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Understanding the Learning Benefits Associated with Transcranial Direct Current Simulation of the Right Ventrolateral Prefrontal Cortex

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Understanding the Learning Benefits Associated with Transcranial Direct Current

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Abstract

Previous work has demonstrated that anodal transcranial direct current stimulation

(tDCS) applied to the right ventrolateral prefrontal cortex (rVLPFC) is capable of

accelerating learning of a threat identification and classification task. However, questions

remain as to the cognitive mechanisms underlying this effect, and whether the observed

tDCS mediated learning is specific to threatening stimuli or, rather, a more generalizable

learning processes. The goal of the current project was to isolate specific aspects of the

threat detection task in order to exemplify previous findings. A number of pre-test

measures were included to attempt to decipher the characteristics of subjects who are

most likely to benefit from stimulation. A novel classification task was devised, during

which subjects learned to classify pictures of European streets into two categories using

two rules. Fifty-four subjects were randomly assigned to receive 30 minutes of anodal (n

= 18), cathodal (n = 18), or sham (n = 18) tDCS. A linear mixed model revealed a

significant interaction between condition and training block in performance increases

after training ($p = 0.002$). Compared to a 4.2% increase in sham subjects, anodal tDCS

increased categorization accuracy by 20.6% ($d = 1.71$) and cathodal tDCS by 14.4% ($d =$

1.16). A logistic regression was run to predict rule learning in the experimental task using

pre-test measures as predictors, with the final model predicting rule learning group by

75.9 %. Overall, these results provide further evidence for the capacity of tDCS applied

to rVLPFC to enhance learning, showing greater than quadrupling of performance in a

difficult novel classification task. These data suggest a generalized learning enhancement,

such that other learning tasks may also benefit from this tDCS protocol. Additionally, the

results point to ways in which individual characteristics might influence subsequent

tDCS-mediated learning.

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Introduction

Since the reemergence of the technique at the turn of this century (Nitsche & Paulus, 2000), transcranial direct current stimulation (tDCS) has been applied across a range of cognitive functions associated with the right prefrontal cortex, including attention (Coffman, Trumbo, & Clark, 2012; Reteig, Talsma, van Schouwenburg, & Slagter, 2017; Sikström et al., 2016), insight and creativity (Mayseless & Shamay-Tsoory, 2015; Weinberger, Green, & Chrysikou, 2017), emotionality (Herrmann, Beier, Simons, & Polak, 2016; Vergallito, Riva, Pisoni, & Romero Lauro, 2018), and learning (Choe, Coffman, Bergstedt, Ziegler, & Phillips, 2016; V. P. Clark et al., 2012; Hauser et al., 2016; McKinley et al., 2013).

tDCS is one of a number of technologies classified as a form of non-invasive brain stimulation (NIBS), methods for modulating brain function without surgery (Huang et al., 2017; Miniussi, Harris, & Ruzzoli, 2013; Rothwell, 2018). Specific NIBS techniques each offer their own advantages and disadvantages. Transcranial magnetic simulation (TMS) is able to elicit action potentials on its own, but is expensive (Miniussi et al., 2013), and while transcranial focused ultrasound is potentially able to target brain areas with millimeter precision, it currently has a limited history of experimentation with human subjects (Tyler, Lani, & Hwang, 2018). In contrast, thousands of subjects have undergone tDCS and have reported a minimal number of adverse effects (Bikson et al., 2016; Nikolin, Huggins, Martin, Alonzo, & Loo, 2018), and the technology needed to successfully implement a tDCS protocol is relatively inexpensive. Yet at the same time, the same features that make tDCS a highly versatile tool also make the results of tDCS

studies highly variable (Ammann, Lindquist, & Celnik, 2017; Chew, Ho, & Loo, 2015; Dyke, Kim, Jackson, & Jackson, 2016; Fonteneau et al., 2019; López-Alonso, Cheeran, Río-Rodríguez, & Fernández-del-Olmo, 2014; Wiethoff, Hamada, & Rothwell, 2014), as different experimental protocols interact with individual characteristics in ways that are only beginning to be understood (Fertonani & Miniussi, 2017; Guerra, López-Alonso, Cheeran, & Suppa, 2017; Guerra et al., 2017; Li, Uehara, & Hanakawa, 2015; Ziemann & Siebner, 2015). Further work is needed to clearly define the protocols and applications that maximize the potential of tDCS (Bikson et al., 2018).

The essential components of a tDCS protocol consist of a two saline-soaked sponges attached to a stimulator that is powered by a 9-volt battery. A small electrical current then flows from the stimulator to one of the sponges (referred to as the anode) from where it passes into the skin and through the skull towards the return sponge (referred to as the cathode), thereby completing a circuit. Typical intensities are between 1 and 2 mA, and these are applied for durations of 10 to 30 minutes. Behavioral effects of tDCS are thought to be the result of changes in the membrane potential of neurons, where in the motor cortex cathodal stimulation has a hyperpolarizing effect and anodal stimulation has a depolarizing effect (Liebetanz, 2002; Nitsche & Paulus, 2000; Nitsche & Paulus, 2001; Nitsche et al., 2005). At the level of individual neurons, tDCS is thought to induce changes in the electric potential of cell membranes (Bikson et al., 2004; Nitsche et al., 2003). Importantly, this effect is insufficient to elicit action potentials (Bindman, Lippold, & Redfearn, 1964; Purpura & McMurtry, 1965). Rather, tDCS enhances or inhibits ongoing neuronal activity (Radman, Ramos, Brumberg, & Bikson, 2009),

meaning that consideration of the behavior undertaken by subjects during stimulation is

vitally important (Bergmann, 2018; Bortoletto, Pellicciari, Rodella, & Miniussi, 2015).

Thus, tDCS acts a neuromodulator, and can be contrasted with TMS which can act as

both a neuromodulator and a neurostimulator, capable of eliciting action potentials

regardless of endogenous activity. Several neurotransmitters are implicated in tDCS

induced changes of synaptic function (Cirillo et al., 2017; Stagg, Antal, & Nitsche, 2018),

but increases in glutamate concentration seem to underlie much of the changes in

behavior that have been observed with tDCS (V. P. Clark, Coffman, Trumbo, &

Gasparovic, 2011; Hunter et al., 2015; Nitsche et al., 2005). This is appropriate given the

role of glutamate as the dominant excitatory neurotransmitter responsible for synaptic

changes associated with learning (Bliss & Collingridge, 1993).

Threat Detection Background

Previous work has demonstrated the capability of tDCS to improve performance and

accelerate learning (Coffman, Clark, & Parasuraman, 2014). Adapting stimuli from the

"DARWARS Ambush!" (Macmillan et al., 2005) program, computer based training

designed to prepare soldiers prior to deployment to the Middle East, it was found that

subjects receiving 2.0 mA anodal stimulation displayed an 87% percent increase in

accuracy in perceiving threats compared to subjects receiving sham (placebo) stimulation

(V. P. Clark et al., 2012). Furthermore, this benefit increased an hour afterwards, with the

stimulation group then evincing a 104% improvement in accuracy over sham. The

profound extent of these effects may be due to the utilization of functional magnetic

imaging (fMRI) prior to training, where areas of activation associated with the ability to

correctly identify a threat were isolated. Foremost among these was the right ventrolateral prefrontal cortex (rVLPFC) (F10 in 10-20 system), which was subsequently designated as the stimulation site (V. P. Clark et al., 2012). This intervention achieved an effect size of $d = 1.2$, larger than effect sizes typically observed in tDCS interventions on cognitive outcomes, (Jacobson, Koslowsky, & Lavidor, 2012) and nearly twice that found in a recent meta-analysis ($d = 0.76$) examining tDCS application during math and language learning (Simonsmeier, Grabner, Hein, Krenz, & Schneider, 2018). Importantly, two subsequent replication studies across multiple site found results of a similar magnitude following stimulation of F10 during the same target identification task (Coffman et al., 2012; Falcone, Coffman, Clark, & Parasuraman, 2012).

Follow up work has sought to clarify the mechanisms through which F10 stimulation contributes to learning in the threat detection task, an investigation with potential implications for enhancing performance across a variety of domains (V. P. Clark & Parasuraman, 2014; Coffman et al., 2014; Parasuraman & McKinley, 2014). One possibility to explain these learning effects is increased attentional ability. This is supported by fMRI and lesion work, which have found the rVLPFC to be implicated in the maintenance of attention and cognitive control (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Aron, Robbins, & Poldrack, 2014; Coull, Frackowiak, & Frith, 1998; Coull, Nobre, & Frith, 2001; Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). Additionally, these data are supported by behavioral results, where subjects receiving 2.0 mA anodal stimulation over F10 demonstrated a greater ability to maintain alertness (Coffman et al., 2012), as measured by the Attention Networks Task (Fan, McCandliss,

Sommer, Raz, & Posner, 2002). Other tDCS studies have found similar beneficial effects of F10 stimulation on the stop-signal task (Hogeveen et al., 2016; Jacobson, Javitt, & Lavidor, 2011; Stramaccia et al., 2015).

