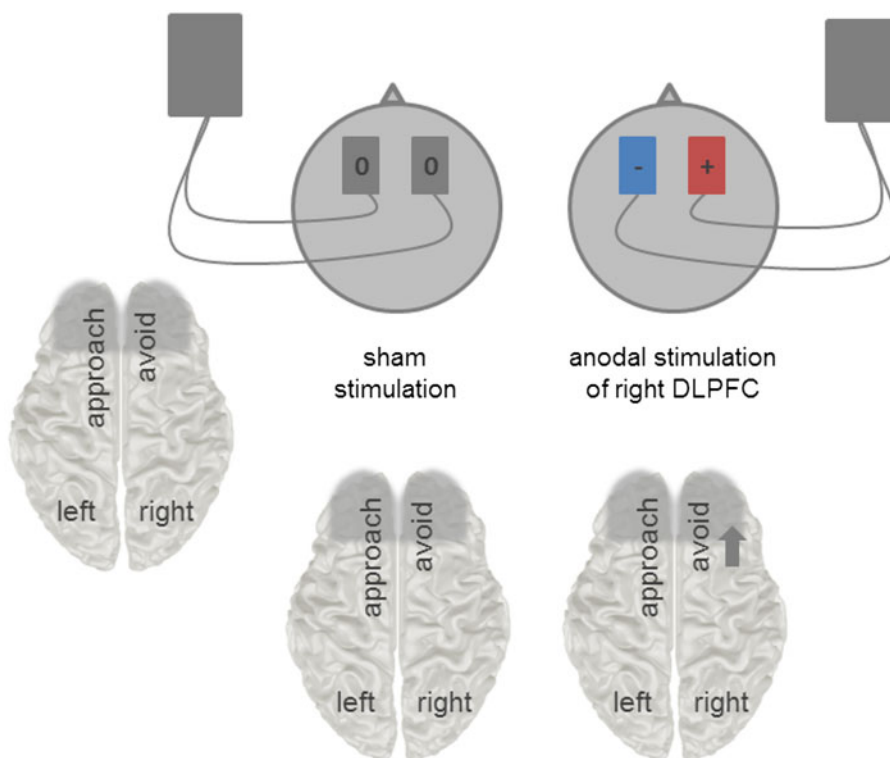


Fig. 1 tDCS setup. DLPFC = dorsolateral prefrontal cortex.

be excluded because their medical conditions at the day of the experiment did not allow for the application of brain stimulation. Thirty-two participants could be included in the analysis and were randomly assigned to one of the two tDCS conditions: stimulation over right dorsolateral prefrontal cortex, $N = 16$ ($N = 7$ male); sham stimulation, $N = 16$ ($N = 6$ male). As the TAP relies on the participant's naivety, it is not suited to be repeated in a within-subject design. Even though the TAP is the best possible measure of our dependent variable, we sacrificed a possible within-subject design.

To induce right-hemispheric fronto-cortical dominance—and thus enhance avoidance motivation—the anode was positioned over the right dorsolateral prefrontal cortex (F4), while the cathode was positioned above the left eyebrow (Figure 1). A DC stimulator with 5×7 cm standard electrodes (neuroConn, Ilmenau, Germany) was used. We induced 2.0 mA direct current for a duration of 750 s (ramping phases 20 s each). To apply sham tDCS, the same procedure was followed as explained above, but the stimulation was switched off immediately after the ramping phases. This mimicked the skin sensation accompanying real tDCS application and deceived participants about which condition they were assigned to. Unlike sham TMS, sham tDCS feels identical to real tDCS and can thus be regarded as a highly effective sham condition.

Statistical analysis

Inferential statistics were conducted by computing multivariate analyses of variance with the 2×2 factors gender (male, female) and stimulation condition (induction of right-hemispheric dominance, sham stimulation). Total aggression, reactive aggression and proactive aggression were included as dependent variables. This was done for both the RPQ and the TAP separately. When a significant interaction effect was found, the sample was split and *post hoc* tests were conducted via independent sample *t*-tests. Bivariate Pearson product-

moment correlation coefficients were computed to estimate the relationship between TAP and RPQ.

RESULTS

Mean values and standard deviations are summarized in Table 1. Results are depicted in Figures 2 and 3.

