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Transcranial Direct Current Stimulation (tDCS) paired with a decision-making task reduces risk-taking in a clinically impulsive sample

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ABSTRACT

Background: Impulsivity is a multidimensional personality trait observed across a variety of psychiatric disorders. Transcranial direct current stimulation (tDCS) applied over dorsolateral prefrontal cortex (DLPFC) has shown promise as an intervention to reduce impulsivity.
Objective: To investigate the effects of tDCS paired with a decision-making task on risk-taking in Veterans with a clinical history of impulsive behavior.
Methods: This was a randomized, single-blind, sham-controlled study. Participants performed the Balloon Analogue Risk Task (BART) while concurrently receiving either active or sham tDCS (right anodal/left cathodal over DLPFC) twice a day for five days. To evaluate generalization, the Risk Task was performed before and after the complete course of intervention. To evaluate durability, the BART and Risk Task were administered again at one and two month follow-up sessions.
Results: Thirty Veterans participated: 15 received active tDCS and 15 received sham tDCS. For the trained BART task, individual growth curve analysis (IGC) examining individual variation of the growth rates over time showed no significant variations in individual trajectory changes over time ($\beta = 0.02$, $p > 0.05$). For the untrained Risk Task, IGC showed that the active tDCS group had a significant 46% decrease in risky choice from pre-to post-intervention, which persisted through the one and two month follow-up sessions. The sham tDCS group showed no significant change in risky choice from pre-to post-intervention.
Conclusions: tDCS over DLPFC paired with a decision-making task effectively reduced risk-taking behavior in a group of Veterans with clinically-relevant impulsivity. Results suggest that this approach may be an effective neuroplasticity-based intervention for patients affected by impulsivity.

Introduction

Impulsivity is a multifaceted personality trait characterized by sensation-seeking, lack of premeditation, and impaired cognitive control [1]. Impulsivity includes a variety of behaviors that are typically inappropriate to the situation and done without consideration [2], including insufficient attention to relevant stimuli, inability to delay gratification, deficient action planning, and increased risk-taking [3–5].

Impulsivity is observed in a number of psychiatric disorders, including substance use disorders [6], gambling disorder [7], attention deficit hyperactivity disorder (ADHD) [8], bipolar disorder [9], post-traumatic stress disorder (PTSD) [10,11], binge eating disorder [12], and personality disorders [13]. The construct of impulsivity in psychiatric illness is important because impulsiveness has been shown to correlate significantly with destructive, suicidal, and aggressive behavior [14–16], is related to poor treatment program adherence [17], and is an important aspect of violence risk assessment and management in clinical outpatient settings [18]. These relationships are particularly important for military Veterans and service members, as impulsivity has been linked to combat exposure [19], depression [20], PTSD [11,21],

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traumatic brain injury (TBI) [20,22], substance use disorders [23], and aggression [24] in these populations.

While impulsivity is a common clinical trait, it has been difficult to treat and manage. Given that impulsivity is found in a myriad of psychiatric disorders, it presents a compelling target for treatment. Cognitive-Behavioral Therapies (CBT) have been used to target impulsive behaviors within the context of various disorders with some success [25,26]. Psychopharmacological treatments e.g. Refs. [27–29] have shown some promising effects with regard to impulsive behaviors, however results remain equivocal (e.g. Refs. [30,31]), and they each have adverse effect profiles that must be considered before administration. There remains a need for a novel, well-tolerated, neuroplasticity-based intervention that targets both the cognitive control issues associated with impulsivity, as well as its underlying neural dysfunction. Transcranial Direct Current Stimulation (tDCS) is a promising, low-risk, non-invasive neuromodulation technique that can modulate brain networks by inducing neural excitability with potentially enduring effects. When paired with an appropriate cognitive task, tDCS has potential as a low-risk method for affecting brain connectivity and psychiatric symptoms [32].

