

TRANSCRANIAL DIRECT CURRENT STIMULATION MODULATES
PERFORMANCE IN CHALLENGING SITUATIONS

by

Eric J. Blumberg
A Dissertation
Submitted to the
Graduate Faculty
of
George Mason University
in Partial Fulfillment of
The Requirements for the Degree
of
Doctor of Philosophy
Psychology

Committee:

_____ Director

_____ Department Chairperson

_____ Program Director

_____ Dean, College of Humanities
and Social Sciences

Date: _____ Spring Semester 2016
George Mason University
Fairfax, VA

Transcranial Direct Current Stimulation Modulates Performance in Challenging
Situations

A Dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy at George Mason University

by

Eric J. Blumberg
Master of Arts
George Mason University, 2012

Director: Matthew S. Peterson, Professor
Department of Psychology

Spring Semester 2016
George Mason University
Fairfax, VA



THIS WORK IS LICENSED UNDER A CREATIVE COMMONS
ATTRIBUTION-NONCOMMERICAL 3.0 UNPORTED LICENSE.

Dedication

I would like to thank all of my friends, relatives, and supporters who have made this happen. My loving wife, Dianna, has been a source of unwavering confidence and love. She kept life in perspective during those late nights and she always made sure I was having fun.

Acknowledgements

First, I would like to thank my dissertation committee Matt Peterson, Tyler Shaw, and Pam Greenwood. Your thoughtful feedback and support made this possible. I would also like to thank Eva Wiese, Carryl Baldwin, and Patrick McKnight for helping me navigate graduate life and keeping me focused on the big picture. I would like to acknowledge Raja Parasuraman, who was a great mentor, researcher, and person. I will continue my career incorporating his wisdom and scientific rigor. Finally, thank you to the entire psychology department staff for answering my never-ending questions.

The following research was supported by Air Force Office of Scientific Research Grant FA9550-10-1-0385 to RP and the Center of Excellence in Neuroergonomics, Technology, and Cognition (CENTEC).

Table of Contents

	Page
List of Tables	vii
List of Figures	viii
Abstract	x
General Introduction	1
Neurophysiological Basis of Cognitive Resources	5
Transcranial Direct Current Stimulation	7
The Current Studies	10
Enhancing multiple object tracking performance with noninvasive brain stimulation: A causal role for the anterior intrapariatal sulcus	13
Abstract	13
Introduction	13
Methodology	19
Results	22
Discussion	29
Activation and inhibition of posterior parietal cortex have bi-directional effects on spatial errors following interruptions	35
Abstract	35
Introduction	36
Methods	39
Results	44
Discussion	51
Anodal stimulation reduces complex task performance: The importance of evaluating individual differences in tDCS research	55
Abstract	55
Introduction	56
Methods	65
Results	72

Discussion	101
General Conclusion	113
Appendix A	116
References	120

List of Tables

Table	Page
Table 1: Means for both accuracy and capacity measure across stimulation condition, tracking load, and subsession.	27
Table 2: Distribution of high ability and low ability participants in each stimulation condition.	80

List of Figures

Figure	Page
Figure 1: The Financial Management Task.....	41
Figure 2: The interruption task. The interruption task replaced the screen for the duration of each interruption.....	42
Figure 3: The mean number of errors made (fewer errors represent improved performance) following an interruption (A) and the mean raw scores (higher scores represent improved performance) on the mental rotation task (B) during baseline and stimulation blocks.....	46
Figure 4: Change (stimulation - baseline) in interruption related errors (A) and MRT scores (B) plotted against the number of errors (A) and mean mental rotation scores (B) at baseline.	49
Figure 5: Change (stimulation - baseline) in interruption related errors plotted against change in mental rotation scores.	51
Figure 6: Sequence of actions within MOT task.	20
Figure 7: MOT accuracy +/- SEM (standard error of the mean) across stimulation sites broken down by time point (baseline and stimulation) and tracking load (low and high). * indicates significance at the 0.05 level.	23
Figure 8: MOT accuracy in the high tracking load condition +/- SEM. * indicates significance at the 0.05 level.	26
Figure 9: Correlation between baseline MOT accuracy and the change in MOT accuracy within the AIPS high tracking load condition.	28
Figure 10: Accuracy per block in the AIPS stimulation high tracking load condition, subsession differentiated by bar color.....	29
Figure 11: Illustration of expected differences between stimulation conditions. For effect, should not be interpreted literally.....	64
Figure 12. The DDD simulation map.....	67
Figure 13. Distribution of enemy vehicles within the DDD scenario.	68
Figure 14: Red zone incursions collapsed across stimulation conditions.	74
Figure 15: Red zone incursions collapsed across period.....	75
Figure 16: Red zone incursions during the combined low task load period.	76
Figure 17: Red zone incursions during the high task load period.	77
Figure 18: Red zone incursions for the high ability cluster collapsed across period.	82
Figure 19: Red zone incursions for the high ability cluster during the low task load period.....	83
Figure 20: Red zone incursions for the high ability cluster during the high task load period.....	84