Gender

A multivariate analysis of variance showed that men behaved more aggressively (total aggression and reactive aggression) than women, regardless of stimulation type (TAP; total aggression: $F = 5.33$, $df = 1,62$, $P = 0.029$; reactive aggression: $F = 4.31$, $df = 1,62$, $P = 0.047$; proactive aggression: $F = 3.94$, $df = 1,62$, $P = 0.057$; Figure 2A). Men considered themselves more proactively aggressive (RPQ; total aggression: $F = 7.49$, $df = 1,62$, $P = 0.011$; reactive aggression: $F = 2.84$, $df = 1,62$, $P = 0.103$; proactive aggression: $F = 13.42$, $df = 1,62$, $P = 0.001$; Figure 2B).

Correlations between behavioral and self-report measures

Proactive behavioral aggression (TAP) correlated positively with self-reported proactive aggression (RPQ) in men, but not in women. For the other types of aggression, there was no relationship between behavioral and self-reported measures (overall sample: total aggression: $r = 0.27$ and $P = 0.132$, reactive aggression: $r = 0.20$ and $P = 0.266$, proactive aggression: $r = 0.50$ and $P = 0.003$; male: total aggression: $r = -0.13$ and $P = 0.678$, reactive aggression: $r = -0.400$ and $P = 0.175$, proactive aggression: $r = 0.62$ and $P = 0.024$; female: total aggression: $r = 0.27$ and $P = 0.268$, reactive aggression: $r = 0.29$ and $P = 0.225$, proactive aggression: $r = 0.059$ and $P = 0.809$).

Table 1 Mean and standard deviation per gender and stimulation condition

	Stimulation				Sham				Male				Female			
	Stimulation		Sham		Stimulation		Sham		Stimulation		Sham		Stimulation		Sham	
	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.
TAP																
Total aggression	3.84	1.16	4.00	1.33	4.16	0.90	4.87	0.86	3.60	1.33	3.48	1.32				
Reactive aggression	4.07	1.25	4.13	1.48	4.52	0.96	4.86	1.09	3.73	1.39	3.69	1.55				
Proactive aggression	2.93	1.25	3.49	1.72	2.74	1.26	4.89	1.50	3.08	1.29	2.69	1.27				
RPQ																
Total aggression	8.44	3.44	9.31	6.16	10.00	5.98	13.17	3.15	7.22	2.95	7.00	5.25				
Reactive aggression	7.00	2.34	7.00	4.03	7.71	3.67	8.67	3.67	6.44	2.56	6.00	4.08				
Proactive aggression	1.44	1.67	2.31	2.75	2.29	3.15	4.50	5.98	0.78	0.83	1.00	1.41				

Note: For TAP, the descriptive statistics are based on mean; for RPQ, the descriptive statistics are based on sum scores.