These findings point to two, potentially overlapping, possibilities for the facilitative effect of F10 stimulation on attention. Either the ability to maintain alertness allows individuals to process more information (Parasuraman & Galster, 2013), or it allows for the ability to sustain attention for longer periods. Evidence for the former being solely responsible appears mixed, as other measures on the ANT designed to assess executive control were not affected by F10 stimulation (Coffman et al., 2012). Similarly, another task that required the tracking of multiple moving objects did not find a benefit to F10 anodal stimulation (Scheldrup et al., 2014) (though see Nelson et al., 2016). As a consequence, the ability to maintain alertness appears more promising, especially when conceived of as the *vigilance decrement*, the decreased ability to notice intermittent stimuli over time (Helton & Russell, 2011). Research in this paradigm has found that the onset of the vigilance decrement can occur in as little as 20 minutes (Hitchcock et al., 2003), and that it increases when viewing targets that are more difficult to discriminate (Warm, Parasuraman, & Matthews, 2008). Mitigation of the vigilance decrement could thus be the vehicle through which improvement occurs, with consequent improvements in learning to identify new images (V. P. Clark et al., 2012; McKinley et al., 2013), or previously seen images (Coffman et al., 2012) being driven by prolonged attentional ability.

Further parsing the factors that contribute to expert performance on the threat detection task is made more difficult by the naturalistic stimuli. Subjects are presented with computer-generated street scenes, within which are hidden threats such as a small explosive device attached to the underside of a car, or the faint shadow of a gun barrel cast from the parapet of a building. In this task, the possible processes affected by F10 anodal stimulation are visual search, categorization (either implicit or explicit), and insight. Each of these often parallel domains possess their own literature, vocabulary, and method for solving research problems (Kuhn, 1970), making combining them difficult.

Visual Search

In order to improve performance in the threat detection paradigm, one must first search the scene for possibly relevant items. Visual search is thought to involve both bottom-up, implicit processes and top-down, consciously driven processes (Wolfe & Horowitz, 2017; Wolfe, Võ, Evans, & Greene, 2011). Bottom-up search is conceptualized in the visual saliency hypothesis, where the two-dimensional visual field is encoded and the likelihood of attending to any point in the visual field is determined by characteristics like color, orientation, and the location of edges (Itti & Koch, 2000). After repeated exposure to a type of scene, implicit processes learn the typical layout, serving to speed future responses (Jiang & Wagner, 2004). Top down search is driven by the cognitive relevancy hypothesis, where items are attended to in accordance with their understood meaning and importance (Torralba, Oliva, Castelhano, & Henderson, 2006).

However, the threat detection task utilizes discovery learning, where information about how to identify a threat or what constitutes a threat can only be learned via feedback (Bruner, 1961). Within this paradigm, meaning can only be ascribed gradually and, even then, likely not permanently. The initial search process thus involves the selection of candidate objects, driven both by apparent saliency and preconscious knowledge about the organization of natural scenes (Wolfe et al., 2011). Where visual search for a known object is occurring, preconscious knowledge forms an effective set size of objects with similar features to the target, upon which attention is then directed (Neider & Zelinsky, 2008). In the case of a task without predefined objects of interest, establishing a premature or inflexible effective set would serve to hinder performance, leading to the erroneous weighting of Bayesian priors for the importance of specific objects (Eckstein, Drescher, & Shimozaki, 2006).

Categorization & Insight

Once pertinent objects have been adduced, the correct associations these objects hold must be determined. In the threat detection task, this likely occurs through a gradual process of categorization punctuated by the occasional insight into category parameters. Categorization processes are frequently conceived of in the COVIS (competition between verbal and implicit systems) framework developed by Gregory Ashby. This framework is centered around a distinction between explicit (known as rule based (RB) categorization) and implicit learning (known as II categorization), both of which contribute to correct category identification (Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Ashby & Valentin, 2017; Squire, 2004). In evolutionary terms, II categorization ability is older,

requires quick and reliable feedback, and is slow to develop. RB learning is a more recent

phylogenic development, relies on the declarative memory system for rule testing, and

occurs more quickly (Ashby & Maddox, 2005; Ashby & Valentin, 2017). Neuroscience

provides compelling evidence for the dual systems account of COVIS, noting that these

systems are competitive (Poldrack & Packard, 2003; Roeder, Maddox, Todd, & Filoteo,

Vincent, 2017; Smith et al., 2015).

Interestingly, COVIS does not account for the concept of insight, defined as a solution

that occurs suddenly after a period of intractability (Ashby & Valentin, 2017; Kounios &

Beeman, 2014; Lagnado, Newell, Kahan, & Shanks, 2006). Instead, learning in COVIS is

always a gradual process mediated by stimulus/response or systematic hypothesis testing.

Part of the confidence behind results in the COVIS paradigm likely comes from the

homogeneity of tasks that are utilized, the ecological validity of which is debatable

(Lagnado et al., 2006). The likelihood of insight playing a role in success on the

DARWARs task is greater due to the association of the rVLPFC with insight and

creativity, with more insightful individuals showing greater activity in the right

hemisphere when at rest (Bowden & Jung-Beeman, 2003a; Jung-Beeman et al., 2004;

Mashal, Faust, Hendler, & Jung-Beeman, 2007; Mihov, Denzler, & Förster, 2010).

Experimental difficulty also maintains the estrangement of RB learning in the COVIS

model and insight learning, as problems can be solved by both and precise methodologies

are required to tease these strategies apart (Bowden, Jung-Beeman, Fleck, & Kounios,

2005; Kounios & Beeman, 2014). Unlike the steady progression of analytical thought, the

period before an insight solution is assumed to occur outside conscious awareness

(Kounios & Beeman, 2014). Evidence for unconscious thinking that precedes insight

comes from a study in which the presentation of subliminal, solution-related primes led

people to regard subsequently conceived solutions as more insightful (Bowden, 1997).

Pointing to a hemispheric asymmetry and a particular role for the right prefrontal cortex,

this priming effect was found to be stronger when cues were presented to the left visual

field (Beeman & Bowden, 2000).

Insight problems can be broken down further into instances that require convergent or

divergent creativity (Guilford, 1957). In divergent creativity, the solution is open ended

such that there are many possibilities, while in convergent creativity there is only one

possible solution, though that one solution is usually distally related to the immediate

problem space. There is evidence for hemispheric asymmetry in convergent and

divergent creativity, with convergent creativity tasks finding more activation in the right

hemisphere and divergent in the left (Benedek et al., 2014; Chermahini & Hommel, 2010;

Fink et al., 2009; Shah et al., 2013). This is echoed in hemispheric differences in neuronal

architecture. Imaging studies have noted that semantic activation in the right hemisphere

is larger compared to the left, while also encompassing more distally related words.

Semantic representation in the left hemisphere is smaller and centered around one

dominant interpretation (Chiarello, Burgess, Richards, & Pollock, 1990). This contrast is

also echoed in physiology as pyramidal neurons in the right hemisphere collect inputs

from a larger area and possess longer axons (Hutsler & Galuske, 2003; Tardif & Clarke,

2001).

Evidence for convergent and divergent hemispheric asymmetry has also been found in tDCS studies, with performance on the Remote Associates Task (RAT), a measure of convergent creativity, and the Alternate Uses Task (AUT), a measure of divergent creativity, evincing right and left sided activation, respectively. Cathodal stimulation of the left prefrontal cortex (PFC) has been successfully implemented to increase performance for uncommon uses in the AUT (Chrysikou et al., 2013; Ivancovsky, Kurman, Morio, & Shamay-Tsoory, 2018), while anodal stimulation of the right PFC has been found to increase performance on the RAT (Cerruti & Schlaug, 2009). Still other studies applied concurrent anodal stimulated to the right PFC and cathodal to the left PFC and saw increased performance in the AUT, finding as well that the reverse montage did not improve performance (Hertenstein et al., 2019; Mayseless & Shamay-Tsoory, 2015).

Further Complications

The previous sections of this introduction have offered different possibilities for the beneficial effect of F10 tDCS, those rooted in visual search, categorization, and insight, with all of these perhaps moderated by attention. However, the PFC is also potentially associated with performance in the threat detection task in additional aspects. Activation of the right lateral PFC is linked with the reduction of the fear response (Klumpers et al., 2010), while decreased activity is associated with worry (Rosenbaum et al., 2018), leaving open the possibility that the outsized effects seen in threat detection tasks is specific to emotionally salient stimuli. This possibility is also supported by tDCS research, with a study finding that subjects receiving anodal stimulation to F10

experienced less skin conductance following unpredictable threats in the form of sudden

noises (Herrmann et al., 2016). Elegant fMRI work by Huth and colleagues has also

demonstrated the rVLPFC to be active during semantic comprehension of narrative

stories containing violence (Huth, de Heer, Griffiths, Theunissen, & Gallant, 2016).

