Summer 7-11-2019

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

Benjamin C. Gibson
University of New Mexico

Benjamin C. Gibson, B.A.
Candidate

Psychology
Department

This thesis is approved, and is acceptable form and quality for publication:

Approved by the Thesis Committee:

Vincent P. Clark, Ph.D., Chairperson

Katie Witkiewitz Ph.D.

Eric Ruthruff, Ph.D.

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

Benjamin C. Gibson

B.A., Urban Planning, California State University Northridge, 2010

THESIS

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Science

Psychology

The University of New Mexico

Albuquerque, NM

July 2019

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

By

Benjamin C. Gibson

B.A., Urban Planning, California State University Northridge, 2010

M.S., Psychology, University of New Mexico, 2019

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.

Table of Contents

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:

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

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.

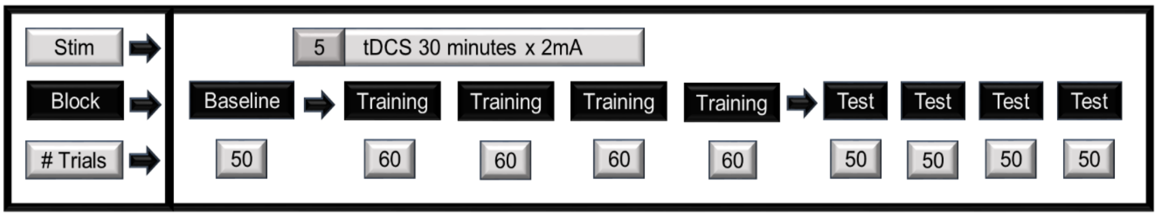


Figure 2: Between-groups differences in categorization accuracy across experimental blocks. Error bars = +/- 1 SE.

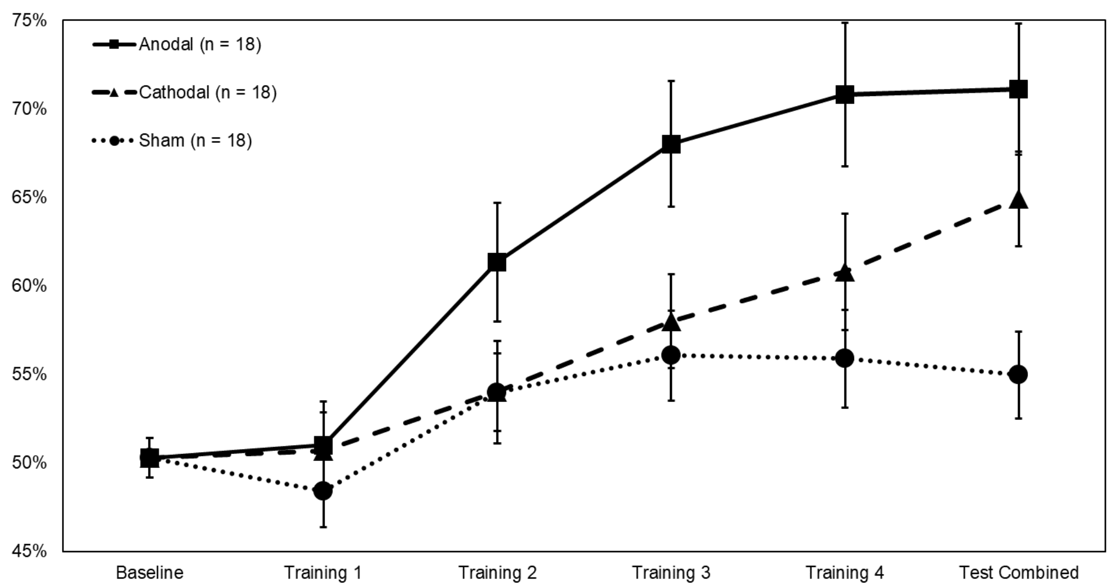


Figure 3: Between-groups differences in response time (in milliseconds) across experimental blocks. Error bars = +/- 1 SE.

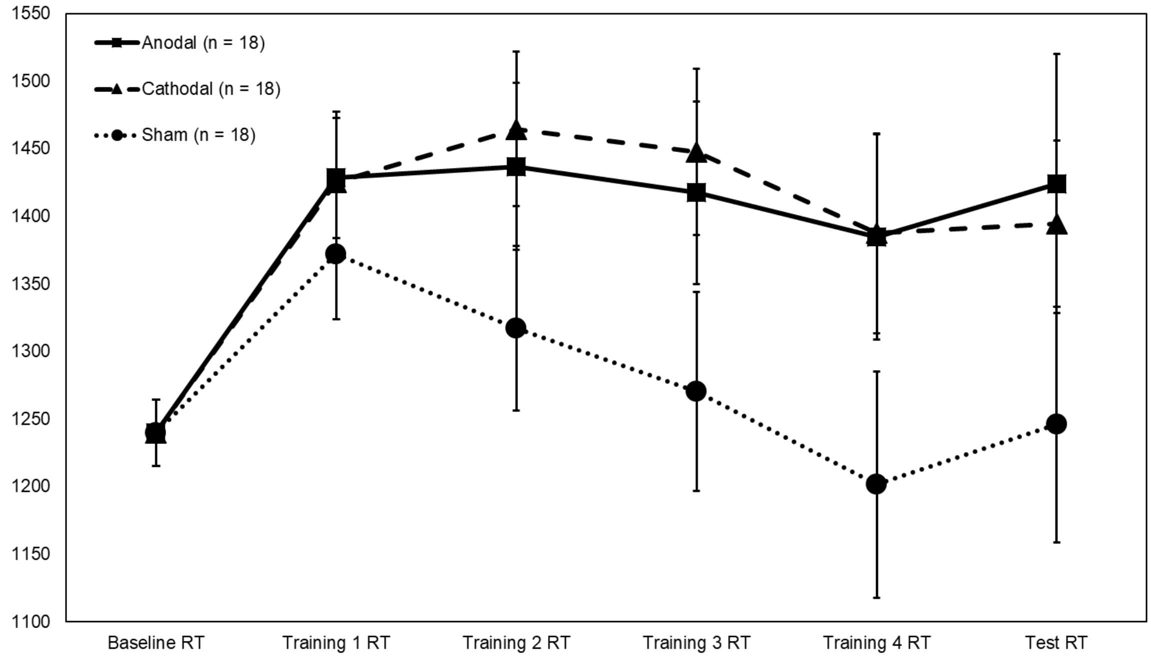


Figure 4: Between-groups differences in self-reported “warmth” (1-7 scale) across experimental blocks. Error bars = +/- 1 SE.

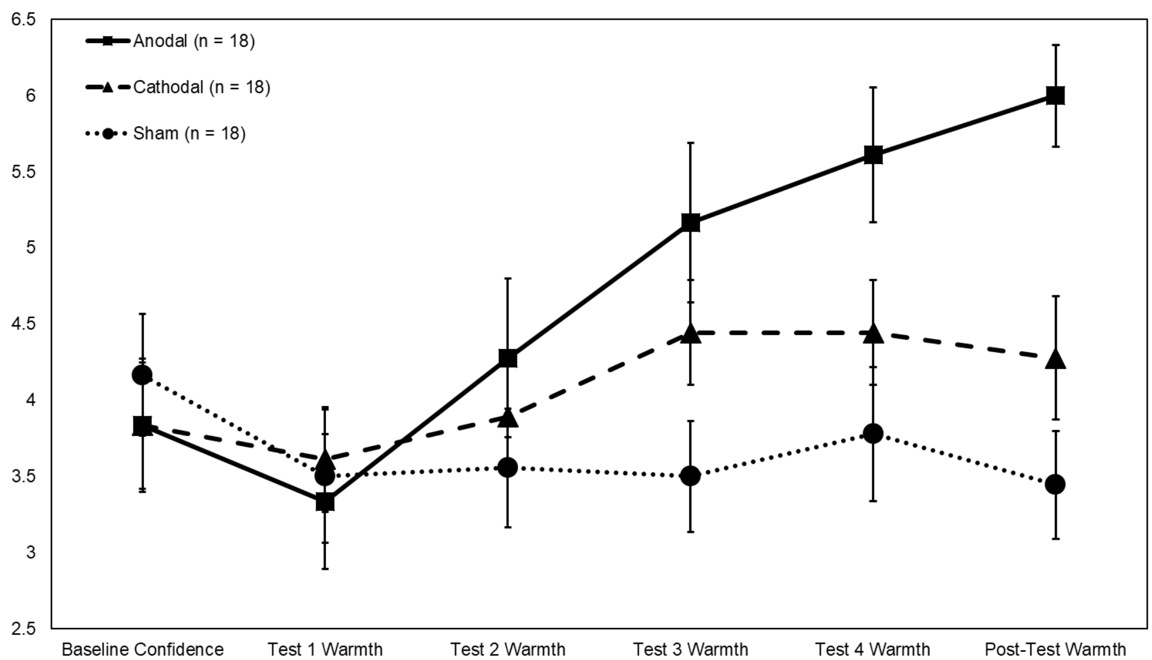


Figure 5: Between-groups accuracy on repeated trials. Error bars = +/- 1 SE.