From a neurobiological perspective, impulsivity derives from dysfunction within thalamo-cortico-striatal neurocircuitry [33], with impairments in the higher order thalamic relay supporting the cortex in cognition [34], combined with excess engagement from the striatum (nucleus accumbens, putamen/caudate) driving the impulsive behaviors, and insufficient top-down control from the cortices, particularly prefrontal regions [35]. The prefrontal cortex plays a key role in cognitive control, modulating functions such as inhibitory control, attention, planning, risk taking, and delay discounting [36–39]. Thus, prefrontal cortex hypoactivity may result in deficits in these functions and lead to greater cognitive and motor impulsivity [5,40].

Previous studies involving healthy subjects have applied tDCS over prefrontal cortex, resulting in significant reduction of different aspects of impulsivity [see Ref. [40] for a review], such as inhibitory control [41–43], planning [44], and risk-taking [45–47]. Fecteau and colleagues investigated the effects of tDCS, in a single session, on risk-taking behavior as measured by the Balloon Analogue Risk Task (BART) [45] or the Risk Task [46]. Participants received either active or sham tDCS stimulation concurrent with task performance. Risk-taking in the BART was reduced with bilateral stimulation of dorsolateral prefrontal cortex (DLPFC), regardless of anode/cathode connection pattern (i.e. right anode/left cathode or left anode/right cathode), compared to either unilateral tDCS or sham [45]. Risk-taking in the Risk Task was reduced with right anode/left cathode over DLPFC (compared to left anode/right cathode and sham) [46]. Both Cheng and Lee [47] and Shen et al. [48] found reduced risk-taking and delay discounting, respectively, with single-session prefrontal tDCS, that was correlated with baseline impulsivity, such that the effect was larger in more impulsive individuals (in healthy samples). Finally, Ditye et al. [43], combined anodal tDCS over right frontal cortex with training on the Stop Signal Task for four consecutive days, resulting in an improvement in the ability to inhibit responses after active tDCS compared to sham.

tDCS has also been used to target impulsive behaviors within the context of specific clinical populations. A single DLPFC stimulation has been shown to reduce craving in alcohol use disorder (AUD) participants [49,50] and in chronic cannabis users [51]. Multiple tDCS sessions over DLPFC combined with an approach bias training have reduced craving in individuals with hazardous drinking and shown promising trends in improving treatment outcome [52,53]. There are encouraging findings of lower relapse incidence in AUD participants [54]. Also, there has been some success in using tDCS to reduce impulsive behaviors in ADHD patients [55,56], although success is not consistent [57].

These results suggest that tDCS may be a valuable therapeutic approach that can enhance executive function in clinical populations characterized by impulsivity. However, the long-term durability of this intervention in clinical populations is still unknown. The current study investigated the combination of tDCS with a decision-making training task over multiple sessions as a method of reducing impulsive behavior in a clinical population of Veterans. Further, we investigated the durability of the effects of combining tDCS and a task out to two months post-intervention. We hypothesized that 1) the active tDCS group would show a greater reduction in impulsive behavior on risk-taking tasks compared to the sham tDCS group, and 2) this reduction in impulsive behavior would persist to one month and two month follow-up sessions.

Material and methods

Participants

Thirty Veterans receiving outpatient services in the Minneapolis Veterans Affairs Health Care System (MVAHCS) participated. Participants were referred from clinical staff, posted flyers, and patient lists from clinics within the MVAHCS based on the participant's clinical history of impulsive behavior. Upon enrollment into the study, participants were randomized into either the active tDCS group or sham tDCS group (details below in *Intervention* section). There were 15 Veterans in the active tDCS group (mean age 60.4 ± 6.6 years, 1 woman), and 15 Veterans in the sham tDCS group (mean age 58.3 ± 7.6 years, 2 women). Participants were blinded to which study condition (active or sham) they were in, while research staff were not. Groups did not differ on age ($t(28) = 0.84$, $p > 0.05$). Consistent with the demographics of Minnesota, the sample was primarily Caucasian (20 Caucasian, 5 African-American, 5 Other/Unreported).