Figure 25: CBFV collapsed across hemispheres and stimulation conditions.....	87
Figure 26: CBFV of the high ability cluster collapsed across periods.	89
Figure 27: Right hemisphere CBFV of the high ability cluster collapsed across periods.	90
Figure 28: CBFV for the sham condition collapsed across periods.	88
Figure 29: Top – Transition 1 right hemisphere CBFV for the high ability cluster.	93
Figure 30: Subjective mental workload. Plotted with standard error of the mean.	96
Figure 31: Correlation between subjective workload and red zone incursions. A significant positive correlation was identified.	97
Figure 32: Correlation between subjective workload and left hemisphere CBFV. A significant positive correlation was identified.	98
Figure 33: Change in MOT accuracy across tracking loads with baseline MOT accuracy as a covariate.	Error! Bookmark not defined.
Figure 34: Change in conflict cost with subsession 1 conflict as a covariate.	101
Figure 31: Percentage of enemy vehicles destroyed across stimulation conditions.	116
Figure 32: The number of enemy attacks across stimulation conditions.	117
Figure 33: Attack efficiency across stimulation conditions.	118
Figure 34: The number of individual vehicle movements across stimulation conditions.	119

Abstract

TRANSCRANIAL DIRECT CURRENT STIMULATION MODULATES PERFORMANCE IN CHALLENGING SITUATIONS

Eric J. Blumberg, Ph.D.

George Mason University, 2016

Dissertation Director: Dr. Matthew S. Peterson

Transcranial direct current stimulation (tDCS) is a promising tool to improve cognitive abilities, however, a number of questions remain. When is it most effective and how does it affect the brain leading to such diverse cognitive benefits? In the following experiments we tested the extent to which tDCS modulates performance during varying levels of task load in three different visuospatial tasks. We targeted stimulation over the right parietal cortex, an area associated with spatial processing.

Experiment 1 tested whether right parietal anodal stimulation could increase multiple object tracking (MOT) accuracy during high tracking load trials. Participants completed a MOT task under low and high tracking load levels prior to and during stimulation. Participants were randomly assigned to one of the three stimulation conditions: right parietal anodal, left prefrontal anodal, left prefrontal sham. Right parietal anodal stimulation significantly increased MOT accuracy under the high tracking

load compared to the other conditions. Stimulation was also more effective for participants who had lower baseline MOT accuracies suggesting that baseline ability moderated the stimulation-based effect.

Experiment 2 tested whether right parietal stimulation could modulate the number of spatial based errors participants committed in a procedural task following an interruption (math problems). Participants were assigned to one of three stimulation conditions: anodal, cathodal or sham. Anodal stimulation significantly reduced the number of spatial errors participants committed while cathodal stimulation significantly increased the number of spatial errors. The results demonstrated that the effects of stimulation are bi-directional and that anodal stimulation can be used to reduce the negative effects associated with interrupted task performance. Stimulation was also more beneficial for participants who committed the greatest numbers of errors suggesting that baseline ability moderated the stimulation-based effect.

Experiment 3 tested whether right parietal stimulation could modulate performance in a real-time strategy simulation where task load was systematically manipulated between low and high levels. Cerebral blood flow velocity (CBFV), an index of mental resource allocation was simultaneously recorded during gameplay to explore how tDCS impacts the brain. Participants were randomly assigned to either the anodal, cathodal, or sham conditions. We ran a cluster analysis in order to account for individual differences in baseline cognitive abilities. The results revealed that anodal stimulation significantly reduced performance compared to cathodal stimulation for those

categorized as having high executive control. However, there were no differences in CBFV between the stimulation conditions.

Together, the experiments provide compelling evidence that right parietal direct current stimulation can modulate performance in challenging situations. In addition, the results indicate that tDCS-based effects are moderated by individual differences in cognitive abilities.