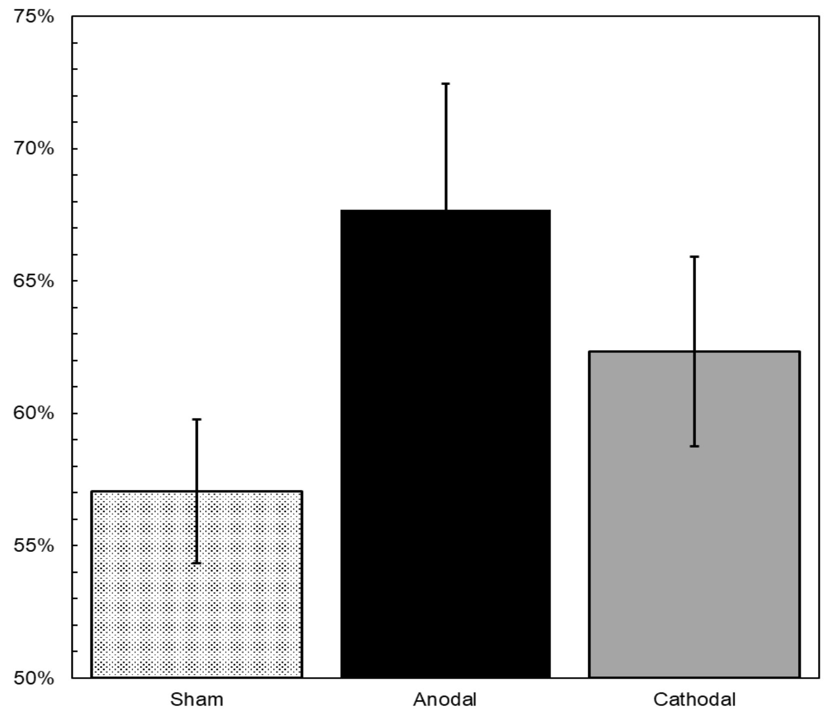


Figure 6: Categorization accuracy by rule group across training with Rule 2 learners represented both on Rule 2 accuracy only and on overall accuracy. Error bars +/- 1 SE.

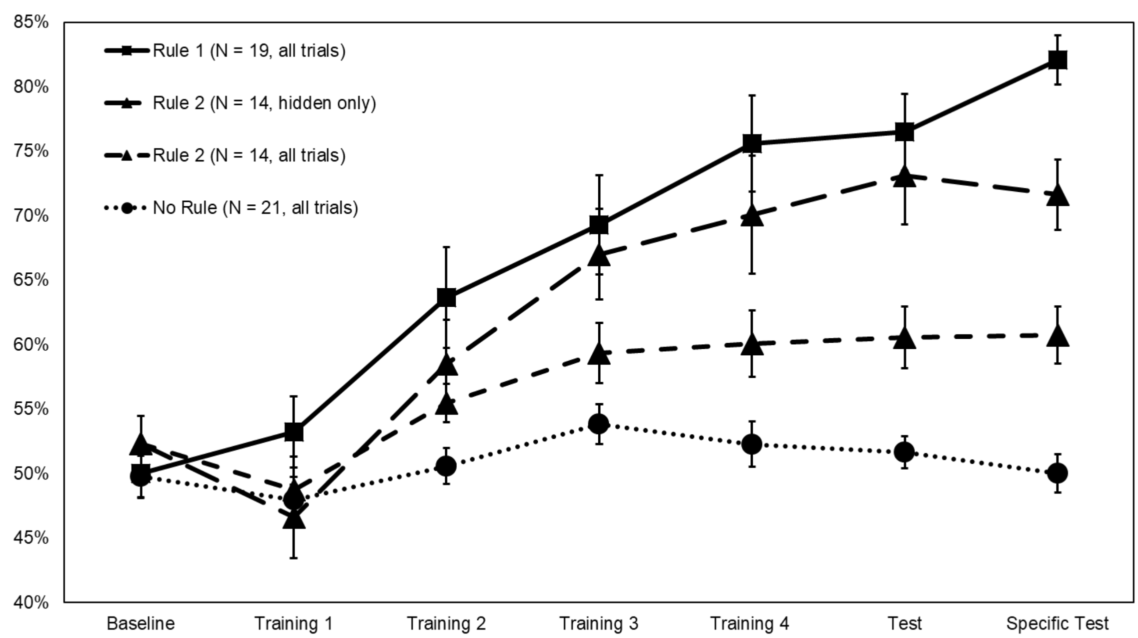
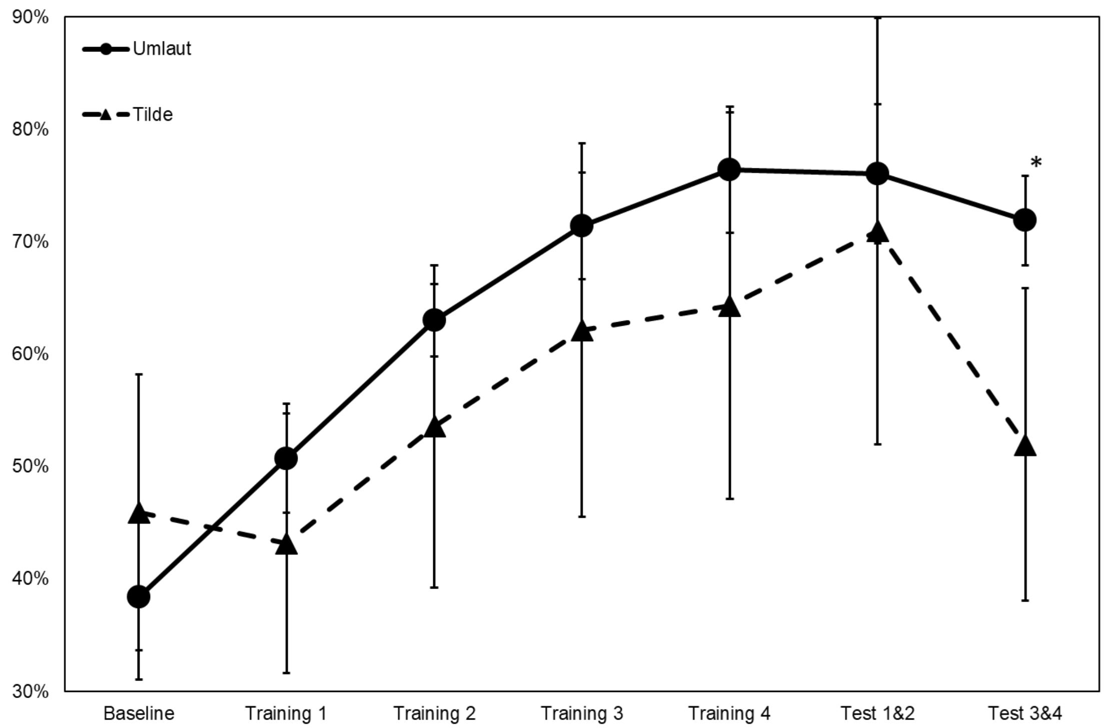


Figure 7: Accuracy on each individual type of hidden object (umlaut or tilde) for Rule 2 learners only. * $p < 0.05$. Error bars +/- 1 SE.



