2006). More recent findings bolster the meta-analytic evidence. The involvement of the DLPFC in aggressive and antisocial behavior has since been documented in other neuroimaging studies (Dalwani et al., 2011; Fairchild et al., 2013; Alegria et al., 2016). Furthermore, while it has been suggested that DLPFC lesions are associated with apathy and diminished motivation (Levy and Dubois, 2006), a meta-analysis of 126 neuropsychological studies measuring executive functions in antisocial populations documented an effect size of $d = 0.44$ for antisocial behavior and $d = 0.41$ for physical aggression, implicating dorsolateral prefrontal dysfunction in aggression (Ogilvie et al., 2011). It is important to recognize, however, that the DLPFC is not the only prefrontal area implicated in antisocial and aggressive behavior. Other subregions include the ventromedial prefrontal cortex (Hare et al., 2014) and the anterior cingulate cortex (Kolling et al., 2016), areas which have widespread connections to the DLPFC. Together, studies suggest that there is multimethod evidence indicating the possible implication of the DLPFC on antisocial behavior, among other brain regions.

Despite these findings, little is known about the causal role of the prefrontal cortex on aggressive behavior. Conclusions from extant research on the neural foundations of aggression have largely been correlational. Three known studies have tested the effect of prefrontal cortex upregulation on aggression using the Taylor Aggression Paradigm and transcranial direct current stimulation (tDCS), a noninvasive technique that influences neural excitability by delivering a direct, continuous, low-intensity electrical current to cortical areas between anodal and cathodal electrodes (Brunoni et al., 2012). However, findings have been mixed. One study documented that upregulating the right DLPFC reduced proactive aggression in males (Dambacher et al., 2015b), while another revealed that increasing left DLPFC activity resulted in more aggressive behavior when participants were angry (Hortensius et al., 2012). In contrast, upregulation of the inferior frontal cortex did not have a significant effect on aggression (Dambacher et al., 2015a). Whether stimulation targeting the DLPFC can reduce intentions to engage in aggressive acts or behavioral aggression using other measures has not been examined and, to our knowledge, no studies have experimentally investigated the intermediary mechanisms linking prefrontal deficits to aggression.

Given the association between prefrontal impairments and aggression, this study tests the hypothesis that upregulating the prefrontal cortex using tDCS will reduce intent to commit an aggressive act. This study additionally extends the limited literature on tDCS and aggression by using a larger sample. As similarities have been found between the neural mechanisms underlying moral cognition in normal individuals and brain mechanisms impaired in antisocial populations (Raine and Yang, 2006), we also assess whether prefrontal upregulation improves judgments of moral wrongfulness, which may in turn partly account for any effect of prefrontal enhancement on reducing intent to commit aggressive acts.

Materials and Methods

Trial design. The study consisted of a double-blind, placebo-controlled, stratified, randomized trial comparing a group that received an anodal tDCS intervention with a sham control group. Baseline assessments and one session of tDCS or sham intervention were conducted during the experimental session, while outcome measures were assessed the following day. Tasks and questionnaires were administered in a fixed order. The study was approved by the Institutional Review Board of the University of Pennsylvania and the trial protocol was registered at ClinicalTrials.gov (NCT02427672).

Participants. Eighty-six healthy adults (age, ≥18 years) were recruited in Philadelphia between April 2015 and April 2016. The experiment took place during one visit to the study site. In addition to assessments conducted at baseline, participants were followed up 1 d after the experimental session using a web-based questionnaire. Exclusion criteria included contraindications to brain stimulation, such as metallic implants near the electrode sites; unstable medical conditions; neurological, cardiovascular, or psychiatric illness; participation in another noninvasive brain stimulation study on the same day; history of adverse reactions to tDCS; and lack of e-mail access. Written informed consent was obtained from all participants.

tDCS intervention. tDCS was administered by trained study personnel using a battery-driven, constant-current stimulator (TCT Research). Two anodal electrodes were placed over the DLPFC bilaterally (F3 and F4) according to the International 10–20 EEG system. A constant current of 2 mA (1 mA to each DLPFC site) was applied for 20 min through saline-soaked sponge electrodes (5 × 5 cm). A single extracephalic cathodal electrode (5 × 7 cm) was placed at the posterior base of the neck to minimize unintentional effects of inhibitory stimulation on brain activity.

Following standard tDCS protocol, stimulation commenced after a 30 s ramp-up period. The current was ramped down over the last 2 s. The tasks performed during tDCS are understood to influence the behavioral after-effects of stimulation (Gill et al., 2015). Thus, during the stimulation session, all participants performed the Psychology Experiment Building Language (Mueller and Piper, 2014) version of two cognitive tasks known to engage the DLPFC: the Psychomotor Vigilance Task (Dinges and Powell, 1985; Cui et al., 2015), followed by the Iowa Gambling Task (Bechara et al., 1994; Ernst et al., 2002). Although participants in both intervention arms received the same electrode placement and ramp-up/down times, stimulation for the sham control group was discontinued after 30 s. This has proven to be effective for blinding as participants habituate to the sensation of stimulation within seconds of current initiation (Gandiga et al., 2006).

Intentions to commit aggression. Behavioral intentions to commit aggressive acts were assessed using two hypothetical vignettes, which have been studied in samples with characteristics similar to ours (Hannon et al., 2000; Mazerolle et al., 2003). Brief scenarios describing two types of aggression, physical assault and sexual assault, were presented to participants, who responded to the anticipated likelihood that they would commit the aggressive act. Responses were measured on a scale ranging from zero (no chance at all) to 10 (100% chance).

Perceptions of moral wrongfulness. To assess moral perceptions of the aggressive acts, participants were asked to rate how morally wrong it would be to act as the protagonist in the scenario on a scale from 0 (not at all) to 10 (very). Aggregate measures of aggressive intent and perception of moral wrongfulness were created by combining responses from the physical and sexual assault scenarios (Armstrong and Boutwell, 2012).

Aggression. The voodoo doll task is a reliable and validated behavioral analog measure of aggression (Dewall et al., 2013). In this task, participants were shown a computer-based image of a doll that represented a partner or a close friend. They were told that they were given the opportunity to release their negative energy to that individual by inserting as many pins (0–51) in the doll as they wished. Instructions did not use the word "voodoo." Stabbing the doll with more pins indicated higher levels of aggression.

Randomization and stratification. At the initial visit, participants were randomized into an active stimulation or sham/placebo condition using a computerized urn randomization procedure (Stout et al., 1994). The stratification factors were age (18/19/≥20 years), sex (male/female), and ethnicity (Caucasian/non-Caucasian). This stratification was used to balance groups on key demographic variables.

Blinding. Participants and experimenters were blind to the tDCS condition assignment. The trial adhered to established procedures to maintain separation between staff that conducted the stimulation and staff that engaged with the participant. In each experimental session, only one experimenter who set up the tDCS procedure had knowledge of the participant's allocation. To further ensure blinding, all participants were kept blind to the objective of the study and outcome measures were not taken in the presence of research staff as they could lead to biased results.