General Introduction

A consistent body of literature has long reported that humans have limited cognitive resources that can be easily degraded (Cowan, 2001; Engle, 2002). These resources are oftentimes conceptualized as a finite tank of “effort” or “attention” that is allocated in response to task demands but also which can be depleted without necessary breaks during demanding tasks (Humphreys & Neville, 1984; Paas & van Merriënboer, 1994). More specifically, these resources can also be characterized by limitations in cognitive faculties of memory and attention (Awh et al., 2007; Bays & Husain, 2008; Luck & Vogel, 1997; Xu & Chun, 2006; Duncan, 1980) to response selection (Dux et al., 2006; Marois & Ivanoff, 2005). These resources are most clearly illustrated in the attention and memory literature where it has become accepted that people can only remember three to four items at any one time (Todd & Marois, 2004; Cowan, 2001).

Unfortunately, yet not surprisingly, these limitations can become disastrous in situations where human abilities are pushed to the limit such as when under high cognitive load. High cognitive load (also commonly referred to as mental load or workload) has been reported to be a contributing factor in aviation accidents (Loukopoulos et al., 2012; Wiener, 1977), power plant failures (Cordes, 1983; Spettell & Liebert, 1986), and more recently space exploration (NTSB Report-SpaceShip2, 2015).

This highlights the importance of conducting research for a goal of improving safety during performance under cognitive load.

Although cognitive load is an intuitive construct, it is often used loosely to describe how an operator handles different situations. Sweller, van Merriënboer, & Pass (1988) developed Cognitive Load Theory to help operationalize the characteristics related to cognitive load. Their theory posits that cognitive load is associated with how one allocates attention (both endogenously and exogenously) during the performance of tasks. The correct allocation of attention results in lower cognitive load.

Paas and van Merriënboer defined cognitive load as a combination of the characteristics of the tasks being completed (e.g., task load), the operator's own characteristics (e.g., executive control), and their interaction (1994). Cognitive load can then be identified by an assessment of the mental effort the user supplies in response to the task demands. Cognitive load could then be thought of as the measureable outcome relating task load and individual abilities.

Given that cognitive load and mental load are oftentimes used interchangeably, it is important to note their subtle differences. Pass and van Merriënboer defined mental load as an a priori value relating to the interaction between task and operator characteristics while mental effort is the actual amount of mental resources allocated to combat task demands (1994). Therefore, cognitive load is comprised of both mental load and mental effort. Within the current paper, cognitive load will be used to define the performance derived from the interaction between task characteristics and operator abilities.

A high or overloaded cognitive state would occur when task demands are equal or beyond an individual's ability. Such situations generally lead to significant drops in performance (Endsley & Rodgers, 1997). Evaluating and preventing these situations can be particularly difficult because of the natural variations in individuals' underlying abilities (Carroll & Maxwell, 1979; Gevins & Smith, 2000; Humphreys & Neville, 1984). There are large individual differences in cognitive abilities in domains such as creativity, problem solving, perception, and memory (Carroll & Maxwell, 1979). Although two individuals may be able to complete a task to a similar level of proficiency, each individual may be allocating a different amount of resources. Therefore, situations may arise in which one person cannot perform with additional cognitive load without disastrous consequences for overall performance, while another person may be able to integrate additional cognitive tasks into their routine without a decrease in performance. Given the serious nature surrounding high cognitive load (Lamble et al., 1999; Svensson et al., 1997), considerable resources have been directed towards developing interventions that can boost performance and thus prevent these situations from occurring. Two of the more common methods are training and automation.

Training has long been used as a method to improve task performance under load with varying levels of success. One type of training, crew resource management has been reported to be successful in aviation (Helmreich, Merritt, & Wilhelm, 1999). Many other training programs follow cognitive load theory, which stipulates that there exist both automatic and controlled processes that vary in the amount of resources that are needed. Exposure and practice to different problems will help individuals make analogies

between novel problems and previously encountered ones. Therefore, after enough practice, specific operations will transition from being controlled processes that are resource intensive to automatic processes that require minimal resources (Paas & van Merriënboer, 1994). This form of training has also been reported to be successful. However, training can take days, weeks, or even months (Green & Bavelier, 2006a) which requires a large amount of effort and dedication to be successful. Also, errors appear to be ubiquitous and may be unrelated to individual expertise; therefore training may not be enough (Loukopoulos et al., 2012; Prakash et al., 2014).