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. * $p < 0.05$; ** $p < 0.01$.

	No Rule versus Rule 1 (reference)		Rule 2 versus Rule 1 (reference)	
Variable	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)

References

Allsop, J., & Gray, R. (2014). Flying under pressure: Effects of anxiety on attention and gaze behavior in aviation. *Journal of Applied Research in Memory and Cognition*, *3*(2), 63–71. https://doi.org/10.1016/j.jarmac.2014.04.010

Ammann, C., Lindquist, M. A., & Celnik, P. A. (2017). Response variability of different anodal transcranial direct current stimulation intensities across multiple sessions. *Brain Stimulation*, *10*(4), 757–763. https://doi.org/10.1016/j.brs.2017.04.003

Ansburg, P. I., & Hill, K. (2003). Creative and analytic thinkers differ in their use of attentional resources. *Personality and Individual Differences*, *34*(7), 1141–1152. https://doi.org/10.1016/S0191-8869(02)00104-6

Antal, A., Nitsche, M. A., Kincses, T., Wolfgang, K., Klaus-Peter, H., & Walter, P. (2004). Facilitation of visuo-motor learning by transcranial direct current stimulation of the motor and extrastriate visual areas in humans. *European Journal of Neuroscience*, *19*(10), 2888–2892. https://doi.org/10.1111/j.1460-9568.2004.03367.x

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience*, *6*(2), 115. https://doi.org/10.1038/nn1003

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: One decade on. *Trends in Cognitive Sciences*, *18*(4), 177–185. https://doi.org/10.1016/j.tics.2013.12.003

Ashby, F. G., Alfonso-reese, L. A., Turken, U., & Waldron, E. M. (1998). A neuropsychological theory of multiple systems in category learning. *Psychological Review*, 442–481.

Ashby, F. G., & Maddox, W. T. (2005). Human Category Learning. *Annual Review of Psychology*, *56*(1), 149–178. https://doi.org/10.1146/annurev.psych.56.091103.070217

Ashby, F. G., & Valentin, V. V. (2017). Multiple Systems of Perceptual Category Learning. In *Handbook of Categorization in Cognitive Science* (pp. 157–188). https://doi.org/10.1016/B978-0-08-101107-2.00007-5

Au, J., Karsten, C., Buschkuehl, M., & Jaeggi, S. M. (2017). Optimizing Transcranial Direct Current Stimulation Protocols to Promote Long-Term Learning. *Journal of Cognitive Enhancement*, *1*(1), 65–72. https://doi.org/10.1007/s41465-017-0007-6

Bailey, J. E., Dawson, G. R., Dourish, C. T., & Nutt, D. J. (2011). Validating the inhalation of 7.5% CO_2 in healthy volunteers as a human experimental medicine:

A model of generalized anxiety disorder (GAD). *Journal of Psychopharmacology*, *25*(9), 1192–1198. https://doi.org/10.1177/0269881111408455

Bailey, J. E., Kendrick, A., Diaper, A., Potokar, J. P., & Nutt, D. J. (2007). A validation of the 7.5% CO2 model of GAD using paroxetine and lorazepam in healthy volunteers. *Journal of Psychopharmacology*, *21*(1), 42–49. https://doi.org/10.1177/0269881106063889

Bar, M. (2009). A cognitive neuroscience hypothesis of mood and depression. *Trends in Cognitive Sciences*, *13*(11), 456–463. https://doi.org/10.1016/j.tics.2009.08.009

Beeman, M. J., & Bowden, E. M. (2000). The right hemisphere maintains solution-related activation for yet-to-be-solved problems. *Memory & Cognition*, *28*(7), 1231–1241. https://doi.org/10.3758/BF03211823

Benedek, M., Jauk, E., Fink, A., Koschutnig, K., Reishofer, G., Ebner, F., & Neubauer, A. C. (2014). To create or to recall? Neural mechanisms underlying the generation of creative new ideas. *NeuroImage*, *88*, 125–133. https://doi.org/10.1016/j.neuroimage.2013.11.021

Bergmann, T. O. (2018). Brain State-Dependent Brain Stimulation. *Frontiers in Psychology*, *9*. https://doi.org/10.3389/fpsyg.2018.02108

Bikson, M., Brunoni, A. R., Charvet, L. E., Clark, V. P., Cohen, L. G., Deng, Z.-D., … Lisanby, S. H. (2018). Rigor and reproducibility in research with transcranial electrical stimulation: An NIMH-sponsored workshop. *Brain Stimulation*, *11*(3), 465–480. https://doi.org/10.1016/j.brs.2017.12.008

Bikson, M., Grossman, P., Thomas, C., Zannou, A. L., Jiang, J., Adnan, T., … Woods, A. J. (2016). Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *9*(5), 641–661. https://doi.org/10.1016/j.brs.2016.06.004

Bikson, M., Inoue, M., Akiyama, H., Deans, J. K., Fox, J. E., Miyakawa, H., & Jefferys, J. G. R. (2004). Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro. *The Journal of Physiology*, *557*(1), 175–190. https://doi.org/10.1113/jphysiol.2003.055772

Bindman, L. J., Lippold, O. C., & Redfearn, J. W. (1964). the Action of Brief Polarizing Currents on the Cerebral Cortex of the Rat. *Journal of Physiology*, *172*, 369–382. https://doi.org/10.1234/12345678

Bishop, S. J. (2009). Trait anxiety and impoverished prefrontal control of attention. *Nature Neuroscience*, *12*(1), 92–98. https://doi.org/10.1038/nn.2242

Bliss, T. V. P., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. *Nature*, *361*(6407), 31–39. https://doi.org/10.1038/361031a0

Bortoletto, M., Pellicciari, M. C., Rodella, C., & Miniussi, C. (2015). The interaction with task-induced activity is more important than polarization: A tDCS study. *Brain Stimulation*, *8*(2), 269–276. https://doi.org/10.1016/j.brs.2014.11.006

Bowden, E. M. (1997). The Effect of Reportable and Unreportable Hints on Anagram Solution and the Aha! Experience. *Consciousness and Cognition*, *6*(4), 545–573. https://doi.org/10.1006/ccog.1997.0325

Bowden, E. M., & Jung-Beeman, M. (2003a). Aha! Insight experience correlates with solution activation in the right hemisphere. *Psychonomic Bulletin & Review*, *10*(3), 730–737. https://doi.org/10.3758/BF03196539

Bowden, E. M., & Jung-Beeman, M. (2003b). Normative data for 144 compound remote associate problems. *Behavior Research Methods, Instruments, & Computers*, *35*(4), 634–639. https://doi.org/10.3758/BF03195543

Bowden, E. M., Jung-Beeman, M., Fleck, J., & Kounios, J. (2005). New approaches to demystifying insight. *Trends in Cognitive Sciences*, *9*(7), 322–328. https://doi.org/10.1016/j.tics.2005.05.012

Bruner, J. S. (1961). The act of discovery. *Harvard Educational Review*, *31*, 21–32.

Buchwald, A., Calhoun, H., Rimikis, S., Lowe, M. S., Wellner, R., & Edwards, D. J. (2019). Using tDCS to facilitate motor learning in speech production: The role of timing. *Cortex*, *111*, 274–285. https://doi.org/10.1016/j.cortex.2018.11.014

Bullard, L. M., Browning, E. S., Clark, V. P., Coffman, B. A., Garcia, C. M., Jung, R. E., … Weisend, M. P. (2011). Transcranial direct current stimulation's effect on novice versus experienced learning. *Experimental Brain Research*, *213*(1), 9–14. https://doi.org/10.1007/s00221-011-2764-2

Cacioppo, J. T., & Petty, R. E. (1982). The need for cognition. *Journal of Personality and Social Psychology*, *42*(1), 116–131. https://doi.org/10.1037/0022-3514.42.1.116

Cacioppo, J. T., Petty, R. E., & Chuan Feng Kao. (1984). The Efficient Assessment of Need for Cognition. *Journal of Personality Assessment*, *48*(3), 306.