To add even more complexity, attention, insight, and emotion are intertwined. There is

evidence linking positive affect to insight and creative ability, both in terms of

endogenous positive affect and induced positive affect (Isen & Daubman, 1987; Kounios

& Beeman, 2014). Also, hemispheric differences in affect (Canli, Desmond, Zhao,

Glover, & Gabrieli, 1998; Gray, Braver, & Raichle, 2002) might follow differences in

divergent and creative thinking, with one study finding that preparation for the former

prompted a positive mood, while preparation of the latter brought about a negative mood

(Chermahini & Hommel, 2012). The mechanism through which positive mood impacts

insight might itself be attention, with mood having a positive impact in broadening

inward, semantic attention *and* outward, visual attention (Rowe, Hirsh, & Anderson,

2007). Indeed, insightful individuals tend to have more diffuse attention as evidenced by

an ability to recall peripherally presented items (Ansburg & Hill, 2003).

Lastly, F10 anodal stimulation might not be beneficial due to the content of the threat

detection task, but rather to the way in which the task is presented to subjects. Before

performing the task, subjects are only told that the images contain threats, but are not told

any specifics about the nature of the threats. Thus, F10 anodal stimulation might offer

specific assistance in a discovery learning paradigm (Bruner, 1961), a possibility

supported by previous categorization and fMRI research (Seger et al., 2000). With these

myriad possibilities, it is readily apparent that further research is needed to explicate the

large learning benefit bestowed by F10 anodal stimulation. The aim of the current work

was to isolate possible mechanisms through which learning enhancement in the F10

protocol occurs, specifically eliminating any semantic or overt representation of threat- or

violence-related stimuli, while maintaining other aspects of the prior task.

Methods

Subjects

Potential participants were recruited through the University of New Mexico (UNM)

research participation portal, as well as through advertisements posted in and around the

UNM campus. Subjects received either class credit or cash payment (approximately $30)

for a single experimental visit lasting approximately 2 hours. Prior to enrollment, subjects

were screened for the following inclusion criteria: right-handed, English as a first

language, age 18-55, no history of seizures, no recent treatment for mood disorders

(within 2 years), no metal implants or pacemakers, not pregnant, no dependence on

alcohol or recent illicit drug use, no recent nicotine consumption, and not taking any

pharmacological agents known to affect nervous system function. Caffeine consumption

was not an exclusion; however, subjects were excluded if they consumed an amount that

exceeded 200 mg daily. At the beginning of the experimental session, subjects were

informed of the details and goals of the study, including the use of tDCS, and consented.

All study materials and procedures were approved by Chesapeake IRB and the U.S.

Army Research Laboratory's Human Research Protection Program**.**

Experimental Task

In the experimental task, subjects learned to classify pictures of European streets into two categories. Pictures were static street segments views accessed on Google Maps Street View (http://maps.google.com). Each trial consisted of one static street view presented for 2.5 seconds. Following a baseline block of 50 trials without feedback, there were four blocks of training, each with 60 trials in which subjects received accuracy feedback following each response. This in turn was followed by the post-test, consisting of four blocks of 50 trials each, all without feedback (Figure 1). The baseline set was framed as a practice block during which subjects were instructed to become accustomed to the timing of the stimuli and to begin hypothesizing about criteria that might differentiate the categories. While signs in the respective languages of these different regions were present in some of the pictures, this was not one of the primary criteria for correct categorization. Instead, pictures could be identified through two arbitrary rules. The first rule differentiated regions based on how the picture was taken in relation to the road. In region L, pictures were taken on the left hand side of the road with traffic approaching, while in region R, pictures were taken on the right hand side of the road with traffic moving away (Rule 1). Traffic pattern was on the right across all pictures. The second rule consisted of symbols added to the pictures (i.e., hidden objects). Two side-by-side dots (umlaut) were added to the pictures for region L, and a curved line (tilde) was added to the pictures in region R (Rule 2). The umlaut and tilde both had the same height and width in pixels. Prior to beginning the study, subjects were only told that there were two regions and were not informed about any of the possible ways to differentiate the regions.

Instead, through discovery learning (Bruner, 1961), they were tasked with gaining knowledge of the pertinent criteria via feedback during the training portion. In the present study, male voices with European accents recited a range of feedback for correct or incorrect responses. In the training portion of the study, Rule 1 was present in all trials, while Rule 2 was present in half of trials. The two rules were consistent with each other throughout baseline, training, and the first two test blocks. The last 2 post-test blocks contained trials designed to test different possible combinations of learning, where each of the rules was isolated from the other. This consisted of 50 repeat images (all hidden object trials from the training portion where the hidden object had been removed) designed to isolate learning of Rule 1, and 50 novel hidden object trials designed to isolate learning of Rule 2 where the street direction previously associated with each of the hidden objects was reversed. Beside the 50 repeat pictures in test blocks 3 and 4, each picture was only used once. To ensure consistency throughout the task, the saliency of specific criteria in individual pictures was rated on a 0 to 3 scale (with 0 being not present and 3 being very salient) by two researchers. Pictures were then randomized to different blocks to ensure an even distribution of difficulty throughout the procedure. The criteria rated were: 1) visibility of written language, 2) helpfulness of visible written language for categorization, 3) saliency of road direction rule, 4) saliency of hidden object rule, 5) and apparent temperature. All pictures were standardized to be 1,670 pixels wide and between 600 and 750 pixels tall.

tDCS

TDCS was applied in a similar manner to that used in prior work (V. P. Clark et al., 2012) and subsequent replications (Coffman et al., 2012; Falcone et al., 2012). Subjects were randomized to receive anodal, cathodal, or sham stimulation over F10. The other electrode was placed on the contralateral triceps. TDCS was administered by an ActivaDoseII Iontophoresis unit. In a double-blind design, two of these units were connected to a blinding box, with one unit set to deliver an active dose of 2.0mA and the other set to deliver a sham dose of 0.1mA. Subjects were randomized to a specific switch on the blinding box, with the experimenter implementing the protocol unaware of the dosages associated with each switch. Two saline-soaked Amrex A5 (5x5 cm) sponges served as the electrodes, and these were attached to the subject's arm with adhesive Coban wrap and to the subject's head with an Amrex Velcro strap. Stimulation lasted 30 minutes and began after the baseline block. At 0 and 4 minutes after the beginning of stimulation, subjects completed a sensation questionnaire asking them to rate the degree of itching, heat, and tingling on a 0-10 Likert-type scale. Subjects were informed that sensations rated 7 or above would prompt the termination of stimulation and end the experiment. After the first five minutes of stimulation, subjects began the 1st training block, with stimulation ending in the last minute of the 3rd training block.

Profile of Mood States

To explore possible interactions between self-reported affect and performance improvements during the categorization task, subjects completed the Profile of Mood States (POMS) prior to stimulation (Grove & Prapavessis, 2016; Shacham, 1983). The POMS includes seven unique subscales, tension, anger, fatigue, depression, esteem,

vigor, and confusion. Subjects also completed the POMS at the end of the experimental

visit to asses any possible affective changes induced by tDCS application or the

experimental task.

Need for Cognition Scale

The Need for Cognition scale (Cacioppo & Petty, 1982; Cacioppo, Petty, & Chuan Feng

Kao, 1984) was completed before training in order to explore the relationship between

cognitive habits and task performance. Questions on the Need for Cognition scale are

designed to measure the degree to which someone enjoys difficult thinking.

Creativity Measures

Before the experimental task, subjects performed the Remote Associates Test (RAT), a

measure of convergent creativity (Bowden & Jung-Beeman, 2003b; Mednick, 1962), and

the creative Alternative Uses Task (AUT), a measure of divergent creativity (Guilford,

1957; Silvia et al., 2008). In the RAT the subject is presented with 3 words and are told to

produce the 4th word that connects to the 3 presented words. A subject might be presented

with the 3 words, "skate, pick, cream" where the appropriate answer would be "ice". The

test consisted of 15 of these items. For the AUT subjects were given an object,

"newspaper", and had 2 minutes to come up with as many non-normal uses as possible.

During the main experimental task, in order to try and differentiate solutions gained via

sudden insights versus solutions gained from more methodical hypothesis testing,

subjects reported on a 1-7 scale how "warm" they felt they were in regards to

understanding the task criteria in between each experimental block. This measure was

taken 6 times, after baseline, each training block, and at the conclusion of the study. As subjects had not yet received specific feedback after baseline, for the first warmth scale subjects were told to rate how confident they were that they would figure out how to correctly differentiate the pictures.

Attention Networks Task

As previous work has found improvements in the Attention Networks Task (ANT) (Fan et al., 2002) following F10 anodal stimulation (Coffman et al., 2012), the current study sought to tie baseline ANT performance with learning in the experimental task by implementing the ANT before tDCS application. The ANT consists of a combination of the flanker and cued reaction time tasks, and yields scores corresponding to 3 attention networks, alerting, orienting, and executive control. The orienting subscale is created by subtracting the average reaction time in trials where there is a spatial cue from trials in which no cue is presented. Larger numbers for the orienting subscale indicate a greater reaction time advantage when a spatial cue is included. The alerting subscale is created by subtracting reaction time on trials with a temporal cue from reaction time on trials without. The executive subscale acts as a measure of inhibitory ability and is calculated by subtracting average response time on congruent flanker trials from average response time on incongruent flanker trials.