Participants' clinical history of impulsivity (Table 1) was gleaned from medical record review, as well as by assessment of neuropsychiatric symptoms via the MINI International Neuropsychiatric Interview (MINI 5.0) [58] given to participants at their baseline session. Additionally, all participants self-reported a history of exposure to sub-concussive or concussive events at some point in their lives, with 18 participants meeting criteria for having sustained a mild TBI (active tDCS: 10 participants, sham: 8

Table 1
Impulsivity Characteristics of the Sample.

	n	Percent of sample (N=30)
Alcohol Dependence/Abuse	26	86.7
Non-Alcohol Substance Dependence/Abuse	19	63.3
Suicidality [a]	16	53.3
Legal Problems [a]	9	30.0
Financial Problems [a]	7	23.3
Aggression	6	20.0
Interpersonal Issues [a]	4	13.3
ADHD/CD [a]	3	10.0
Impulse Control Disorder	3	10.0
Number of Impulsivity Characteristics per Participant		
1	1	3.3
2 - 3	20	66.7
4 - 6	9	30.0

[a] Suicidality: those meeting criteria for Suicidality per the MINI were all determined to be at low current suicide risk (all ≤ 2 on a scale of 1-46). Legal Problems include DWI, arrests for assault, robbery, disorderly conduct, drug possession, soliciting sex Financial Problems include impulsive spending, bankruptcy, gambling problems. Interpersonal Issues include history of multiple marriages/divorces, conflicts with commanding officers, inappropriate social interactions. ADHD/CD: Attention Deficit Hyperactivity Disorder and/or Conduct Disorder.

participants; Chi-square test showed no significant difference in number of participants who sustained an mTBI between groups: $X^2(1) = 1.01$, $p = 0.32$).

Participants provided written informed consent before enrollment in the study, and were compensated $20 per hour for participation after each session. The study protocol was reviewed and approved by the Minneapolis Veterans Affairs Medical Center Institutional Review Board and the Defense Centers of Excellence Human Research Protection Program Office.

Measures

Barratt Impulsiveness Scale (BIS-11). To evaluate self-reported impulsiveness we used the BIS-11 [59], a 30-item self-report questionnaire that contains statements describing common impulsive and non-impulsive behaviors. The BIS-11 total score indicates the level of impulsiveness, with higher scores indicating a higher level of impulsivity. The BIS-11 was administered at pre-intervention baseline, post-intervention (following the final tDCS session), and at the one month and two month follow-ups.

Balloon Analogue Risk Task (BART). The BART [60] is a behavioral measure of risk taking that correlates with real-world risk behavior e.g. Ref. [61], and trait measures of risk-taking propensity [60,62]. In the BART, participants inflate a computerized balloon by pressing the 'p' key on the keyboard to pump it up. Each balloon had its own explosion threshold, varying between 1 and 128 pumps. Participants had to decide after each pump whether to keep pumping and risk explosion of the balloon, or to stop (by pressing the 's' key). Participants received 10 points for each pump they made, but if the balloon exploded, the points earned for that trial (balloon) were lost. Therefore, with each pump, the probability of losing the points, as well as the amount of the loss, increased. Risk-taking is measured by the average number of "adjusted pumps", the number of pumps on trials where the participant decided to stop pumping before the balloon exploded. Higher scores indicate greater risk-taking propensity. There were a total of 30 trials (balloons) per session. The BART was used as the "training" task, performed at each of the ten tDCS sessions, concurrently with tDCS.

Risk Task. The Risk Task is a computerized behavioral measure of the propensity for risk-taking within a decision-making task [63]. For each trial, there were six boxes, colored red or blue, arranged horizontally at the top of the screen. The participant was told that there was a yellow token hidden under one of the boxes, and that the token was equally likely to be hidden under any of the boxes. Participants had to decide whether the token was hidden under a red box or a blue box, and indicate their choice by pressing '1' for red or '2' for blue. Participants were rewarded with points for correctly choosing the color of the box hiding the token, and penalized points for choosing incorrectly. The ratio of red and blue boxes varied from trial to trial (5:1, 4:2, or 3:3), as did the balance between the reward (or penalty) points associated with each color (90:10, 80:20, 70:30, 60:40, and 50:50, which were presented on the screen for each trial). For each trial, the ratio of red-to-blue boxes effectively determined the probability of finding that winning token and thus the level of risk of the choice. Importantly, on all trials with an unequal ratio of red and blue boxes (i.e., 5:1 or 4:2), the larger reward was always associated with the least likely outcome (i.e., the color with the fewest number of boxes; the higher risk option), creating a conflict between level of risk and balance of reward that is inherent in risk-taking situations [63]. Participants' aim was to earn as many points as possible. Risk-taking in the Risk Task was measured as the average percent of the time that participants chose the high risk option. The Risk Task was used to test generalization of effects to an untrained task.