Campanella, S., Schroder, E., Monnart, A., Vanderhasselt, M.-A., Duprat, R., Rabijns, M., … Baeken, C. (2017). Transcranial Direct Current Stimulation Over the Right Frontal Inferior Cortex Decreases Neural Activity Needed to Achieve Inhibition: A Double-Blind ERP Study in a Male Population. *Clinical EEG and Neuroscience*, *48*(3), 176–188. https://doi.org/10.1177/1550059416645977

Canli, T., Desmond, J. E., Zhao, Z., Glover, G., & Gabrieli, J. D. E. (1998). Hemispheric asymmetry for emotional stimuli detected with fMRI. *NeuroReport*, *9*(14), 3233.

Cao, B., Li, W., Li, F., & Li, H. (2016). Dissociable roles of medial and lateral PFC in rule learning. *Brain and Behavior*, *6*(11), e00551. https://doi.org/10.1002/brb3.551

Cerruti, C., & Schlaug, G. (2009). Anodal Transcranial Direct Current Stimulation of the Prefrontal Cortex Enhances Complex Verbal Associative Thought. *Journal of Cognitive Neuroscience*, *21*(10), 1980–1987.

Cheng, G. L. F., & Lee, T. M. C. (2016). Altering risky decision-making: Influence of impulsivity on the neuromodulation of prefrontal cortex. *Social Neuroscience*, *11*(4), 353–364. https://doi.org/10.1080/17470919.2015.1085895

Chermahini, S. A., & Hommel, B. (2010). The (b)link between creativity and dopamine: Spontaneous eye blink rates predict and dissociate divergent and convergent thinking. *Cognition*, *115*(3), 458–465. https://doi.org/10.1016/j.cognition.2010.03.007

Chermahini, S. A., & Hommel, B. (2012). Creative mood swings: Divergent and convergent thinking affect mood in opposite ways. *Psychological Research*, *76*(5), 634–640. https://doi.org/10.1007/s00426-011-0358-z

Chew, T., Ho, K.-A., & Loo, C. K. (2015). Inter- and Intra-individual Variability in Response to Transcranial Direct Current Stimulation (tDCS) at Varying Current Intensities. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *8*(6), 1130–1137. https://doi.org/10.1016/j.brs.2015.07.031

Chiarello, C., Burgess, C., Richards, L., & Pollock, A. (1990). Semantic and associative priming in the cerebral hemispheres: Some words do, some words don't … sometimes, some places. *Brain and Language*, *38*(1), 75–104. https://doi.org/10.1016/0093-934X(90)90103-N

Choe, J., Coffman, B. A., Bergstedt, D. T., Ziegler, M. D., & Phillips, M. E. (2016). Transcranial Direct Current Stimulation Modulates Neuronal Activity and Learning in Pilot Training. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00034

Chrysikou, E. G., Hamilton, R. H., Coslett, H. B., Datta, A., Bikson, M., & Thompson-Schill, S. L. (2013). Noninvasive transcranial direct current stimulation over the left prefrontal cortex facilitates cognitive flexibility in tool use. *Cognitive Neuroscience*, *4*(2), 81–89. https://doi.org/10.1080/17588928.2013.768221

Cirillo, G., Di Pino, G., Capone, F., Ranieri, F., Florio, L., Todisco, V., … Di Lazzaro, V. (2017). Neurobiological after-effects of non-invasive brain stimulation. *Brain Stimulation*, *10*(1), 1–18. https://doi.org/10.1016/j.brs.2016.11.009

Clark, R., & Saxberg, B. (2018). Engineering Motivation Using the Belief-Expectancy-Control Framework. *Interdisciplinary Education and Psychology*, *2*(1). https://doi.org/10.31532/InterdiscipEducPsychol.2.1.004

Clark, V. P., Coffman, B. A., Mayer, A. R., Weisend, M. P., Lane, T. D. R., Calhoun, V. D., … Wassermann, E. M. (2012). TDCS guided using fMRI significantly accelerates learning to identify concealed objects. *NeuroImage*, *59*(1), 117–128. https://doi.org/10.1016/j.neuroimage.2010.11.036

Clark, V. P., Coffman, B. A., Trumbo, M. C., & Gasparovic, C. (2011). Transcranial direct current stimulation (tDCS) produces localized and specific alterations in neurochemistry: A 1H magnetic resonance spectroscopy study. *Neuroscience Letters*, *500*(1), 67–71. https://doi.org/10.1016/j.neulet.2011.05.244

Clark, V. P., & Parasuraman, R. (2014). Neuroenhancement: Enhancing brain and mind in health and in disease. *NeuroImage*, *85*, 889–894. https://doi.org/10.1016/j.neuroimage.2013.08.071

Coffman, B. A., Clark, V. P., & Parasuraman, R. (2014). Battery powered thought: Enhancement of attention, learning, and memory in healthy adults using transcranial direct current stimulation. *NeuroImage*, *85*, 895–908. https://doi.org/10.1016/j.neuroimage.2013.07.083

Coffman, B. A., Trumbo, M. C., & Clark, V. P. (2012). Enhancement of object detection with transcranial direct current stimulation is associated with increased attention. *BMC Neuroscience*, *13*, 108. https://doi.org/10.1186/1471-2202-13-108

Coffman, B. A., Trumbo, M. C., Flores, R. A., Garcia, C. M., van der Merwe, A. J., Wassermann, E. M., … Clark, V. P. (2012). Impact of tDCS on performance and learning of target detection: Interaction with stimulus characteristics and experimental design. *Neuropsychologia*, *50*(7), 1594–1602. https://doi.org/10.1016/j.neuropsychologia.2012.03.012

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The Reorienting System of the Human Brain: From Environment to Theory of Mind. *Neuron*, *58*(3), 306–324. https://doi.org/10.1016/j.neuron.2008.04.017

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, *3*(3), 201–215. https://doi.org/10.1038/nrn755

Coull, J. T., Frackowiak, R. S. J., & Frith, C. D. (1998). Monitoring for target objects: Activation of right frontal and parietal cortices with increasing time on task. *Neuropsychologia*, *36*(12), 1325–1334. https://doi.org/10.1016/S0028-3932(98)00035-9

Coull, J. T., Nobre, A. C., & Frith, C. D. (2001). The Noradrenergic α2 Agonist Clonidine Modulates Behavioural and Neuroanatomical Correlates of Human Attentional Orienting and Alerting. *Cerebral Cortex*, *11*(1), 73–84. https://doi.org/10.1093/cercor/11.1.73

Crescentini, C., Seyed-Allaei, S., Pisapia, N. D., Jovicich, J., Amati, D., & Shallice, T. (2011). Mechanisms of Rule Acquisition and Rule Following in Inductive Reasoning. *Journal of Neuroscience*, *31*(21), 7763–7774. https://doi.org/10.1523/JNEUROSCI.4579-10.2011

Cunillera, T., Brignani, D., Cucurell, D., Fuentemilla, L., & Miniussi, C. (2016). The right inferior frontal cortex in response inhibition: A tDCS–ERP co-registration study. *NeuroImage*, *140*, 66–75. https://doi.org/10.1016/j.neuroimage.2015.11.044

Derakshan, N., Ansari, T. L., Hansard, M., Shoker, L., & Eysenck, M. W. (2008). Anxiety, Inhibition, Efficiency, and Effectiveness. *Experimental Psychology*, *56*(1), 48–55. https://doi.org/10.1027/1618-3169.56.1.48

Derakshan, N., & Eysenck, M. W. (2009). Anxiety, processing efficiency, and cognitive performance: New developments from attentional control theory. *European Psychologist*, *14*(2), 168–176. https://doi.org/10.1027/1016-9040.14.2.168

Derryberry, D., & Reed, M. A. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology*, *111*(2), 225–236. https://doi.org/10.1037/0021-843X.111.2.225

Dixon, M., & Christoff, K. (2012). The Decision to Engage Cognitive Control Is Driven by Expected Reward-Value: Neural and Behavioral Evidence. *PloS One*, *7*, e51637. https://doi.org/10.1371/journal.pone.0051637