Power Analysis

A number of previous studies have implemented F10 anodal stimulation during the DARWARS program. Collectively, these have achieved a corrected mean effect size

(Hedge's g) of 1.16; 95% CI: [0.89, 1.43] (V. P. Clark et al., 2012; Coffman et al., 2012, 2012; Falcone et al., 2012). Using G*Power, a repeated measures ANOVA with 3 groups, 7 measurement points, $f^2 = 0.58$, $\alpha = 0.05$, and power of 0.80 requires a total sample size of 9. However, one of the goals of this project is to understand individual differences that lead to disparate effects of tDCS across subjects receiving the same protocol. Compared to the effect above, individual differences prior to tDCS are more subtle, with prior research suggesting $f^2 = 0.17$ (Katz et al., 2017). Rerunning the above power analysis with this effect size calls for a total sample of 54, with 18 in each experimental arm.

Statistical Analysis

All analyses were conducted in SPSS. Differences in average sensations reported across tDCS conditions were analyzed with analysis of variance (ANOVA). To test the effectiveness of participant blinding, we examined whether individuals correctly guessed their assigned condition at the end of the experimental session using a cross-tabulation and χ^2 test. In addition, Bonferroni-corrected paired t-tests were conducted to compare scores on seven POMS subscales at the beginning and end of the experiment. One-way ANOVAs were conducted to identify any between-group differences on the POMS subscales at the conclusion of the experiment.

As the data violated the assumption of sphericity necessary for a repeated measures ANOVA, a linear mixed effects model was instead used to test differences across tDCS conditions on accuracy, reaction time, and self-reported warmth. These three separate

models were estimated using maximum likelihood. The models fixed effects of condition (anodal, cathodal, or sham tDCS) and random effects of block (baseline, 4 trainings, and combined test) within subjects. Models used an autoregressive variance-covariance structure that accounted for decreasing correlations over non-consecutive blocks in individual subjects.

In order to explicate learning of Rule 1 and 2 within the experimental task, subjects were categorized as learners of Rule 1, Rule 2, or neither based on their accuracy in test blocks 3 and 4. A subject was classified as a Rule 1 learner if there was less than a 5% chance of having achieved their level of accuracy in the repeated images by chance alone. The value associated with a 5% chance was calculated from the distribution of categorization accuracy at baseline, such that scores above 60% were regarded as above chance. Rule 2 learners were similarly classified based on their performance in hidden object stimuli in test blocks 3 and 4. Based on these criteria, 19 subjects were classified as Rule 1 learners, 14 as Rule 2 learners, and 21 subjects learned neither rule. No subjects had categorization accuracy above chance for both Rule 1 and 2.

A multinomial logistic regression was used to model the effect of performance on measures associated with rVLPFC and learning of the different rules in the experimental task. The full model contained 2 categorical variables, stimulation condition and sex, and 5 continuous variables, orienting subscale from the ANT, number of correct responses on the RAT, creativity score on the AUT, and tension and vigor subscales from the POMS. Model fit indices (AIC and BIC) were then used to reduce the full model, and nested

comparisons were conducted to test for significant differences in fit between these

models. Interaction terms were created for the continuous and categorical variables in the

reduced model, with those reaching statistical significant being included in the final

model.

Hypotheses

The present study had the following a priori hypotheses:

1) Subjects who received anodal stimulation would demonstrate greater learning of both

rule 1 and 2 compared to subjects who received cathodal and sham stimulation, while

subjects who received cathodal stimulation would demonstrate greater learning compared

to those who received sham stimulation.

2) Subjects who received anodal stimulation would demonstrate greater accuracy on

repeated trials compared to subjects who received cathodal and sham stimulation.

3) Subjects who received anodal stimulation would have faster response times over the

course of training and test blocks compared to subjects who received cathodal

stimulation.

Results

Subjects

Six subjects were replaced from the final analysis. Two of these were replaced due to

technical issues during data collection. An additional three subjects, one in each

experimental group, were replaced because of insufficient task engagement. Subjects

were regarded as having insufficient task engagement if three criteria were met:

LEARNING BENEFITS ASSOCIATED WITH tDCS OF THE rVLPFC

classification accuracy was at chance (below 60% accuracy) throughout training and test

blocks, average response time was less than one second, and the pattern of response was

indicative of disengagement. A response pattern was deemed as indicative of

disengagement if responses were unidirectional (consistent 1's or 2's) or if the pattern of

response consistently alternated across responses (1, 2, 1, 2, 1, 2…). One subject

receiving cathodal stimulation reported a metallic taste and chose to leave the study

during the first five minutes of stimulation. This left 54 subjects in the final analysis, 18

in each stimulation group. Demographic data by stimulation group is presented in Table 1

Sensation and Participant Blinding

One-way ANOVAs indicated significant differences for reported sensations between

groups. Subjects in the anodal (M = 3.07, SD = 1.87) and cathodal groups (M= 2.50, SD

= 2.22) reported greater tingling than those in the sham group (M = 0.67, SD = 0.72),

(F(2, 43) = 7.821, p = 0.001). Additionally, subjects receiving anodal stimulation (M =

2.47, SD = 1.92) reported significantly greater itching than subjects receiving sham

stimulation (M = 0.87, SD = 1.19), (F(2, 43) = 3.353, p = 0.044). Despite these

differences, a chi-square test of independence did not indicate a significant association

between assigned condition (active or sham) and condition guessed by subjects at the

conclusion of the experiment χ^2 (1) = 0.35, p = 0.554. Results from the Bonferroni

corrected paired t-tests indicated that subjects reported significantly more confusion and

fatigue, and significantly less vigor after the experiment (Table 2). An additional one-way

ANOVA was conducted to describe differences in these and each of the other POMS

subscales (depression, anger and tension) attributable to stimulation group membership, none of which approached significance (all p's > 0.05) (Table 3).

Linear Mixed Models

The average response time and accuracy of the two test blocks combined were used in the analysis. Responses occurring later than 2500 milliseconds after stimulus onset were not included in the calculation of accuracy or response time, and one-way ANOVAs confirmed that there were no significant differences between groups on number of no-response trials in any of the blocks. The mixed model examining accuracy indicated a significant fixed effect of block ($F(1, 131.525) = 63.461$, $p < 0.001$) and an interaction between block and condition, ($F(2, 131.525) = 6.766$, $p = 0.002$). Estimates of fixed effects indicated that subjects in the anodal group increased accuracy by an average of 4.65%, 95% CI [4.61%, 8.31%] percent per block, compared to 2.82%, 95% CI [1.27%, 6.92%] in the cathodal group and 1.35%, 95% CI [-1.95%, 1.66%] in the sham group. Pairwise comparisons revealed that accuracy in the anodal stimulation group was significantly better than sham ($p = 0.002$) and cathodal stimulation groups ($p = 0.04$). No other comparisons reached significance. As shown in Figure 2, from baseline to test, anodal tDCS increased the average categorization accuracy by 20.6% (SD = 16.9%), cathodal tDCS increased accuracy by 14.4% (SD = 11.9%) and sham subjects only increased accuracy by a non-significant 4.2% (SD = 12.6%). The improvement in performance equated to a within-group effect size of $d = 1.71$, 95% CI [0.95, 2.47] in the anodal group and $d = 1.16$, 95% CI [0.45, 1.86] in the cathodal group (Morris, 2008).

For the mixed effects models of reaction time, subjects receiving sham stimulation had decreasing response times over the length of the experiment, with an average decrease of 15.03 milliseconds [95% CI: -91.91, -4.99] per block. Subjects in the cathodal group had response times that increased by an average of 18.35 milliseconds [95% CI: -11.45, 48.15] per block, while subjects in the anodal group response times increased by 22.05 milliseconds [95% CI: -16.49, 68.01] per block. However, neither the fixed effects of time nor the interaction between time and condition reached significance.

The model examining self-reported warmth found significant effects of condition ($F(2, 285.041) = 3.540$ $p = 0.03$), time ($F(1, 107.732) = 9.667$ $p = 0.002$), and their interaction ($F(1, 107.750) = 8.996$ $p = <0.001$). Pairwise comparisons indicated one significant between-group difference, with anodal subjects reporting significantly greater warmth compared to sham subjects ($p = .02$).

Hypothesis 2 regarding performance on repeated trials in test blocks 3 and 4 was not supported. The mean difference between accuracy in the anodal group and sham group trended towards but did not reach significance, (M = 67.71%, SD = 20.14%) versus (M = 57.06%, SD = 11.49%), $p = 0.05$ (Figure 5). Hypothesis 3 regarding between-groups reaction times across the task was also not supported. In both of these cases, this was due to subjects gravitating either towards Rule 1 (street direction rule), Rule 2 (hidden objects rule), or not learning either (performance on both at chance).

Multinomial Logistic Regression

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For all models, Rule 1 learners were defined as the reference category and compared to no rule and Rule 2 learners. The AIC and BIC of the full model were 97.87 and 133.67, respectively. While the Chi-square for the full model was significant $\chi^2 = 55.29$, $p < 0.001$, indicating that the full model provides better model fit than the intercept alone, the AIC and BIC were in disagreement. The AIC of the intercept only model was 121.16, greater than the full model, while the intercept only BIC of 125.14 was smaller than that of the full model. The likelihood ratio tests of the full model indicated that model fit could be improved by the removal of 2 variables. These were the vigor subscale of the POMS (corresponding to a reduced model AIC and BIC of 94.41 and 126.23) and the AUT creativity score (corresponding to a reduced model AIC and BIC of 96.96 and 127.79). Subsequent models with these variables removed were compared. Both the AIC and BIC were improved by removal of the 2 variables (AIC = 92.48 and BIC = 120.33), and the degree of improvement according to the BIC was very strong according to the guidelines noted by Raferty (Raftery, 1996). However, the Chi square difference test for the reduced model did not indicate significantly better model fit $\chi^2 = 2.074$, $p = 0.354$, despite the reduced model having marginally better classification accuracy of 75.9% compared to 74.1% in the full model.