Intervention

Transcranial Direct Current Stimulation (tDCS). tDCS was performed with the StarStim wireless neurostimulator system (Neuroelectrics, Inc., Barcelona, SP). Direct current was induced by two circular carbon rubber core electrodes in saline-soaked surface sponges (25 cm^2), placed in a neoprene headcap with marked locations based on the 10-10 EEG system. The anodal electrode was placed at location F4 (right frontal), and the cathodal electrode was placed at location F3 (left frontal). For active stimulation, participants received a constant current of 2 mA intensity for 25 min (30 s ramp up/down). tDCS started 5 min before the BART began and was delivered during the entire course of the task, which lasted ~10 min, and beyond for a total of 25 min. For sham stimulation, current was ramped down (30 s) immediately after the initial ramp up period, and then ramped up (30 s) right before the final ramp down portion of the session.

Intervention sessions took place twice per day, separated by 2 h, on five consecutive days, for a total of 10 sessions. The BART was administered at each intervention session, concurrent with tDCS, as well as at the one month and two month follow-up sessions (without tDCS). The Risk Task was administered at pre-intervention baseline, post-intervention (following the final tDCS session), and at the one month and two month follow-ups. Participants were administered a questionnaire before and after each tDCS session assessing the presence and severity of a variety of potential side effects, including headache, neck pain, scalp pain, tingling, itching, burning sensation, skin redness, sleepiness/fatigue, poor concentration, acute mood change, and nausea. Severity was rated on a scale: 0 (absent), 1 (mild), 2 (moderate), 3 (severe).

Data analysis

BIS-11 total scores, Risk Task, and BART data were analyzed with individual growth curve (IGC) models, using mixed effect models with maximum likelihood (ML) estimation. This method modeled individual change over time, determined the shape of the growth curves, explored systematic differences in change, and examined the effects of group differences (i.e. active vs. sham tDCS) in the initial status and the rate of growth. This approach, when modeling change over time, creates a two-level hierarchical model that nests time within individual [64]. IGC analyses were carried out using SPSS 19 (IBM Co., 2010).

IGC analysis for each task was carried out in three steps. First, an unconditional mean model was used. In this model, no predictor was included. It served as a baseline model to examine individual variation in the outcome variable without regard to time. This model assessed i) the mean of the outcome variable and ii) the amount of outcome variation that exists in intra- and interindividual levels. Using the parameters from this model, the intraclass correlation coefficient (ICC) was calculated. The ICC describes the amount of variance in the outcome that is attributed to differences between individuals. Second, a linear growth curve model was used that examined individual variation of the growth rates. This model examined any significant variations in individual trajectory changes over time. Third, given significant results in step 2, any effect of tDCS condition on the shape of individual growth trajectories was tested. Group (active tDCS vs. sham tDCS) was examined as a time-invariant covariate to explore any group differences in change over time (i.e., interaction with time).

Results

Missing Data. Three participants (2 active tDCS, 1 sham) were missing data for the one-month follow-up session, and four (3

active tDCS, 1 sham) were missing the two-month follow-up session due to attrition. Additionally, from the BART, one active tDCS participant was missing data for session 1 (the first tDCS session) and one sham tDCS participant was missing session 2 (the second tDCS session), both due to technical difficulties with the task.

BIS-11

First, to assess any differences between groups (active vs. sham tDCS) in baseline BIS-11 Total Score, we performed an independent samples *t*-test. Groups did not significantly differ (Mean (SD) BIS-11 Total Scores: active tDCS = 68.5 (8.6), sham tDCS = 66.9 (13.8); $t(28) = 0.38$, $p = 0.71$). Next, IGC analyses showed that, for the BIS-11, the ICC was 0.87, suggesting that about 87% of the total variation in BIS-11 Total Scores was due to interindividual differences. In the linear growth curve model examining individual variation of the growth rates over time, the Time parameter was not significant ($\beta = 0.01$, SE = 0.02, $p = 0.52$). Comparing within-individual variation in initial status between the first and second models, there was a decline in the residual variance of 7.14 (20.75–13.61), suggesting that only about 7% of the within-individual variation in BIS-11 Total Scores was associated with linear rate of change.