Dockery, C. A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of Planning Ability by Transcranial Direct Current Stimulation. *Journal of Neuroscience*, *29*(22), 7271–7277. https://doi.org/10.1523/JNEUROSCI.0065-09.2009

Dyke, K., Kim, S., Jackson, G. M., & Jackson, S. R. (2016). Intra-Subject Consistency and Reliability of Response Following 2 mA Transcranial Direct Current Stimulation. *Brain Stimulation*, *9*(6), 819–825. https://doi.org/10.1016/j.brs.2016.06.052

Eckstein, M. P., Drescher, B. A., & Shimozaki, S. S. (2006). Attentional Cues in Real Scenes, Saccadic Targeting, and Bayesian Priors. *Psychological Science*, *17*(11), 973–980. https://doi.org/10.1111/j.1467-9280.2006.01815.x

Ettinger, U., Ffytche, D. H., Kumari, V., Kathmann, N., Reuter, B., Zelaya, F., & Williams, S. C. R. (2008). Decomposing the Neural Correlates of Antisaccade Eye Movements Using Event-Related fMRI. *Cerebral Cortex*, *18*(5), 1148–1159. https://doi.org/10.1093/cercor/bhm147

Eysenck, M. W., & Calvo, M. G. (1992). Anxiety and Performance: The Processing Efficiency Theory. *Cognition and Emotion*, *6*(6), 409–434. https://doi.org/10.1080/02699939208409696

Eysenck, M. W., & Derakshan, N. (2011). New perspectives in attentional control theory. *Personality and Individual Differences*, *50*(7), 955–960. https://doi.org/10.1016/j.paid.2010.08.019

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion*, *7*(2), 336–353. https://doi.org/10.1037/1528-3542.7.2.336

Falcone, B., Coffman, B. A., Clark, V. P., & Parasuraman, R. (2012). Transcranial Direct Current Stimulation Augments Perceptual Sensitivity and 24-Hour Retention in a Complex Threat Detection Task. *PLOS ONE*, *7*(4), e34993. https://doi.org/10.1371/journal.pone.0034993

Fales, C. L., Barch, D. M., Burgess, G. C., Schaefer, A., Mennin, D. S., Gray, J. R., & Braver, T. S. (2008). Anxiety and cognitive efficiency: Differential modulation of transient and sustained neural activity during a working memory task. *Cognitive, Affective, & Behavioral Neuroscience*, *8*(3), 239–253. https://doi.org/10.3758/CABN.8.3.239

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the Efficiency and Independence of Attentional Networks. *Journal of Cognitive Neuroscience*, *14*(3), 340–347. https://doi.org/10.1162/089892902317361886

Fertonani, A., & Miniussi, C. (2017). Transcranial Electrical Stimulation: What We Know and Do Not Know About Mechanisms. *The Neuroscientist*, *23*(2), 109–123. https://doi.org/10.1177/1073858416631966

Fink, A., Grabner, R. H., Benedek, M., Reishofer, G., Hauswirth, V., Fally, M., … Neubauer, A. C. (2009). The creative brain: Investigation of brain activity during creative problem solving by means of EEG and FMRI. *Human Brain Mapping*, *30*(3), 734–748. https://doi.org/10.1002/hbm.20538

Fleck, M. S., Samei, E., & Mitroff, S. R. (2010). Generalized "Satisfaction of Search": Adverse Influences on Dual-Target Search Accuracy. *Journal of Experimental Psychology. Applied*, *16*(1). https://doi.org/10.1037/a0018629

Fonteneau, C., Mondino, M., Arns, M., Baeken, C., Bikson, M., Brunoni, A. R., … Brunelin, J. (2019). Sham tDCS: A hidden source of variability? Reflections for further blinded, controlled trials. *Brain Stimulation*. https://doi.org/10.1016/j.brs.2018.12.977

Friedman, N. P., & Miyake, A. (2004). The Relations Among Inhibition and Interference Control Functions: A Latent-Variable Analysis. *Journal of Experimental Psychology: General*, *133*(1), 101–135. https://doi.org/10.1037/0096-3445.133.1.101

Garner, M., Attwood, A., Baldwin, D. S., James, A., & Munafò, M. R. (2011). Inhalation of 7.5% Carbon Dioxide Increases Threat Processing in Humans. *Neuropsychopharmacology*, *36*(8), 1557–1562. https://doi.org/10.1038/npp.2011.15

Goel, V., Tierney, M., Sheesley, L., Bartolo, A., Vartanian, O., & Grafman, J. (2007). Hemispheric Specialization in Human Prefrontal Cortex for Resolving Certain and Uncertain Inferences. *Cerebral Cortex*, *17*(10), 2245–2250. https://doi.org/10.1093/cercor/bhl132

Gray, J. R., Braver, T. S., & Raichle, M. E. (2002). Integration of emotion and cognition in the lateral prefrontal cortex. *Proceedings of the National Academy of Sciences*, *99*(6), 4115–4120. https://doi.org/10.1073/pnas.062381899

Grove, R., & Prapavessis, H. (2016). *Abbreviated POMS Questionnaire (items and scoring key)*.

Guerra, A., López-Alonso, V., Cheeran, B., & Suppa, A. (2017). Variability in non-invasive brain stimulation studies: Reasons and results. *Neuroscience Letters*. https://doi.org/10.1016/j.neulet.2017.12.058

Guilford, J. P. (1957). Creative abilities in the arts. *Psychological Review*, *64*(2), 110–118. https://doi.org/10.1037/h0048280

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: Inhibition and attentional control. *NeuroImage*, *50*(3), 1313–1319. https://doi.org/10.1016/j.neuroimage.2009.12.109

Hauser, T. U., Rütsche, B., Wurmitzer, K., Brem, S., Ruff, C. C., & Grabner, R. H. (2016). Neurocognitive Effects of Transcranial Direct Current Stimulation in

Arithmetic Learning and Performance: A Simultaneous tDCS-fMRI Study. *Brain Stimulation*, *9*(6), 850–858. https://doi.org/10.1016/j.brs.2016.07.007

Helton, W. S., & Russell, P. N. (2011). Working memory load and the vigilance decrement. *Experimental Brain Research*, *212*(3), 429–437. https://doi.org/10.1007/s00221-011-2749-1

Hembree, R. (1988). Correlates, Causes, Effects, and Treatment of Test Anxiety. *Review of Educational Research*, *58*(1), 47–77. https://doi.org/10.3102/00346543058001047

Herrmann, M. J., Beier, J. S., Simons, B., & Polak, T. (2016). Transcranial Direct Current Stimulation (tDCS) of the Right Inferior Frontal Gyrus Attenuates Skin Conductance Responses to Unpredictable Threat Conditions. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00352

Hertenstein, E., Waibel, E., Frase, L., Riemann, D., Feige, B., Nitsche, M. A., … Nissen, C. (2019). Modulation of creativity by transcranial direct current stimulation. *Brain Stimulation*. https://doi.org/10.1016/j.brs.2019.06.004

Hitchcock, E. M., Warm, J. S., Matthews, G., Dember, W. N., Shear, P. K., Tripp, L. D., … Parasuraman, R. (2003). Automation cueing modulates cerebral blood flow and vigilance in a simulated air traffic control task. *Theoretical Issues in Ergonomics Science*, *4*(1–2), 89–112. https://doi.org/10.1080/14639220210159726

Hogeveen, J., Grafman, J., Aboseria, M., David, A., Bikson, M., & Hauner, K. K. (2016). Effects of High-Definition and Conventional tDCS on Response Inhibition. *Brain Stimulation*, *9*(5), 720–729. https://doi.org/10.1016/j.brs.2016.04.015

Huang, Y. Z., Lu, M. K., Antal, A., Classen, J., Nitsche, M., Ziemann, U., … Rothwell, J. (2017). Plasticity induced by non-invasive transcranial brain stimulation: A position paper. *Clinical Neurophysiology*, *128*(11), 2318–2329. https://doi.org/10.1016/j.clinph.2017.09.007