Interaction terms were then created between the three remaining continuous variables and the two categorical variables, sex and stimulation condition, with the latter dummy coded. Continuous variables were centered prior to the creation of interaction terms (Kraemer & Blasey, 2004). However, when included none of these interaction terms reached significance, and so they were subsequently removed from the model.

Stimulation group and sex by Rule group are presented in Table 3 and age by Rule group in Table 4. Means of continuous variables are presented in Table 5. Categorization accuracy for the respective rule groups across the experimental task is presented in Figure 6.

Given the variables included in the model, four criteria were found to significantly predict subjects being categorized as Rule 1 as opposed to No Rule learners. Being female increased the probability of belonging to the No Rule learner group by a factor of 10.7 (Wald statistic $= 3.95$, $p = 0.047$). In contrast, receiving anodal stimulation made it 97.9% less likely that a subject would belong to the No Rule group rather than the Rule 1 group (Wald statistic $= 6.759$, $p = 0.009$). The three continuous variables, orienting score, number of correct responses on the remote associates test, and tension sub-score, were significant predictors of belonging to the No Rule learned group as opposed to Rule 1 learners. The same three continuous variables were also significant predictors of belonging to the Rule 2 group as opposed to the Rule 1 group. Beta's and odds ratios for both comparison are presented in Table 7.

Discussion

In the current study, a novel classification task was devised in order to attempt to explicate the learning benefits previously seen following F10 anodal tDCS. When compared with sham stimulation, 2 mA of anodal tDCS over F10 with the cathode on the left arm improved categorization accuracy by a factor of 4.9 (20.6% vs. 4.2%). Similarly, 2 mA of cathodal tDCS over F10 with the anode on the left arm improved categorization accuracy 3.4 times

over sham (14.4% vs. 4.2%). Both the magnitude of performance improvement and effect sizes demonstrated here were larger than in previous studies where stimuli with threat target cues were learned and categorized. These results demonstrate that application of this tDCS protocol is not specific to learning to detect and classify threats or process violent imagery, but rather to more generalizable classification processes.

We also hypothesized the tDCS montage used in the current study may promote attention and vigilance. This hypothesis was supported by the finding that average performance in the sham group peaked during the 3rd training block and diminished for the 4th and post-test blocks afterwards, while performance continued to increase in both stimulation groups into the 4th and subsequent test blocks. This suggests that subjects receiving active stimulation were better able to maintain engagement with this task, even in its later stages. Further evidence for continued task engagement facilitated by tDCS comes from the average between-groups' response times. Subjects receiving both anodal and cathodal tDCS had consistently longer reaction times throughout the training blocks, indicating that they continued to test potential categorization criteria. This contrasts with those receiving sham stimulation, who displayed decreasing reaction times over the training blocks, coupled with chance-level categorization accuracy, suggesting disengagement with the task. Changes in POMS scores following the task also support this interpretation. Subjects across the experimental groups reported increases in fatigue and decreases in vigor following the task, but only in the sham group did performance not significantly improve from baseline to test.

The naturalistic stimuli utilized here make parsing the underlying cognitive mechanisms of tDCS difficult, as there are a number of potential intermediary processes between improved attention and improved performance. These include visual search driven by both bottom-up, implicit processes and top-down, consciously driven processes (Jiang & Wagner, 2004; Torralba et al., 2006; Wolfe & Horowitz, 2017; Wolfe et al., 2011); rule-based categorization relying on declarative memory (Ashby & Maddox, 2005; Ashby & Valentin, 2017); and insight and convergent creativity (Kounios & Beeman, 2014). Indeed, in complex stimuli it may be impossible to distinguish between rule-based categorization learning achieved via methodical hypothesis testing and sudden insights that prompt hypotheses outside the previously conceived problem space (Bowden et al., 2005; Kounios & Beeman, 2014). In the current study, enhancement of insight may also have been involved in the response to tDCS, given its association with the right hemisphere (Beeman & Bowden, 2000; Bowden & Jung-Beeman, 2003a; Jung-Beeman et al., 2004; Mashal et al., 2007; Mihov et al., 2010) and the rVLPFC stimulation used here.

Explicating the similarities between this and previous studies showing evidence of behavioral effects of F10 tDCS is crucial for defining other applications that might benefit from this protocol. Notably, both tasks capitalized on two factors previously shown to moderate the effects of tDCS: the timing of stimulation, and the individual's baseline level of expertise during stimulation. While some studies have shown subsequent benefit when applying stimulation before a task (offline stimulation) (Buchwald et al., 2019; Pirulli, Fertonani, & Miniussi, 2013), stimulation during learning

appears more appropriate as online tDCS is able to modulate task-specific networks (Au,

Karsten, Buschkuehl, & Jaeggi, 2017; Martin, Liu, Alonzo, Green, & Loo, 2014;

Sriraman, Oishi, & Madhavan, 2014; Stagg et al., 2011), such as those within the

rVLPFC responsible for executive control (Campanella et al., 2017; Cunillera, Brignani,

Cucurell, Fuentemilla, & Miniussi, 2016; Sallard, Mouthon, Pretto, & Spierer, 2018). In a

recent meta-analysis of studies exploring tDCS augmented math and language learning,

the authors found that tDCS administered during the learning phase was far more

effective than tDCS administered during the performance phase, with effect sizes of $d =$

0.712 and $d = 0.207$, respectively (Simonsmeier et al., 2018). For novel tasks, early

online stimulation also appears to be more effective, as has been demonstrated for both

anodal and cathodal stimulation. Cathodal stimulation at the beginning of an intervention

has previously been shown to improve performance in recognition memory (Zwissler et

al., 2014), visual discrimination (Peters, Thompson, Merabet, Wu, & Shams, 2013), and

planning ability (Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009). Similarly,

anodal stimulation has been shown to facilitate learning when applied at the beginning of

working memory training (Lally, Nord, Walsh, & Roiser, 2013), and in an object tracking

task (Antal et al., 2004). Importantly, timing effects have also been demonstrated in the

threat detection task, where applying anodal stimulation during the first hour of training

led to significantly better classification accuracy than anodal stimulation applied during

the second hour of training (Bullard et al., 2011). For the current study as well,

stimulation during the initial phase of learning might be critical to maximizing the

subthreshold neuromodulatory capabilities of tDCS (Radman et al., 2009).

An individual's level of expertise on or familiarity with the task performed during tDCS

has also been shown to moderate the effectiveness of tDCS, with initially lower

performers or novices often benefiting more from anodal stimulation than initially higher

performers. This contrasts with what is normally seen in cognitive interventions, where

those with greater resources tend to benefit more (Lövdén, Brehmer, Li, & Lindenberger,

2012; Verhaeghen & Marcoen, 1996). These baseline differences in tDCS have been seen

in a number of domains, including dual task performance (Scheldrup, Dwivedy, Fisher,

Holmbald, & Greenwood, 2016; Strobach et al., 2018), impulsivity (Cheng & Lee, 2016;

Shen et al., 2016), and musical ability (Sánchez-Kuhn, Pérez-Fernández, Moreno,

Sánchez-Santed, & Flores, 2018; Schaal et al., 2017). In a working memory training

intervention featuring 7 sessions of n-back coupled with anodal tDCS, Katz and

colleagues found that a 1 standard deviation increase in baseline performance reduced the

overall effect of anodal stimulation by .47 standard deviations (Katz et al., 2017).

The overall mitigation of baseline differences in the design of the current study, as well

as the threat detection task before it, could be maximizing the effect of tDCS across

subjects by utilizing a form of discovery learning (Bruner, 1961). Instead of exposing

subjects to a paradigm where there are inherent differences in baseline individual ability,

such as in a working memory task, discovery learning introduces a totally undefined

problem space. This serves to moderate any preexisting differences, as everyone's

classification accuracy at the start of stimulation is at chance. The rVLPFC stimulation

site originally identified in V.P. Clark et al. 2012 has been consistently associated in

fMRI research with the search for consistencies and irregularities and the generation of

hypotheses (Cao, Li, Li, & Li, 2016; Crescentini et al., 2011; Goel et al., 2007; Seger & Cincotta, 2006). The rVLPFC was also previously identified in fMRI work when subjects assessed the initially presented stimuli within a discovery learning visual classification task (Seger et al., 2000). Activation of the same brain area has been shown to negatively correlate with experience among online stock traders (Raggetti, Ceravolo, Fattobene, & Di Dio, 2017), and to be activated while associating possible rules with feedback cues (Dixon & Christoff, 2012). Future stimulation studies should use a similar discovery learning paradigm in order to further isolate the mechanisms behind these substantial effect sizes.