BART

Fig. 1 shows mean adjusted pumps in the BART for each group at each session. For the BART, the ICC was 0.71, suggesting that about 71% of the total variation in the number of adjusted pumps was due to interindividual differences. In the linear growth curve model examining individual variation of the growth rates over time (across all 10 tDCS sessions and the 1- and 2-month follow-ups) the Time parameter was not significant ($\beta = 0.02$, SE = 0.03, $p = 0.46$). Comparing within-individual variation in initial status between the first and second models, there was a decline in the residual variance of 3.5 (87.2–83.7), suggesting that only about 3.5% of the within-individual variation in number of adjusted pumps was associated with linear rate of change.

Risk task

Fig. 2 shows mean choice of the high risk option during the Risk Task for each group at each session. For the untrained Risk Task, the ICC was 0.52, suggesting that about 52% of the total variation in the choice of the high risk option was due to interindividual differences. The linear growth curve model showed significant values for both the intercept and linear slope parameters, indicating that the initial status and linear growth rate were not constant over time. There was a significant linear decrease in the choice of the high risk option in the Risk Task ($\beta = -0.14$, SE = 0.04, $p < 0.01$). The mean estimated initial status and linear growth rate for the sample were 24.6 and −0.14, respectively, suggesting that the mean high risk choice was 24.6% and decreased with time. The random error terms associated with the intercept and linear effect were significant ($p < 0.01$), suggesting that the variability in these parameters could be explained by between-individual predictors (e.g. tDCS condition). Comparing within-individual variation in initial status between the first and second models, there was a decline in the residual variance of 32.3 (104.5–72.2). This suggested that about 32% of the within-individual variation in the choice of the high risk option was associated with linear rate of change.

Finally, we included Group as a time-invariant covariate to explore any group differences in change over time in the untrained Risk Task. We performed these analyses in two ways: 1) examining overall effects by including all four time points (pre-intervention, post-intervention, 1 month follow-up, 2 month follow-up) in the growth curve model, and 2) examining, separately, short-term (pre-to post-intervention only) and long-term effects (post-intervention through both monthly follow-ups). For the overall model, there was no effect of Group on the linear change over time (Group: $\beta = -2.04$, SE = 2.63, $p = 0.45$; Group x Time interaction: $\beta = -0.04$, SE = 0.04, $p = 0.28$). Analysis of short-term effects, however, showed that the active tDCS group showed a significant decrease in the choice of the high risk option from pre-to post-intervention as compared with the sham group (a Group x Time interaction: $\beta = -1.0$, SE = 0.37, $p = 0.01$). Post-intervention through the follow-ups, there was no effect of Group on the linear change over time (Group: $\beta = -4.3$, SE = 2.8, $p = 0.14$; Group x Time interaction: $\beta = 0.002$, SE = 0.04, $p = 0.96$), i.e. both active and sham tDCS groups' degree of risk aversion remained stable. The active tDCS group's decreased choice of the high risk option stabilized and remained at that level across follow-up sessions.

Adverse effects of tDCS

Average ratings on the questionnaire were <1 for all symptoms at each timepoint, there were no significant changes from pre-to