Hunt, A. R., Olk, B., von Mühlenen, A., & Kingstone, A. (2004). Integration of competing saccade programs. *Cognitive Brain Research*, *19*(2), 206–208. https://doi.org/10.1016/j.cogbrainres.2003.12.004

Hunter, M. A., Coffman, B. A., Gasparovic, C., Calhoun, V. D., Trumbo, M. C., & Clark, V. P. (2015). Baseline effects of transcranial direct current stimulation on glutamatergic neurotransmission and large-scale network connectivity. *Brain Research*, *1594*, 92–107. https://doi.org/10.1016/j.brainres.2014.09.066

Huth, A. G., de Heer, W. A., Griffiths, T. L., Theunissen, F. E., & Gallant, J. L. (2016). Natural speech reveals the semantic maps that tile human cerebral cortex. *Nature*, *532*(7600), 453–458. https://doi.org/10.1038/nature17637

Hutsler, J., & Galuske, R. A. W. (2003). Hemispheric asymmetries in cerebral cortical networks. *Trends in Neurosciences*, *26*(8), 429–435. https://doi.org/10.1016/S0166-2236(03)00198-X

Isen, A. M., & Daubman, K. A. (1987). Positive Affect FacilitatesCreative Problem Solving. *Journal of Personality and Social Psychology*, *52*(6), 1122–1131.

Itti, L., & Koch, C. (2000). A saliency-based search mechanism for overt and covert shifts of visual attention. *Vision Research*, *40*(10), 1489–1506. https://doi.org/10.1016/S0042-6989(99)00163-7

Ivancovsky, T., Kurman, J., Morio, H., & Shamay-Tsoory, S. (2018). Transcranial direct current stimulation (tDCS) targeting the left inferior frontal gyrus: Effects on creativity across cultures. *Social Neuroscience*, *0*(0), 1–9. https://doi.org/10.1080/17470919.2018.1464505

Jacobson, L., Javitt, D. C., & Lavidor, M. (2011). Activation of Inhibition: Diminishing Impulsive Behavior by Direct Current Stimulation over the Inferior Frontal Gyrus. *Journal of Cognitive Neuroscience*, *23*(11), 3380–3387. https://doi.org/10.1162/jocn_a_00020

Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: A meta-analytical review. *Experimental Brain Research*, *216*(1), 1–10. https://doi.org/10.1007/s00221-011-2891-9

Jiang, Y., & Wagner, L. C. (2004). What is learned in spatial contextual cuing—configuration or individual locations? *Perception & Psychophysics*, *66*(3), 454–463. https://doi.org/10.3758/BF03194893

Jung-Beeman, M., Bowden, E. M., Haberman, J., Frymiare, J. L., Arambel-Liu, S., Greenblatt, R., … Kounios, J. (2004). Neural Activity When People Solve Verbal Problems with Insight. *PLOS Biology*, *2*(4), e97. https://doi.org/10.1371/journal.pbio.0020097

Katz, B., Au, J., Buschkuehl, M., Abagis, T., Zabel, C., Jaeggi, S. M., & Jonides, J. (2017). Individual Differences and Long-term Consequences of tDCS-augmented Cognitive Training. *Journal of Cognitive Neuroscience*, *29*(9), 1498–1508. https://doi.org/10.1162/jocn_a_01115

Klumpers, F., Raemaekers, M. A. H. L., Ruigrok, A. N. V., Hermans, E. J., Kenemans, J. L., & Baas, J. M. P. (2010). Prefrontal Mechanisms of Fear Reduction After

Threat Offset. *Biological Psychiatry*, *68*(11), 1031–1038. https://doi.org/10.1016/j.biopsych.2010.09.006

Kounios, J., & Beeman, M. (2014). The Cognitive Neuroscience of Insight. *Annual Review of Psychology*, *65*(1), 71–93. https://doi.org/10.1146/annurev-psych-010213-115154

Kraemer, H. C., & Blasey, C. M. (2004). Centring in regression analyses: A strategy to prevent errors in statistical inference. *International Journal of Methods in Psychiatric Research*, *13*(3), 141–151. https://doi.org/10.1002/mpr.170

Kuhn, T. S. (1970). *The structure of scientific revolutions* ([2d ed., enl). Chicago: University of Chicago Press.

Lagnado, D. A., Newell, B. R., Kahan, S., & Shanks, D. R. (2006). Insight and strategy in multiple-cue learning. *Journal of Experimental Psychology: General*, *135*(2), 162–183. https://doi.org/10.1037/0096-3445.135.2.162

Lally, N., Nord, C. L., Walsh, V., & Roiser, J. P. (2013). Does excitatory fronto-extracerebral tDCS lead to improved working memory performance? *F1000Research*, *2*. https://doi.org/10.12688/f1000research.2-219.v2

Li, L. M., Uehara, K., & Hanakawa, T. (2015). The contribution of interindividual factors to variability of response in transcranial direct current stimulation studies. *Frontiers in Cellular Neuroscience*, *9*. https://doi.org/10.3389/fncel.2015.00181

Liebetanz, D. (2002). Pharmacological approach to the mechanisms of transcranial DC-stimulation-induced after-effects of human motor cortex excitability. *Brain*, *125*(10), 2238–2247. https://doi.org/10.1093/brain/awf238

López-Alonso, V., Cheeran, B., Río-Rodríguez, D., & Fernández-del-Olmo, M. (2014). Inter-individual Variability in Response to Non-invasive Brain Stimulation Paradigms. *Brain Stimulation*, *7*(3), 372–380. https://doi.org/10.1016/j.brs.2014.02.004

Lövdén, M., Brehmer, Y., Li, S.-C., & Lindenberger, U. (2012). Training-induced compensation versus magnification of individual differences in memory performance. *Frontiers in Human Neuroscience*, *6*. https://doi.org/10.3389/fnhum.2012.00141

Martin, D. M., Liu, R., Alonzo, A., Green, M., & Loo, C. K. (2014). Use of transcranial direct current stimulation (tDCS) to enhance cognitive training: Effect of timing of stimulation. *Experimental Brain Research*, *232*(10), 3345–3351. https://doi.org/10.1007/s00221-014-4022-x

Mashal, N., Faust, M., Hendler, T., & Jung-Beeman, M. (2007). An fMRI investigation of the neural correlates underlying the processing of novel metaphoric expressions. *Brain and Language*, *100*(2), 115–126. https://doi.org/10.1016/j.bandl.2005.10.005

Massen, C. (2004). Parallel programming of exogenous and endogenous components in the antisaccade task. *The Quarterly Journal of Experimental Psychology Section A*, *57*(3), 475–498. https://doi.org/10.1080/02724980343000341

Mayseless, N., & Shamay-Tsoory, S. G. (2015). Enhancing verbal creativity: Modulating creativity by altering the balance between right and left inferior frontal gyrus with tDCS. *Neuroscience*, *291*, 167–176. https://doi.org/10.1016/j.neuroscience.2015.01.061

McKinley, R. A., McIntire, L., Bridges, N., Goodyear, C., Bangera, N. B., & Weisend, M. P. (2013). Acceleration of image analyst training with transcranial direct current stimulation. *Behavioral Neuroscience*, *127*(6), 936–946. https://doi.org/10.1037/a0034975

Mednick, S. (1962). The associative basis of the creative process. *Psychological Review*, *69*(3), 220–232. https://doi.org/10.1037/h0048850

Mihov, K. M., Denzler, M., & Förster, J. (2010). Hemispheric specialization and creative thinking: A meta-analytic review of lateralization of creativity. *Brain and Cognition*, *72*(3), 442–448. https://doi.org/10.1016/j.bandc.2009.12.007

Miniussi, C., Harris, J. A., & Ruzzoli, M. (2013). Modelling non-invasive brain stimulation in cognitive neuroscience. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1702–1712. https://doi.org/10.1016/j.neubiorev.2013.06.014

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The Unity and Diversity of Executive Functions and Their Contributions to Complex “Frontal Lobe” Tasks: A Latent Variable Analysis. *Cognitive Psychology*, *41*(1), 49–100. https://doi.org/10.1006/cogp.1999.0734