The results of this study support the hypothesis that the rVLPFC tDCS protocol is associated with increases in the ability to maintain task engagement over longer periods. Additionally, the results of the multinomial logistic regression indicate that the quality of the attention subjects had as they began the task also affected their subsequent learning. Subjects who learned Rule 2 featuring hidden objects had the largest tension sub-scores prior to stimulation at 5.14, compared to 1.16 in subjects who learned Rule 1 featuring street direction. Rule 2 learners also had a gain in reaction time after receiving a spatial cue (Orienting) in the ANT, a difference of 44 milliseconds compared to 29 milliseconds in Rule 1 learners. While these might initially seem like disparate factors, the attention differences captured by the orienting subscale might themselves be the result of differences in state anxiety.

Anxiety has often been found to be detrimental to cognitive performance, with

performance decrements increasing with greater complexity and attentional demands.

(Derakshan & Eysenck, 2009; Eysenck & Calvo, 1992; Hembree, 1988; Moran, 2016;

Orem, Petrac, & Bedwell, 2008). Attentional control theory provides an account of how

anxiety impacts attention and negatively impacts higher level cognitive processing

(Eysenck, Derakshan, Santos, & Calvo, 2007). This theory proposes that there are two

competing systems of attention; a purpose-driven, top-down system, and stimulus-driven,

bottom-up system. Anxiety serves to alter the balance of these competing systems in

favor of bottom-up processing (Derryberry & Reed, 2002; Eysenck et al., 2007).

Neuroscience research has supported this dichotomy, revealing different substrates for

these two systems (Corbetta, Patel, & Shulman, 2008; Corbetta & Shulman, 2002).

Adding more complexity to interpretation of the present results and possible interactions

with stimulation in the current study, changes in the relative activity of these attention

systems is also associated with altered functioning of the prefrontal (Bishop, 2009;

Eysenck & Derakshan, 2011) and ventrolateral prefrontal cortices (Ettinger et al., 2008;

Fales et al., 2008).

The antisaccade task has served as a behavioral analogue for measuring changes in the

balance of the two attention systems (Derakshan, Ansari, Hansard, Shoker, & Eysenck,

2008; Miyake et al., 2000). In the antisaccade task, subjects are required to inhibit a

reflexive saccade towards a sudden visual stimulus presented in the periphery and instead

generate a purposeful saccade in the opposite direction. Purposeful and automatic

saccades thus compete, with anxiety suppressing purposeful looking (Hunt, Olk, von

Mühlenen, & Kingstone, 2004; Massen, 2004). Administration of 7.5% CO_2 has been

used as a temporary way of increasing self-report anxiety and modeling generalized

anxiety disorder in healthy volunteers (Bailey, Dawson, Dourish, & Nutt, 2011; Bailey,

Kendrick, Diaper, Potokar, & Nutt, 2007). Appropriately, subjects given 7.5% CO_2 have

demonstrated a decreased ability to purposefully control eye movements in the

antisaccade task (Garner, Attwood, Baldwin, James, & Munafò, 2011). This connects

directly to the orienting network, which directs attention through space. Subjects given

7.5% CO_2 exhibit greater orienting and alerting scores on the ANT, demonstrating that

these scales provide a valid measure of attentional changes resulting from anxiety. While

both trait and state anxiety have been shown to impede cognitive performance (Eysenck

et al., 2007), state anxiety has demonstrated a more robust positive association with

orienting scores (Pacheco-Unguetti, Acosta, Callejas, & Lupiáñez, 2010).

In the current study, differences in orienting scores were likely related to state anxiety,

and these differences influenced subject learning during the experimental task. Rule 2

learners demonstrated a stronger reflexive saccade towards the positional cue in the ANT.

Subsequently, Rule 2 learners were more likely influenced by stimuli within the pictures

presented during the experimental task. Rule 2 learners started the training with a higher

level of visual entropy, meaning that their scanning of the stimuli was more random and

driven by items in the picture rather than top-down goals (Allsop & Gray, 2014; Schieber

& Gilland, 2008). Anxiety might have also disrupted working memory updating in Rule 2

learners, further hindering systematic hypothesis testing (Eysenck & Calvo, 1992;

Eysenck et al., 2007; Friedman & Miyake, 2004). In contrast, the lower relative anxiety

of Rule 1 learners allowed them to better control their attention, likely giving them an advantage in explicitly testing possible rules.

Differences in convergent creativity, as measured by the RAT, may have also played a role in rule learning, as Rule 2 learners had the largest average number of correct responses (7.6) compared to Rule 1 (7.1) and no rule (7.0) learners. While these averages were not significantly different from each other, these differences might be further evidence for the interaction between anxiety and rule learning. Previous research has shown that performing a convergent creativity task like the RAT is associated with decreases in mood (Chermahini & Hommel, 2012), and that this relationship is reciprocal (Bar, 2009), such that mood affects subsequent convergent creativity performance. Thus the same anxiety that promoted Rule 2 learning could have also facilitated performance on the RAT. This may have also interacted with stimulation, as convergent creativity is associated with the right hemisphere (Benedek et al., 2014; Cerruti & Schlaug, 2009; Shah et al., 2013).

Limitations

Several limitations within the current study should be noted. Beyond the use of new stimuli, there were three other differences between the task used in the current study and that in the original target detection task. While the original study presented stimuli for 2 seconds, due to the complex naturalistic stimuli used here, the presentation time was increased to 2.5 seconds. Also, there were half as many baseline trials presented in the current study, 50 vs. the previous 100, as no subjects were significantly above chance at

baseline when piloting the stimuli, possibly related to the arbitrary cues used here.

Finally, the visual feedback was different. In the original study, audio feedback was

played over a computer animated video showing the consequences of a subject's

classification choice, while in the current study, the visual feedback was a non-specific

"Correct" or "Incorrect". Given the significant behavioral found here, it is unlikely that

any of these differences weakened the magnitude of tDCS effects. Another possible

limitation was a lack of double-blinding between the cathodal and anodal conditions, as

research assistants were aware of the specific electrodes were placed on an individual

subject. An additional limitation was a significant difference in categorization accuracy

among Rule 2 learners on the different types of hidden trials (umlaut and tilde) on the

specific test blocks (Figure 7). As the process for randomizing stimuli according to

apparent difficulty was the same across the blocks, it is unclear how the isolation of the

hidden rule differentially affected Rule 2 learners ability to classify the respective types

of hidden objects. It is possible that there was some associative learning between Rule 1

and Rule 2, where this association was stronger for the tilde hidden object.

While the results of the multinomial logistic regression speak to the first rule subjects

gravitate towards, they do not provide an answer as to why they stop at 1 rule. Research

has conceptualized this phenomenon as *satisfaction of search*, originally defined in

radiology where the successful detection of 2nd specific target drastically decreases after

identification of the first (Tuddenham, 1962). This effect has been shown to be

exacerbated by time constraints (Fleck, Samei, & Mitroff, 2010), as were present in the

current study. Future use of this stimuli should attempt to define the parameters necessary for learning of multiple rules.

Conclusion

Prior work examining the impact of rVLPFC tDCS on learning rate during the threat categorization task, coupled with recent fMRI studies implicating the rVLPFC in processing violence-related semantic stimuli, suggested that tDCS of rVLPFC may have been effective on only threat-related content. The results of the present study do not support this hypothesis, suggesting instead that the rVLPFC or F10 tDCS protocol provides a general benefit to classification learning.

The pattern of differences over time, with participants receiving sham tDCS tending to submit to frustration sooner than those receiving either anodal or cathodal tDCS, implies that this protocol may be associated with greater perseverance, which itself has been associated with greater learning and performance (R. Clark & Saxberg, 2018). Future work should specifically test the effects of this protocol on both perseverance during tedious tasks, and on learning across additional forms of stimulus categorization, especially in discovery learning paradigms. If this protocol provides resilience to tedious and difficult tasks, regardless of the task content, it may ultimately prove beneficial for a great variety of real-world tasks.
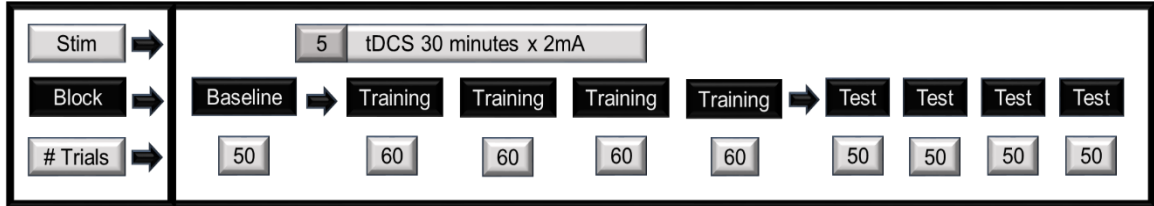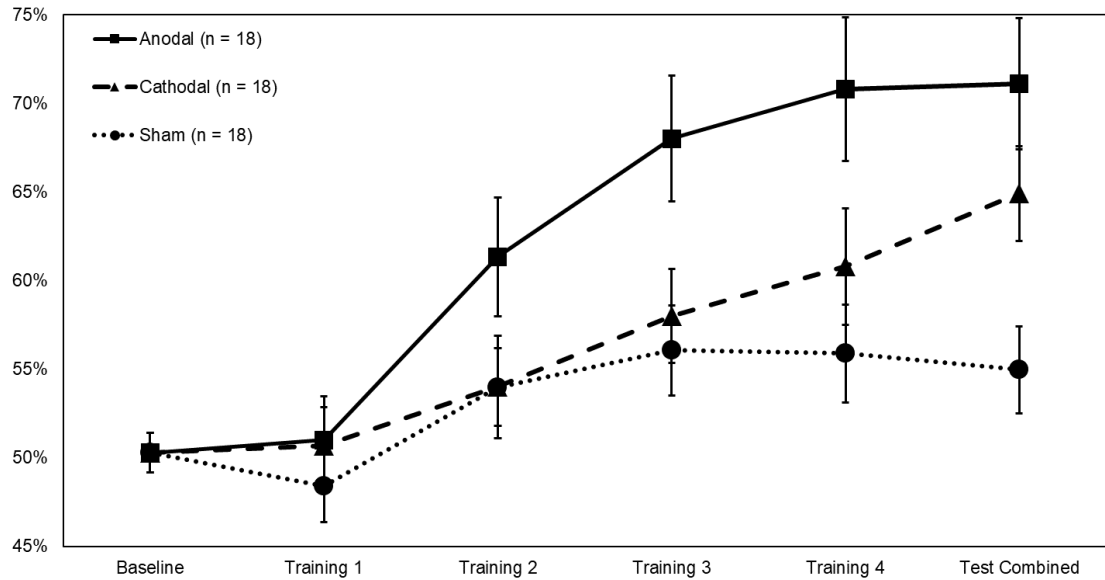
Figures