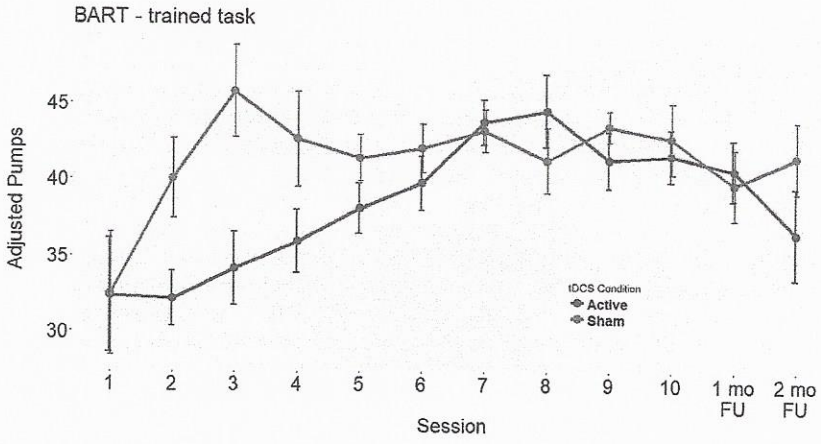

Fig. 1. Mean number of adjusted pumps (number of pumps on balloons that did not explode) in the trained Balloon Analogue Risk Task (BART) for each group at each session. Error bars indicate standard error. Active tDCS: red line, sham tDCS: blue line. Sessions 1–10 were tDCS sessions (two per day for five days) where the BART was performed concurrently with active tDCS or sham stimulation; follow-up sessions were at 1 month (1 mo FU) and 2 months (2 mo FU) post-intervention. Growth curve analysis showed no significant variations in individual trajectory changes over time. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

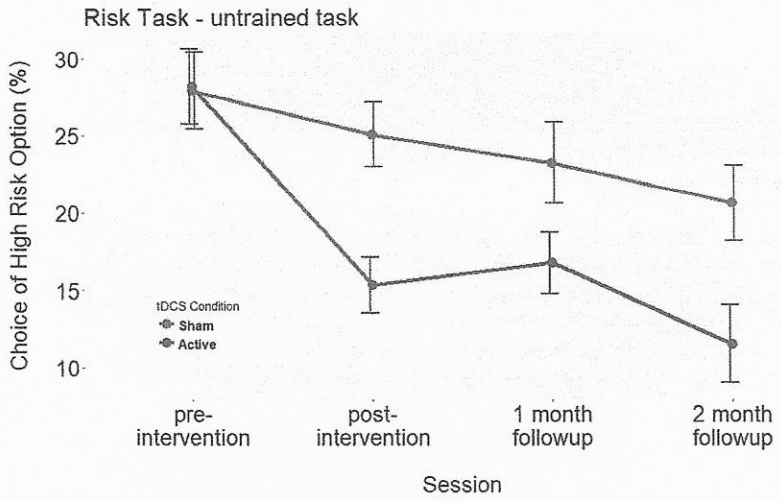

Fig. 2. Mean percentage of times the high risk option was chosen in the untrained Risk Task for each group at each session. Error bars indicate standard error. Active tDCS: red line, sham tDCS: blue line. Pre-intervention session was the baseline session (before tDCS sessions started) and post-intervention session was immediately after the final tDCS session; follow-up sessions were at 1 month and 2 months post-intervention. Growth curve analysis showed that the active tDCS group had a significant decrease in risky choice from pre-to post-intervention, which remained stable through the 1 and 2 month follow-up sessions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

post-tDCS session, and there were no differences between active tDCS and sham groups for any symptom.

Discussion

This is the first study to investigate the combination of tDCS and a cognitive task as an intervention to decrease impulsive behavior in a clinical population of Veterans. Our aim was to investigate the cumulative effects over multiple sessions of tDCS plus a training task (BART) on generalization to an untrained task (Risk Task), and the long-term persistence of these effects beyond the course of training. Results from the untrained Risk Task supported our hypotheses that active tDCS combined with a cognitive task would reduce short-term (immediately following the course of training) risk-taking behavior, and, notably, that this reduced risk-taking behavior would persist for two months post-intervention.

While effects were seen in the untrained Risk Task, we did not see any group differences in the trained BART. To our knowledge, this is the first study to use the BART as a training task simultaneous with tDCS over multiple sessions with the goal of reducing impulsive behavior in a clinical population. Previous studies using the BART have done so in single sessions. Only one prior study presented the BART concurrently with tDCS [45], finding reduced risk-taking behavior in healthy subjects. In another study using healthy subjects [65], the BART was performed while in an fMRI scanner, before and after tDCS (i.e. tDCS and BART were not performed concurrently). There was no effect of tDCS on risk taking behavior, however, tDCS-related changes in task-related brain activation and connectivity, both in the targeted DLPFC and other frontal and parietal regions, were found [65]. A study of abstinent cocaine users [66] found that tDCS reduced risky behavior on the BART.