Moran, T. P. (2016). Anxiety and working memory capacity: A meta-analysis and narrative review. *Psychological Bulletin*, *142*(8), 831–864. https://doi.org/10.1037/bul0000051

Morris, S. B. (2008). Estimating Effect Sizes From Pretest-Posttest-Control Group Designs. *Organizational Research Methods*, *11*(2), 364–386. https://doi.org/10.1177/1094428106291059

Neider, M. B., & Zelinsky, G. J. (2008). Exploring set size effects in scenes: Identifying the objects of search. *Visual Cognition*, *16*(1), 1–10. https://doi.org/10.1080/13506280701381691

Nelson, J., McKinley, R. A., Phillips, C., McIntire, L., Goodyear, C., Kreiner, A., & Monforton, L. (2016). The Effects of Transcranial Direct Current Stimulation (tDCS) on Multitasking Throughput Capacity. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00589

Nikolin, S., Huggins, C., Martin, D., Alonzo, A., & Loo, C. K. (2018). Safety of repeated sessions of transcranial direct current stimulation: A systematic review. *Brain Stimulation*, *11*(2), 278–288. https://doi.org/10.1016/j.brs.2017.10.020

Nitsche, M. A., Fricke, K., Henschke, U., Schlitterlau, A., Liebetanz, D., Lang, N., … Paulus, W. (2003). Pharmacological Modulation of Cortical Excitability Shifts Induced by Transcranial Direct Current Stimulation in Humans. *The Journal of Physiology*, *553*(1), 293–301. https://doi.org/10.1113/jphysiol.2003.049916

Nitsche, Michael A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology*, *527*(Pt 3), 633–639. https://doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x

Nitsche, Michael A., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology*, *57*(10), 1899–1901. https://doi.org/10.1212/WNL.57.10.1899

Nitsche, Michael A., Seeber, A., Frommann, K., Klein, C. C., Rochford, C., Nitsche, M. S., … Tergau, F. (2005). Modulating parameters of excitability during and after transcranial direct current stimulation of the human motor cortex. *The Journal of Physiology*, *568*(Pt 1), 291–303. https://doi.org/10.1113/jphysiol.2005.092429

Orem, D. M., Petrac, D. C., & Bedwell, J. S. (2008). Chronic self-perceived stress and set-shifting performance in undergraduate students. *Stress*, *11*(1), 73–78. https://doi.org/10.1080/10253890701535103

Pacheco-Unguetti, A. P., Acosta, A., Callejas, A., & Lupiáñez, J. (2010). Attention and Anxiety: Different Attentional Functioning Under State and Trait Anxiety. *Psychological Science*, *21*(2), 298–304. https://doi.org/10.1177/0956797609359624

Parasuraman, R., & Galster, S. (2013). Sensing, assessing, and augmenting threat detection: Behavioral, neuroimaging, and brain stimulation evidence for the critical role of attention. *Frontiers in Human Neuroscience*, *7*. https://doi.org/10.3389/fnhum.2013.00273

Parasuraman, R., & McKinley, R. A. (2014). Using Noninvasive Brain Stimulation to Accelerate Learning and Enhance Human Performance. *Human Factors*, *56*(5), 816–824. https://doi.org/10.1177/0018720814538815

Peters, M. A. K., Thompson, B., Merabet, L. B., Wu, A. D., & Shams, L. (2013). Anodal tDCS to V1 blocks visual perceptual learning consolidation. *Neuropsychologia*, *51*(7), 1234–1239. https://doi.org/10.1016/j.neuropsychologia.2013.03.013

Pirulli, C., Fertonani, A., & Miniussi, C. (2013). The Role of Timing in the Induction of Neuromodulation in Perceptual Learning by Transcranial Electric Stimulation. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *6*(4), 683–689. https://doi.org/10.1016/j.brs.2012.12.005

Poldrack, R. A., & Packard, M. G. (2003). Competition among multiple memory systems: Converging evidence from animal and human brain studies. *Neuropsychologia*, *41*(3), 245–251. https://doi.org/10.1016/S0028-3932(02)00157-4

Purpura, D. P., & McMurtry, J. G. (1965). Intracellular Activities and Evoked Potential Changes During of motor cortex. *Neurophysiol*, *28*(1), 166–185. https://doi.org/10.1152/jn.1965.28.1.166

Radman, T., Ramos, R. L., Brumberg, J. C., & Bikson, M. (2009). Role of cortical cell type and morphology in subthreshold and suprathreshold uniform electric field stimulation in vitro. *Brain Stimulation*, *2*(4), 215-228.e3. https://doi.org/10.1016/j.brs.2009.03.007

Raftery, A. E. (1996). Approximate Bayes factors and accounting for model uncertainty in generalised linear models. *Biometrika*, *83*(2), 251–266. https://doi.org/10.1093/biomet/83.2.251

Raggetti, G., Ceravolo, M., Fattobene, L., & Di Dio, C. (2017). Neural Correlates of Direct Access Trading in a Real Stock Market: An fMRI Investigation. *Frontiers in Neuroscience*, *11:536*. https://doi.org/10.3389/fnins.2017.00536

Reteig, L. C., Talsma, L. J., van Schouwenburg, M. R., & Slagter, H. A. (2017). Transcranial Electrical Stimulation as a Tool to Enhance Attention. *Journal of Cognitive Enhancement*, *1*(1), 10–25. https://doi.org/10.1007/s41465-017-0010-y

Roeder, J. L., Maddox, Todd, & Filoteo, Vincent. (2017). The Neuropsychology of Perceptual Category Learning. In *Handbook of Categorization in Cognitive Science*. Retrieved from https://labs.la.utexas.edu/maddox/files/2015/10/Roeder_Maddox_FiloteoChapter12_19.pdf

Rosenbaum, D., Thomas, M., Hilsendegen, P., Metzger, F. G., Haeussinger, F. B., Nuerk, H.-C., … Ehlis, A.-C. (2018). Stress-related dysfunction of the right inferior frontal cortex in high ruminators: An fNIRS study. *NeuroImage: Clinical*, *18*, 510–517. https://doi.org/10.1016/j.nicl.2018.02.022

Rothwell, J. (2018). Transcranial brain stimulation: Past and future. *Brain and Neuroscience Advances*, 4.

Rowe, G., Hirsh, J. B., & Anderson, A. K. (2007). Positive affect increases the breadth of attentional selection. *Proceedings of the National Academy of Sciences*, *104*(1), 383–388. https://doi.org/10.1073/pnas.0605198104

Sallard, E., Mouthon, M., Pretto, M. D., & Spierer, L. (2018). Modulation of inhibitory control by prefrontal anodal tDCS: A crossover double-blind sham-controlled fMRI study. *PLOS ONE*, *13*(3), e0194936. https://doi.org/10.1371/journal.pone.0194936

Sánchez-Kuhn, A., Pérez-Fernández, C., Moreno, M., Sánchez-Santed, F., & Flores, P. (2018). Differential effects of transcranial direct current stimulation (tDCS) depending on previous musical training. *Frontiers in Psychology*, *9*. https://doi.org/10.3389/fpsyg.2018.01465

Schaal, N. K., Kretschmer, M., Keitel, A., Krause, V., Pfeifer, J., & Pollok, B. (2017). The Significance of the Right Dorsolateral Prefrontal Cortex for Pitch Memory in Non-musicians Depends on Baseline Pitch Memory Abilities. *Frontiers in Neuroscience*, *11*. https://doi.org/10.3389/fnins.2017.00677

Scheldrup, M., Greenwood, P. M., McKendrick, R., Strohl, J., Bikson, M., Alam, M., … Parasuraman, R. (2014). Transcranial direct current stimulation facilitates cognitive multi-task performance differentially depending on anode location and subtask. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00665

Scheldrup, M. R., Dwivedy, P., Fisher, J., Holmbald, J., & Greenwood, P. (2016). Modulation of complex multitask performance by tDCS depends on individual differences in baseline task ability. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, *60*(1), 42–46. https://doi.org/10.1177/1541931213601010

Schieber, F., & Gilland, J. (2008). Visual Entropy Metric Reveals Differences in Drivers' Eye Gaze Complexity across Variations in Age and Subsidiary Task Load. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, *52*(23), 1883–1887. https://doi.org/10.1177/154193120805202311

Seger, C. A., & Cincotta, C. M. (2006). Dynamics of Frontal, Striatal, and Hippocampal Systems during Rule Learning. *Cerebral Cortex*, *16*(11), 1546–1555. https://doi.org/10.1093/cercor/bhj092

Seger, C. A., Poldrack, R. A., Prabhakaran, V., Zhao, M., Glover, G. H., & Gabrieli, J. D. E. (2000). Hemispheric asymmetries and individual differences in visual concept learning as measured by functional MRI. *Neuropsychologia*, *38*(9), 1316–1324. https://doi.org/10.1016/S0028-3932(00)00014-2

Shacham, S. (1983). A Shortened Version of the Profile of Mood States. *Journal of Personality Assessment*, *47*(3), 305.