Figure 1: Timing of stimulation and design of experimental task.

Figure 2: Between-groups differences in categorization accuracy across experimental blocks. Error bars = +/- 1 SE.

Figure 3: Between-groups differences in response time (in milliseconds) across experimental blocks. Error bars = +/- 1 SE.

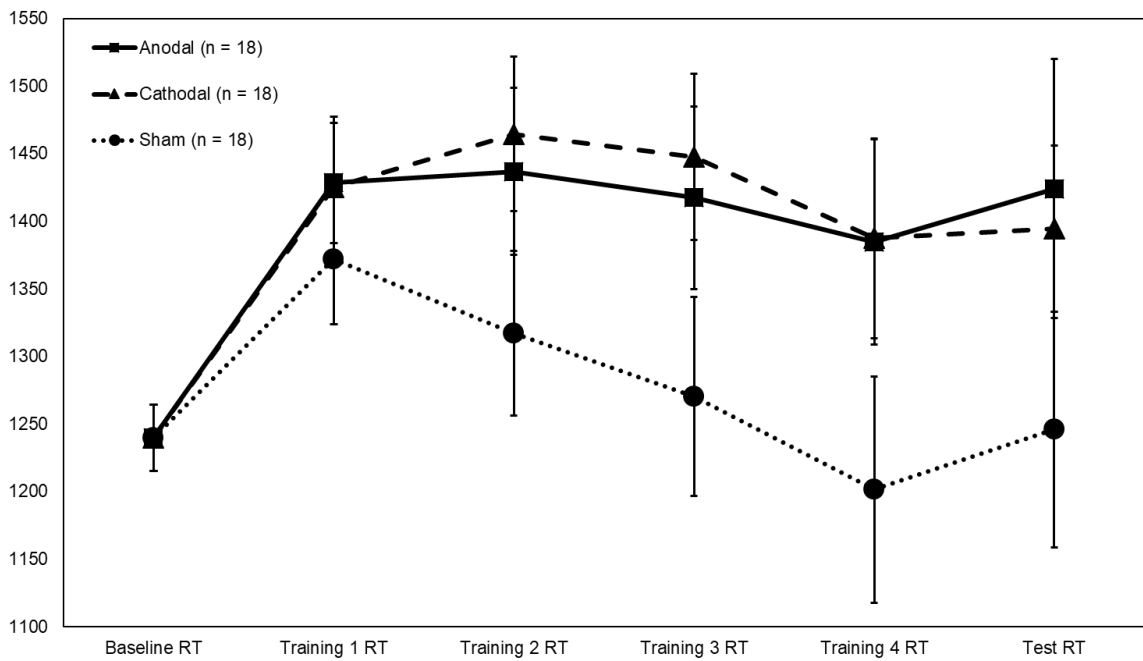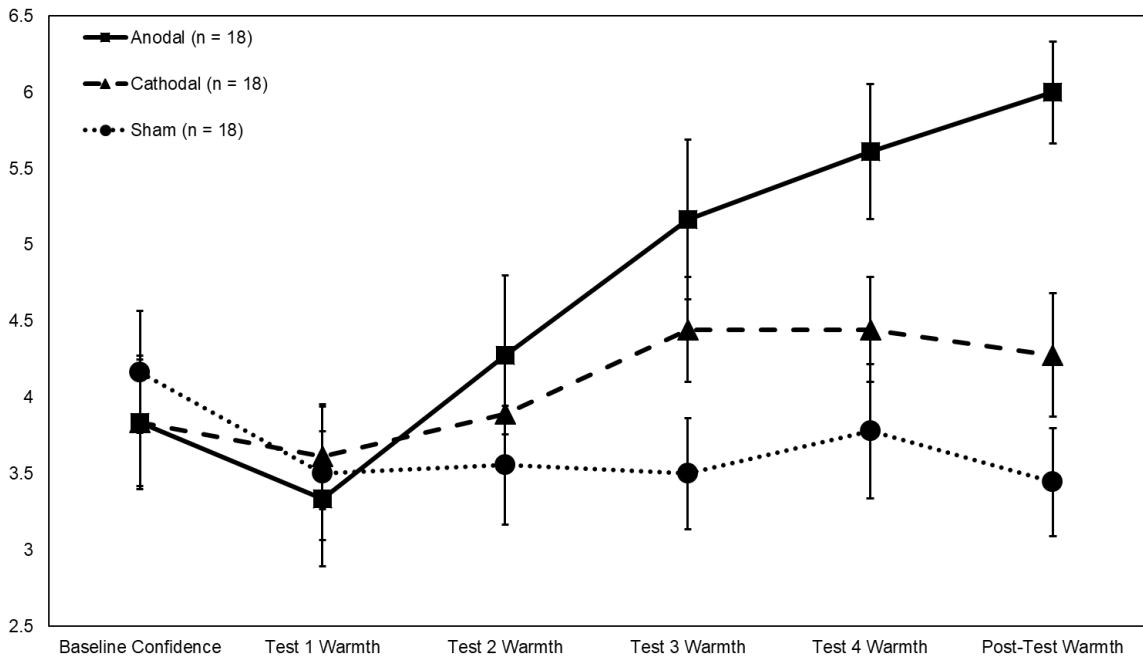Figure 4: Between-groups differences in self-reported "warmth" (1-7 scale) across experimental blocks. Error bars = +/- 1 SE.