Further, differences in participant samples and methodology potentially account for inconsistencies. First, there are limitations to being able to generalize results in healthy participants to clinical populations [67]. Methods shown to work acutely in a healthy population may not extend to clinical populations in which the problematic behavior has been present for years and the underlying neural circuitry may differ. Second, task-related differences between the BART and Risk Task may contribute to differences in results. While both are decision-making tasks involving risk, the BART involves an ambiguous decision, in that the decision whether to make another pump has an unknown probability of success; whereas, in the Risk Task probabilities are known and the lower probability outcome is worth more than the higher probability outcome [45,46]. Decision-making situations under risk and under ambiguity have also been shown to involve different, although overlapping, patterns of neural activity [68,69]. The different populations, conditions, and task properties make it difficult to directly compare results of these various studies. Future work taking a systematic approach to studying the relationship between tDCS and risk-taking would be helpful.

Anatomical and functional neural targeting

Dysfunctional thalamo-cortical-striatal neurocircuitry underlies impulsivity [33], with insufficient top-down control from prefrontal cortices playing a key role [35,70]. The DLPFC, in particular, has been shown to be integrally involved in risky decision-making [68,71], with indications of a right hemisphere preference in activation during risk processing [71]. Given that tDCS modulates brain activity in the area beneath the stimulation site and, consequently, in anatomically and functionally connected neuronal networks, the DLPFC is a convenient target for tDCS intervention to reduce impulsive behavior.

While this anatomical targeting is important for enhancing the efficacy of tDCS, anatomical specificity is limited without also considering the ongoing activity of the involved brain regions. A growing consensus suggests tDCS acts as a modulator of ongoing synaptic activity to facilitate task-relevant plasticity. This functional targeting has been illustrated in studies showing that tDCS preferentially facilitates long-term potentiation (LTP) in a neural network that is already activated (e.g. by a task or experimental stimulation), while not modulating separate neural networks that are inactive [32,72].

The current study leveraged combining anatomical and functional neural targeting by applying tDCS over DLPFC concurrently with performance of a risk-taking decision task. Importantly, effects of this approach generalized to the untrained Risk Task, and persisted for two months post-intervention. Given previous

indications of a right hemisphere preference in activation during risk processing [71], we applied excitatory anodal stimulation over right DLPFC coupled with inhibitory cathodal stimulation over the contralateral, left DLPFC. Fecteau et al. also showed that this bilateral DLPFC configuration successfully reduced risk-taking behavior in the Risk Task [46], as well as in the BART (in which effects were seen using either right anodal/left cathodal or right cathodal/left anodal bilateral stimulation) [45], whereas there were no effects using unilateral DLPFC stimulation. Taken together, these results suggest that a balance of activity across the hemispheres underlies the reduction of risk-taking behavior: relative hyperactivation of right DLPFC coupled with inhibition of cortical excitability of left DLPFC cf [46]. This interhemispheric balance during decision-making may be dysfunctional in those with clinically-relevant impulsivity, and bilateral tDCS stimulation can serve to modulate this imbalance. Further investigation is necessary, however, to determine the precise nature of this interhemispheric interaction in risk-taking, impulsive behavior.

Clinical implications

Both cognitive training and tDCS, separately, have shown promise as interventions to reduce impulsive behavior in clinical populations. For example, working memory training programs used in participants with substance use disorder (SUD) [73,74] and its common comorbidities (e.g. mood disorder [75] and anxiety [76]) have shown improvements to clinical measures of impulsivity and self-regulation post-intervention. Although results are mixed, several studies investigating cognitive training in disordered eating behavior have revealed improvements in cognitive flexibility pre-to post-intervention [77]. With regard to tDCS, there has been some success in using it to reduce impulsive behaviors in those with SUDs [49–51,54] and ADHD [55,56]. The current and previous findings suggest that a combined tDCS and cognitive training intervention may be a valuable therapeutic approach to enhance global executive function, improve functional outcomes, and alleviate symptoms in clinical populations characterized by impulsivity. Military service members and Veterans, in particular, could benefit from development of a novel, low-risk, neuroplasticity-based intervention for impulsive behavior, as impulsivity and risky behaviors 1) have been associated with combat exposure [19], aggression [24], and multiple psychiatric disorders [11,20,21,24] commonly found in these populations, and 2) impact mortality rates [78,79] and the growing public health costs for service members and Veterans.