Shah, C., Erhard, K., Ortheil, H.-J., Kaza, E., Kessler, C., & Lotze, M. (2013). Neural correlates of creative writing: An fMRI Study. *Human Brain Mapping*, *34*(5), 1088–1101. https://doi.org/10.1002/hbm.21493

Shen, B., Yin, Y., Wang, J., Zhou, X., McClure, S. M., & Li, J. (2016). High-definition tDCS alters impulsivity in a baseline-dependent manner. *NeuroImage*, *143*, 343–352. https://doi.org/10.1016/j.neuroimage.2016.09.006

Sikström, S., Jürgensen, A.-M., Haghighi, M., Månsson, D., Smidelik, D., & Habekost, T. (2016). Self-Rated Attentiveness Interacts with Transcranial Direct Current Stimulation and Noise Stimulation in Reaction Time in a Go/No-Go Task. *Neural Plasticity*. https://doi.org/10.1155/2016/5302538

Silvia, P. J., Winterstein, B. P., Willse, J. T., Barona, C. M., Cram, J. T., Hess, K. I., … Richard, C. A. (2008). Assessing creativity with divergent thinking tasks: Exploring the reliability and validity of new subjective scoring methods. *Psychology of Aesthetics, Creativity, and the Arts*, *2*(2), 68–85. https://doi.org/10.1037/1931-3896.2.2.68

Simonsmeier, B. A., Grabner, R. H., Hein, J., Krenz, U., & Schneider, M. (2018). Electrical brain stimulation (tES) improves learning more than performance: A meta-analysis. *Neuroscience & Biobehavioral Reviews, 84*, 171–181. https://doi.org/10.1016/j.neubiorev.2017.11.001

Smith, J. D., Zakrzewski, A. C., Herberger, E. R., Boomer, J., Roeder, J. L., Ashby, F. G., & Church, B. A. (2015). The time course of explicit and implicit categorization. *Attention, Perception, & Psychophysics*, *77*(7), 2476–2490. https://doi.org/10.3758/s13414-015-0933-2

Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory*, *82*(3), 171–177. https://doi.org/10.1016/j.nlm.2004.06.005

Sriraman, A., Oishi, T., & Madhavan, S. (2014). Timing-dependent priming effects of tDCS on ankle motor skill learning. *Brain Research, 1581*, 23–29. https://doi.org/10.1016/j.brainres.2014.07.021

Stagg, C. J., Jayaram, G., Pastor, D., Kincses, Z. T., Matthews, P. M., & Johansen-Berg, H. (2011). Polarity and timing-dependent effects of transcranial direct current stimulation in explicit motor learning. *Neuropsychologia*, *49*(5), 800–804. https://doi.org/10.1016/j.neuropsychologia.2011.02.009

Stagg, Charlotte J., Antal, A., & Nitsche, M. A. (2018). Physiology of Transcranial Direct Current Stimulation. *The Journal of ECT*, *34*(3), 144. https://doi.org/10.1097/YCT.0000000000000510

Stramaccia, D. F., Penolazzi, B., Sartori, G., Braga, M., Mondini, S., & Galfano, G. (2015). Assessing the effects of tDCS over a delayed response inhibition task by targeting the right inferior frontal gyrus and right dorsolateral prefrontal cortex. *Experimental Brain Research*, *233*(8), 2283–2290. https://doi.org/10.1007/s00221-015-4297-6

Strobach, T., Antonenko, D., Abbarin, M., Escher, M., Flöel, A., & Schubert, T. (2018). Modulation of dual-task control with right prefrontal transcranial direct current stimulation (tDCS). *Experimental Brain Research*, *236*(1), 227–241. https://doi.org/10.1007/s00221-017-5121-2

Tardif, E., & Clarke, S. (2001). Intrinsic connectivity of human auditory areas: A tracing study with DiI. *European Journal of Neuroscience*, *13*(5), 1045–1050. https://doi.org/10.1046/j.0953-816x.2001.01456.x

Torralba, A., Oliva, A., Castelhano, M. S., & Henderson, J. M. (2006). Contextual guidance of eye movements and attention in real-world scenes: The role of global features in object search. *Psychological Review*, *113*(4), 766–786. https://doi.org/10.1037/0033-295X.113.4.766

Tuddenham, W. J. (1962). Visual Search, Image Organization, and Reader Error in Roentgen Diagnosis. *Radiology*, *78*(5), 694–704. https://doi.org/10.1148/78.5.694

Tyler, W. J., Lani, S. W., & Hwang, G. M. (2018). Ultrasonic modulation of neural circuit activity. *Current Opinion in Neurobiology*, *50*, 222–231. https://doi.org/10.1016/j.conb.2018.04.011

Vergallito, A., Riva, P., Pisoni, A., & Romero Lauro, L. J. (2018). Modulation of negative emotions through anodal tDCS over the right ventrolateral prefrontal cortex. *Neuropsychologia*, *119*, 128–135. https://doi.org/10.1016/j.neuropsychologia.2018.07.037

Verhaeghen, P., & Marcoen, A. (1996). On the mechanisms of plasticity in young and older adults after instruction in the method of loci: Evidence for an amplification model. *Psychology and Aging*, *11*(1), 164–178. https://doi.org/10.1037/0882-7974.11.1.164

Warm, J. S., Parasuraman, R., & Matthews, G. (2008). Vigilance Requires Hard Mental Work and Is Stressful. *Human Factors*, *50*(3), 433–441. https://doi.org/10.1518/001872008X312152

Weinberger, A. B., Green, A. E., & Chrysikou, E. G. (2017). Using Transcranial Direct Current Stimulation to Enhance Creative Cognition: Interactions between Task, Polarity, and Stimulation Site. *Frontiers in Human Neuroscience*, *11*. https://doi.org/10.3389/fnhum.2017.00246

Wiethoff, S., Hamada, M., & Rothwell, J. C. (2014). Variability in Response to Transcranial Direct Current Stimulation of the Motor Cortex. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *7*(3), 468–475. https://doi.org/10.1016/j.brs.2014.02.003

Wolfe, J. M., & Horowitz, T. S. (2017). Five factors that guide attention in visual search. *Nature Human Behaviour*, *1*(3), 0058. https://doi.org/10.1038/s41562-017-0058

Wolfe, J. M., Võ, M. L.-H., Evans, K. K., & Greene, M. R. (2011). Visual search in scenes involves selective and nonselective pathways. *Trends in Cognitive Sciences*, *15*(2), 77–84. https://doi.org/10.1016/j.tics.2010.12.001

Ziemann, U., & Siebner, H. R. (2015). Inter-subject and Inter-session Variability of Plasticity Induction by Non-invasive Brain Stimulation: Boon or Bane? *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *8*(3), 662–663. https://doi.org/10.1016/j.brs.2015.01.409

Zwissler, B., Sperber, C., Aigeldinger, S., Schindler, S., Kissler, J., & Plewnia, C. (2014). Shaping Memory Accuracy by Left Prefrontal Transcranial Direct Current Stimulation. *Journal of Neuroscience*, *34*(11), 4022–4026. https://doi.org/10.1523/JNEUROSCI.5407-13.2014