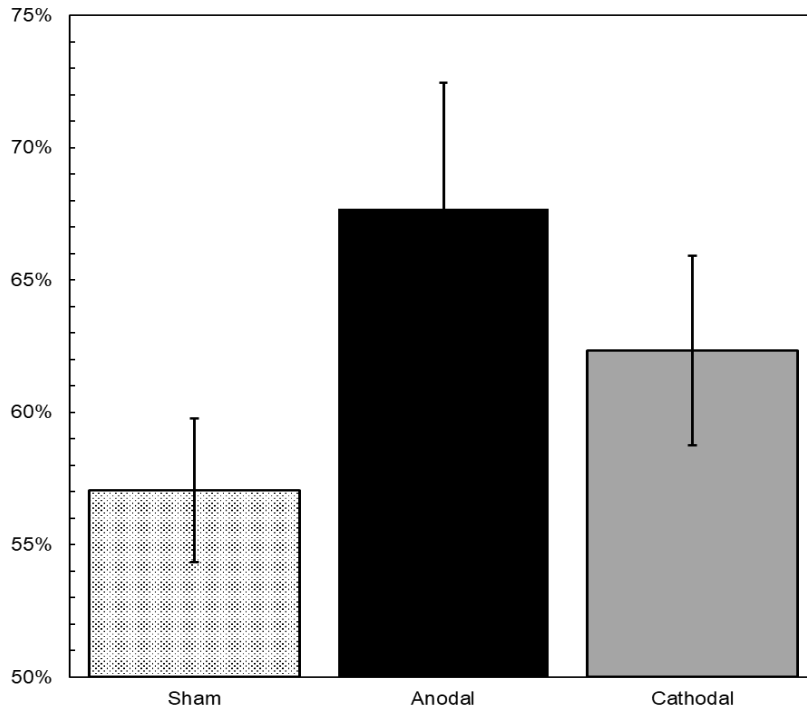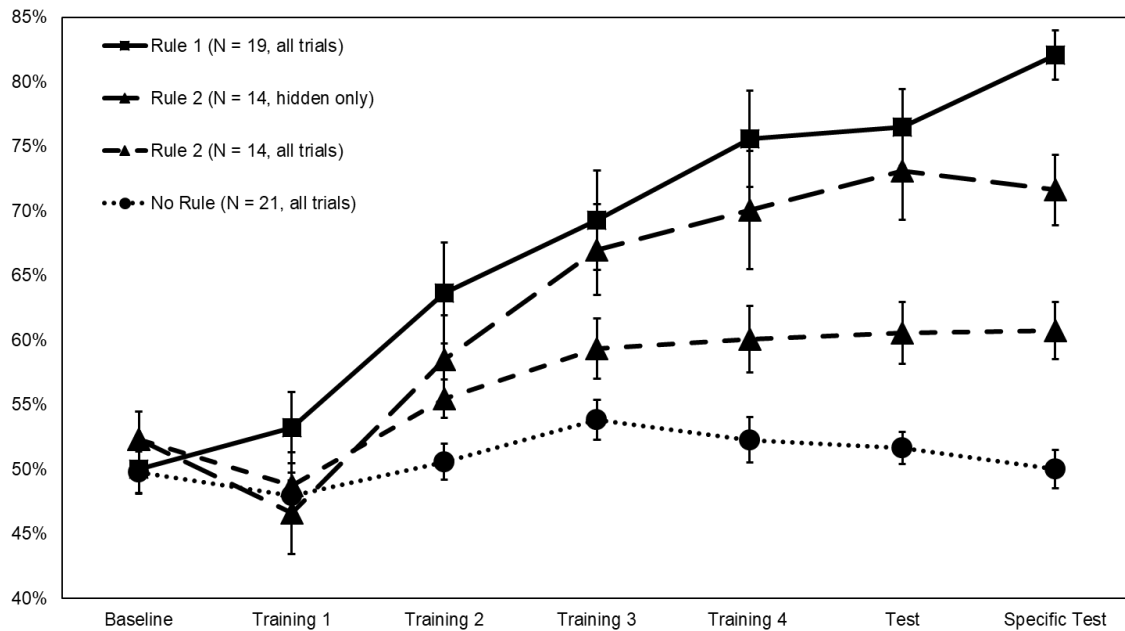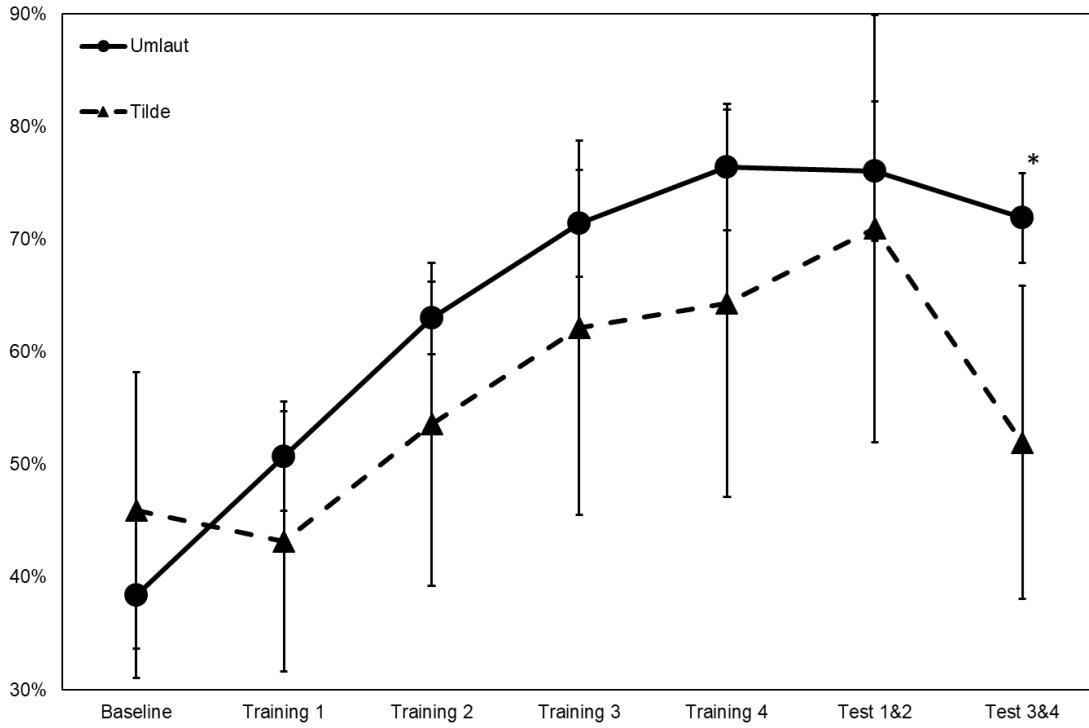Figure 5: Between-groups accuracy on repeated trials. Error bars = +/- 1 SE.

Figure 6: Categorization accuracy by rule group across training with Rule 2 learners represented both on Rule 2 accuracy only and on overall accuracy. Error bars +/- 1 SE.

Figure 7: Accuracy on each individual type of hidden object (umlaut or tilde) for Rule 2 learners only. * $p < 0.05$. Error bars +/- 1 SE.

Tables

Table 1: Subject demographics across stimulation groups.

		Age			Male		Female	
Condition	N	Mean	SD	Range	N	%	N	%
Anodal	18	22.85	7.59	30	9	50%	9	50%
Cathodal	18	24.59	11.35	38	9	50%	9	50%
Sham	18	22.16	5.19	17	5	28%	13	72%
Total	54	23.20	8.34	38	23	43%	31	57%

Table 2: POMS results across groups before and after stimulation.

	Pre	Post		
Subscale	M (SD)	M (SD)	t	p
Confusion	1.75 (2.18)	3.59 (2.91)	-4.782	< 0.001
Fatigue	2.88 (2.94)	3.80 (2.86)	-3.084	0.003
Esteem Related Affect	15.33 (3.06)	12.55 (3.87)	5.504	< 0.001
Vigor	7.25 (4.22)	4.84 (4.46)	6.087	< 0.001

Table 3: POMS results within groups. No significant between groups differences before or after stimulation.

		Confusion		Fatigue		Vigor	
		Pre	Post	Pre	Post	Pre	Post
Condition	N	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Anodal	18	1.78 (2.61)	2.78 (2.34)	2.22 (1.89)	3.56 (2.15)	6.56 (3.57)	4.56 (3.89)
Cathodal	18	1.61 (1.65)	3.94 (3.17)	3.22 (3.17)	3.94 (2.69)	8.11 (4.86)	5.83 (5.35)
Sham	18	1.89 (2.22)	3.94 (3.06)	3.28 (3.52)	4.11 (3.55)	7.44 (4.13)	4.51 (3.97)

Table 4: Rule group membership within stimulation group and sex. Chi-square test of independence for stimulation condition χ^2 (4, N = 54) = 15.49, p = 0.004; and for sex, χ^2 (2, N = 54) = 5.25, p = 0.073.

Rule	Total	Anodal	Cathodal	Sham	Male	Female
	N	N	N	N	N	N
Rule 1	19	8	8	3	12	7
	35.2%	44.4%	44.4%	16.7%	52.2%	22.6%
Rule 2	14	8	4	2	5	9
	25.9%	44.4%	22.2%	11.1%	21.7%	29.0%
No Rule	21	2	6	13	6	15
	38.9%	11.1%	33.3%	72.2%	26.1%	48.4%
Total	54	18	18	18	23	31

Table 5: Age differences by Rule group. No significant differences between groups.

	Age		
Rule	Mean	SD	Range
Rule 1	21.92	5.34	21
Rule 2	20.24	3.41	13
No Rule	26.34	11.53	38
Total	23.20	8.34	38

Table 6: Means and standard deviations for continuous variables by rule learning group.

	Orienting		RAT # Correct		Tension	
Rule	Mean	SD	Mean	SD	Mean	SD
Rule 1	29.09	22.65	7.11	3.23	1.16	1.50
Rule 2	44.19	39.19	7.64	2.95	5.14	3.92
No Rule	55.35	37.83	7.05	2.59	2.52	2.21

Table 7: Predictors of rule learning in multinomial logistic regression. $* p < 0.05$; $** p < 0.01$.

Variable	No Rule versus Rule 1 (reference)		Rule 2 versus Rule 1 (reference)	
	B (SE)	OR (95% CI)	B (SE)	OR (95% CI)
Orienting	0.065 (0.025)**	1.067 (1.016, 1.120)	0.053 (0.025)*	1.055 (1.004, 1.108)
RAT # Correct	0.483 (0.226)*	1.857 (1.095, 3.150)	0.534 (0.250)*	1.706 (1.045, 2.784)
Tension	0.890 (0.423)*	2.435 (1.062, 5.581)	1.194 (0.435)**	3.300 (1.407, 7.740)
Female	2.370 (1.192) *	10.696 (1.034, 110.691)	2.411 (1.348)	11.145 (0.794, 156.502)
Cathodal Stim	-1.458 (1.096)	0.233 (0.027, 1.995)	-0.062 (1.465)	0.940 (0.053, 16.591)
Anodal Stim	-3.875 (1.490)**	0.021 (0.001, 0.385)	-0.211 (1.598)	0.810 (0.035, 18.566)

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