Limitations

The following limitations should be considered when interpreting current results, and underlie the importance of the need for their future systematic replication. First, while all Veterans participating in the study were characterized by a history of impulsive behavior, the source and type of that impulsivity was heterogeneous across participants. The majority of Veterans had a history of alcohol dependence or abuse, and all but one had a history of multiple impulsive behaviors (see Table 1). Thus, it was not possible to disentangle the effects of different impulsive behaviors. While this heterogeneity, combined with a relatively small sample size, may limit interpretation with regard to effectiveness of the current approach on specific impulsive behaviors or clinical diagnoses, this heterogeneity is more representative of the population of Veterans with impulsivity issues, as a whole, increasing generalizability of results.

Second, while the approach of combining tDCS with a decision-making task reduced risk-taking behavior in the Risk Task, we cannot make a statement about the clinical significance of the results. Performance on neither the BART nor the Risk Task correlated with self-reported trait impulsivity as measured by BIS-11 total scores (all p-values > 0.22). Including more measures of state impulsivity and functional outcomes in future studies could address any clinical and real-world benefit of the current intervention.

Third, potential effects on other aspects of impulsivity need to be explored. The current study addressed the risk-taking aspect of impulsivity. However, impulsivity is theorized to encompass four neurocognitive domains: i) Choice Impulsivity, difficulty in delaying gratification, ii) Decision-Making Impulsivity, a tendency towards decision-making deficits, including increased risk-taking, iii) Motor Impulsivity, a tendency towards deficient impulse control, and iv) Reflection Impulsivity, insufficient information sampling before making a choice [70]. Both the trained (BART) and untrained (Risk Task) tasks in the current study measured the risk-taking aspect of Decision-Making Impulsivity. Also, while the BART is a cognitively complex task requiring executive functioning, it was not designed as a cognitive training task; it is neither particularly engaging nor adaptive across multiple sessions. Hofmann et al. [80] make the case that the training of general executive functions (e.g. working memory operations, behavioral inhibition, and task-switching), rather than domain-specific training, may hold promise as an intervention for persons having problems with self-regulation and cognitive control. Thus, future studies should combine tDCS with tasks i) designed for cognitive training, ii) that target the Executive Function system more generally, iii) that are engaging for the participant, and iv) that adapt to their performance, to investigate the effects of this approach across impulsivity domains.

Finally, potential non-linear effects of tDCS at the parameters used in the current study should be considered when interpreting results. For example, Batsikadze et al. [81] found that cathodal stimulation at 2 mA for 20 min induced excitatory effects, similar to those from anodal stimulation, that lasted up to 120 min post-stimulation. However, differences in samples (their young, healthy adults vs. our older, clinically impulsive sample) and other tDCS parameters (e.g. their focus on unilateral motor cortex; our bilateral DLPFC target) preclude direct inferences about non-linear effects in the current study. Thus, while much work has been done investigating the effects of the various parameters that can be manipulated in tDCS (e.g. current strength, electrode placement, stimulation time), there is much investigation to be done to gain a fuller understanding of the impact of these parameters on cognition and clinical disorders.

Conclusions

Impulsive behavior is a component of a myriad of psychiatric disorders. Currently, there are limited treatment options to target impulsivity directly. As such, impulsive behavior presents a compelling target for treatment. The present study was the first to investigate the combination of tDCS and a cognitive task as an intervention to decrease impulsive behavior in a clinical population of Veterans. This study provides evidence that tDCS targeting the DLPFC combined with a decision-making task can reduce risk-taking behavior. Notably, this reduced risky behavior endured for two months post-intervention. These results provide support for developing neuroplasticity-based interventions that combine cognitive training and tDCS to reduce impulsive behavior across multiple domains. Such approaches could improve clinical and functional outcomes and quality of life for Veterans and other patients affected by impulsivity.

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