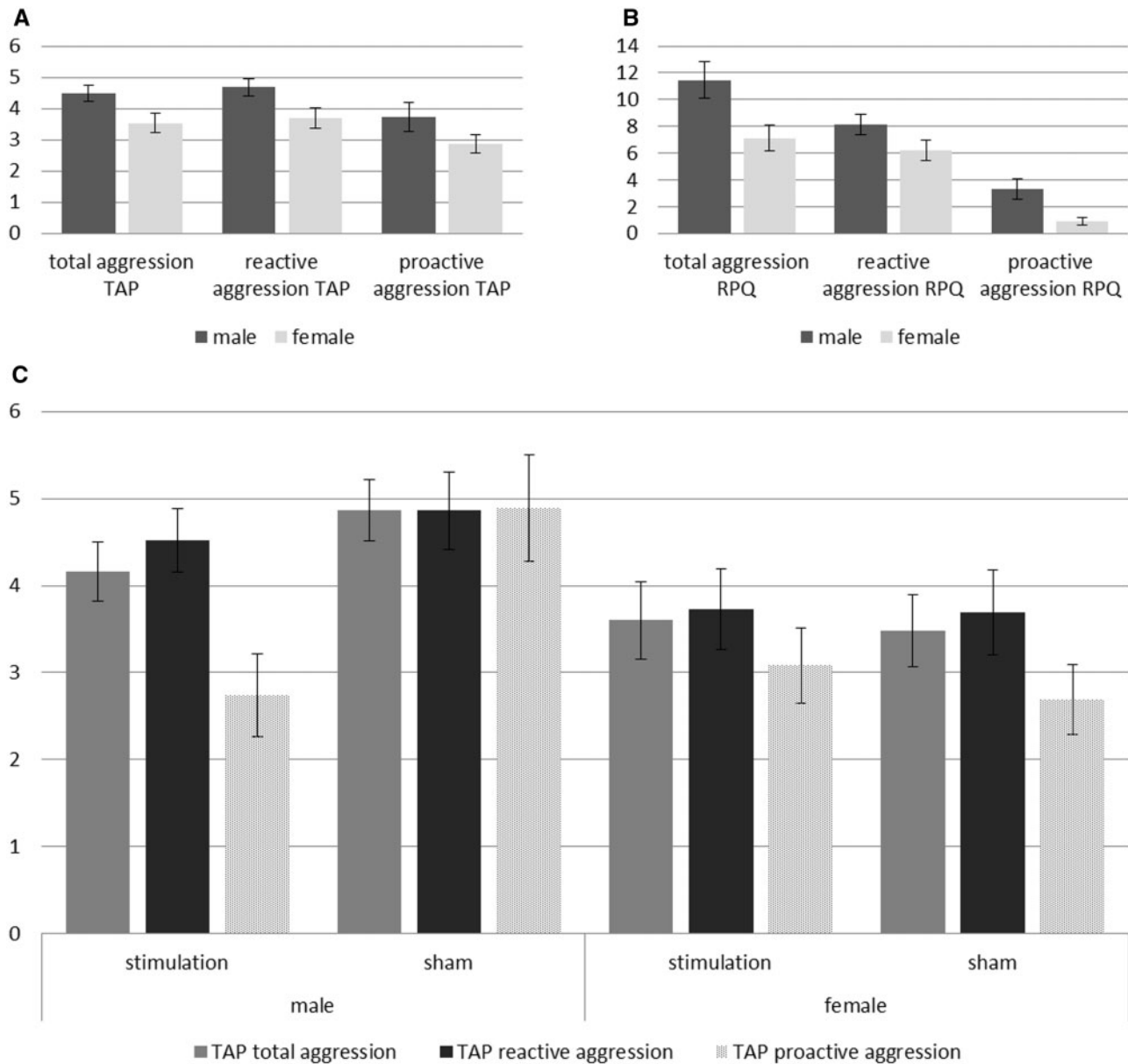


Fig. 2 Aggression scores per gender and stimulation condition. For TAP, the descriptive statistics are based on mean; for RPQ, they are based on sum scores.

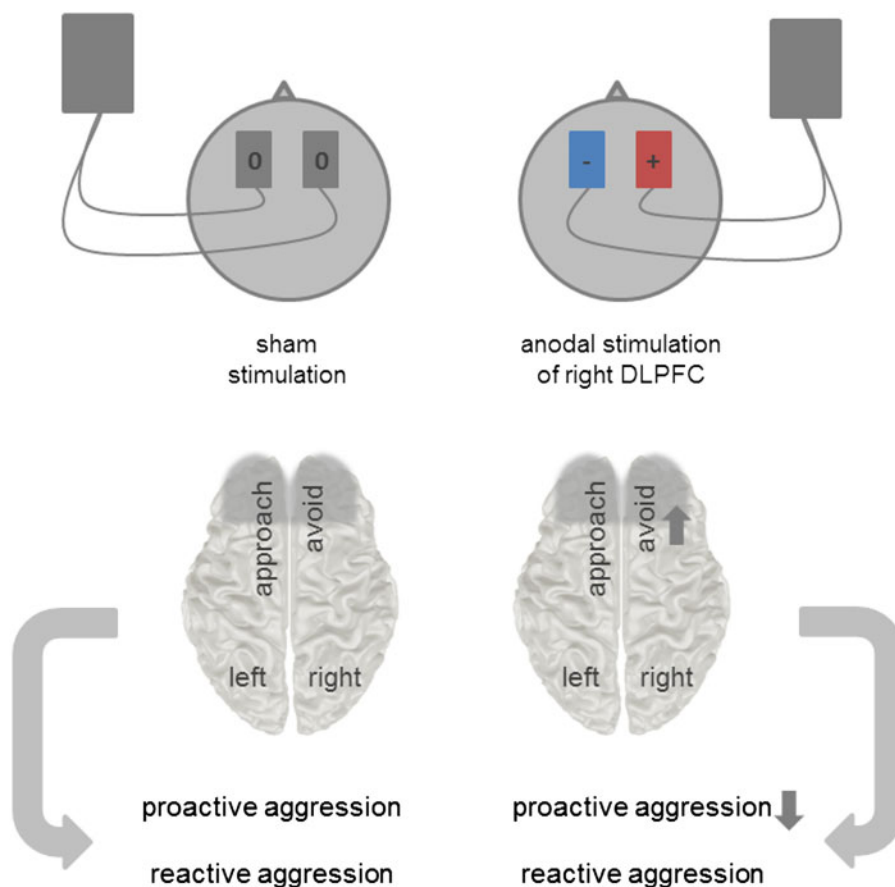


Fig. 3 Results. DLPFC = dorsolateral prefrontal cortex.

tDCS effects

For total and reactive aggression in the TAP, a multivariate analysis of variance revealed that there was no main effect of stimulation condition (total aggression: $F=0.485$, $df=1,62$, $P=0.492$; reactive aggression: $F=0.103$, $df=1,62$, $P=0.750$). No interaction effects between stimulation condition and gender were found (total aggression: $F=0.953$, $df=1,62$, $P=0.337$; reactive aggression: $F=0.167$, $df=1,62$, $P=0.686$). In contrast, for proactive aggression, there was a significant interaction effect between gender and stimulation condition ($F=7.35$, $df=1,62$, $P=.011$), with *post hoc* contrast analyses revealing that this interaction was driven by the induction of right-hemispheric dominance significantly reducing proactive aggression in men (mean = 2.74 and mean = 4.89, $df=11$, $P=0.018$, Cohen’s $d=1.55$; Figures 2C and 3), but not in women (mean = 3.08 and mean = 2.66, $df=17$, $P=0.480$, Cohen’s $d=0.33$; Figure 2C). Reactive aggression was not altered by brain stimulation in either men (mean = 4.52 and mean = 4.86, $df=11$, $P=0.554$, Cohen’s $d=0.34$; Figure 2C) or women (mean = 3.73 and mean = 3.69, $df=17$, $P=0.952$, Cohen’s $d=0.03$; Figure 2C).

DISCUSSION

This study revealed that anodal compared with sham tDCS applied to the right dorsolateral prefrontal cortex reduced proactive aggression in men.

Gender differences

Exploring gender differences in our sample, we demonstrated that men reported more aggressive tendencies than women did. They also

behaved more aggressively compared with women. A vast body of literature is in line with this finding. It has repeatedly been suggested that men display more physical aggression than women, who in turn tend to revert to more indirect forms of aggression (Eagly and Steffen, 1986; Lagerspetz *et al.*, 1988; Bjorkqvist, 1994; Archer, 2004). Several biological factors such as testosterone levels contribute to this phenomenon (Book *et al.*, 2001; Mehta and Beer, 2010). The TAP, in which the actual aggressive act is to assign to the opponent a noise feedback evoking a rather unpleasant and almost painful auditory experience, can be understood as a measure of physical aggression. It is therefore to be expected that—due to its characteristics—the TAP is well suited to generate aggression in men.

Relationship between behavioral and self-reported aggression

There was no relationship between total and reactive behavioral and self-reported aggression scores. It is a long and well-known problem in aggression research that behavioral measures of social constructs do not necessarily overlap with measures on a self-reported level (Scheier *et al.*, 1978). Especially in this domain, effects of social desirability are obstacles that measurement tools have to overcome (Vigil-Colet *et al.*, 2012). Our self-reported data were probably likewise affected as we measured exclusively university students, a sample for which it might be very difficult to admit aggressive tendencies.

We found a positive relationship between behavioral and self-reported aggression in the proactive domain for the overall sample and for men. This might hint toward the fact that conceptually, the proactive aspect of the TAP overlaps more precisely with the proactive sub-scale of the RPQ than the reactive aspect of the TAP with the

reactive sub-scale of the RPQ. Biases regarding self-reported aggression might be more relevant for reactive than for proactive aggression. In our societies, it is emphasized that everyone should react rationally to provocation. Proactive aggression might be less frequent and more exceptional and, thus, less prone to social biases. The data collected in this study could give a hint in this direction. However, more empirical evidence needs to be collected in larger samples to substantiate this claim.

Effects of brain stimulation

In line with our hypothesis, we found that the induction of right-hemispheric neural activation dominance reduced aggressive behavior compared with sham brain stimulation, although the effect was only significant in men.

Dissociation of proactive vs reactive aggression

Proactive aggression refers to the instrumental use of aggression to obtain a reward or a prey (Anderson and Bushman, 2002). Therefore, the motivation to approach seems central. The experimental manipulation in this study was meant to enhance activity in the right dorsolateral prefrontal cortex. This area is said to be responsible for emotional and cognitive processes generating avoidance motivation (Harmon-Jones, 2004; Carver and Harmon-Jones, 2009). The assumption that the applied brain stimulation protocol enhanced avoidance and thus lowered approach motivation fits with our finding that it reduced proactive aggression.

The current findings can also be explained in the light of social information-processing theories. It has been shown that reactive and proactive aggression revert to biases in different stages of social information processing. Thereby, reactive aggression seems to result from deviations in rather early stages, such as an increased attentional bias for angry faces or a hostile interpretation bias (Anderson and Bushman, 2002; Lobbestael et al., 2013; Brugman et al., 2014). For proactive aggression, the later stages seem more impaired and lead to a more positive evaluation of aggressive action options (Walters, 2007). A proactive attitude likely also steers coping processes, meaning that proactively aggressive individuals have the tendency to approach their goals using aggression. The evaluation of the option to act proactively aggressive is more closely related to approach motivation than to attention and interpretation biases. It seems likely that an alteration of such motivational states (on a neural level) influences proactive rather than reactive aggression.

With this study, we demonstrated that it is possible to specifically manipulate proactive aggression. Usually, this form of aggression is more difficult to deal with in clinical contexts; proactive aggression is potentially very dangerous as it is a planned behavior and not emotionally driven. It is often prevalent in patients with psychopathic traits. So far, neuroscience and especially neuroimaging research mostly neglected the differentiation between proactive and reactive aggression. In the light of the current results, it seems promising to consider the difference in further neuroscientific research on aggression. This could lead to more elaborate theories on which specific neural mechanisms underlie proactive aggression compared with reactive aggression and how these mechanisms can be manipulated in order to ultimately change behavior.

Limitations and outlook

This study demonstrates that tDCS can reduce aggressive behavior. Our findings still have to be considered in light of the limitations that the current experimental setting was accompanied by. Our sample ($N=32$) was restricted to university students. The field would profit from investigating larger samples and more

heterogeneous populations. The lack of a stimulation effect in women might be caused by a floor effect considering that female students in our restricted sample displayed low aggression levels. Applying tDCS in the context of aggression to larger and, further, more variable female sample might lead to a clearer picture on whether aggressive behavior can or cannot be reduced in women compared with men. Furthermore, research should also zoom in on larger male samples enabling the inclusion of more control variables (such as, e.g. perception of the opponent, perception of feedback, influence of brain stimulation side effects) and different brain stimulation conditions.

To further examine the specificity of the present effects, other stimulation parameters, such as bilateral stimulation setups and frequency-dependent protocols, might be of use in further investigating the effects of cortical asymmetry on aggression. Future experiments should consider including different stimulation sides within the prefrontal cortex (based on imaging literature) in order to investigate if lateralization effects are bound to the right dorsolateral prefrontal cortex.

We demonstrated the effects of brain stimulation on aggression measured by the Taylor paradigm. The question of whether the findings are generalizable and specific to aggression remains to be answered. It is especially interesting to assess to what degree the very same mechanism plays a role in both aggressive and prosocial approach.

CONCLUSION

This study demonstrates that non-invasive brain stimulation can significantly reduce aggression, and dissociate between proactive and reactive aggression. This is a promising step in order to better understand how cortical brain states connect to aggressive behavior. It enables the examination of how interventions in clinical settings dealing with aggression can be improved.

CONFLICTS OF INTEREST

None declared.

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