Another method for reducing operator load is automation, now commonly implemented to improve performance, efficiency, and safety by transferring responsibilities that were once manually managed by a human operator to a machine or computer (Parasuraman & Riley, 1997; Parasuraman et al., 2000). Research suggests that poorly designed automation introduces additional problems (Parasuraman & Riley, 1997). In many human-automation systems, the human operator acts as a supervisor, monitoring the function of the automation over extended periods of time. This has been shown to be a flawed approach because research has been very consistent in reporting that humans have poor sustained attention abilities (Parasuraman & Manzey, 2010; Parasuraman, Mouloua, & Molloy, 1996; Warm et al., 2008). Without being actively involved in the moment-to-moment actions in the system, humans become “out of the loop,” losing situation awareness of system states and ways to correctly intervene when the automation does fail (Parasuraman & Riley, 1997). Therefore, while automation may help reduce load it is not without its own problems.

Although the proper implementation of training and automation interventions can significantly increase safety (Salas et al., 2006), there are limitations to each intervention. They do not directly address the underlying problems associated with cognitive load, the neurophysiological bases of limited cognitive resources in the brain (Fukuda et al., 2010; Ma et al., 2014; Todd & Marois, 2005; Xu & Chun, 2006). Therefore understanding the neurophysiological underpinnings of cognitive resources will help inform alternative interventions that may more directly tackle this problem.

Neurophysiological Basis of Cognitive Resources

Previous work provides some insight into the bases of limited cognitive resources. Neurophysiological research using fMRI demonstrates clear cognitive limitations, with ceilings observed in the number of unique spatial locations that can be attended, the number of items that can be held in memory, and the fidelity of those memory representations (Luck & Vogel, 1997; Ma et al., 2014; Xu & Chun, 2006). These limits are thought to originate in the parietal cortex, a brain region involved in spatial processing including attention, memory storage, orienting, and biological motion (Colby & Goldberg, 1999; Culham & Kanwisher, 2001; Todd & Marois, 2004). With activation in this region increasing as participants remember three to four items and before their performance asymptotes (Linden et al., 2003; Todd & Marois, 2004; 2005; Xu & Chun, 2006). These findings are particularly relevant as attention is involved in almost every aspect of cognition.

Recently, strong evidence has emerged to support a more network centric view of cognition. This network view has led to the theory of neural efficiency, which states that

intelligence (i.e., ability) is inversely related to the amount of distributed activation in the brain. This is interpreted to mean that more intelligent individuals require lower brain activation or fewer neural resources (Haier et al., 1988; Haier, Siegel, Tang, Abel, & Buchsbaum, 1992). Following the initial statement of the theory, Neubauer and Fink reviewed the literature and reported a more nuanced finding suggesting that for complex tasks with high levels of difficulty, greater distributed network activation significantly correlates with better performance (2009). In addition, neural efficiency is also more commonly reported for activity in the prefrontal cortex as opposed to the parietal cortex. These views suggest that a broader understanding of task complexity and network dynamics need to be considered when describing cortical activation and task performance.

Recent work examining network dynamics suggest that two large networks appear to be involved with attention, the default mode network (DMN) and the dorsal attention network (DAN). Reports suggest that while both of these networks engage different regions of frontal and parietal cortices, they do so in functionally different ways. The DMN is related to internally directed attention such as during memory retrieval (Fornito et al., 2012) while the DAN is related to externally directed attention such as in response to cues (Corbetta & Shulman, 2002). Interestingly, these two networks appear to be anti-correlated, whereby DAN activation results in decreased DMN activation and vice versa (Fox et al., 2005; Singh & Fawcett, 2008). All together, a number of neurophysiological factors govern the complex landscape of cognitive load. Therefore, moving beyond traditional behavioral interventions such as training and automation to interventions that

more directly affect neurophysiological function (e.g., cortical activation locally and cortical activation in the context of network connectivity) may be more effective in improving performance under high load. That is, altered cortical activation or functional connectivity may lead to improved performance under high cognitive load.

Transcranial Direct Current Stimulation

One such intervention may be transcranial direct current stimulation (tDCS), a form of non-invasive brain stimulation that may be suited for the problem of degraded performance under high cognitive load. Over the past two decades a growing body of literature has identified tDCS as a tool that can safely modulate brain function (Coffman et al., 2014; Nitsche & Paulus, 2000). TDCS involves the application of low levels of direct current via electrode pads targeted towards specific brain areas. In vitro, placing the positive electrode (anode) over the target region leads to excitatory effects on the neurons beneath and enhanced performance, while the negative electrode (cathode) leads to inhibitory effects and decreased performance. These excitatory and inhibitory neuronal effects have been observed in studies examining the effects on single neurons, reporting modulation of the resting potential of those cortical neurons (Antal et al., 2001; Bindman et al., 1964). Additional evidence suggests that tDCS may also impact synaptic efficacy (Rahman et al., 2013). Given that cognitive load is routinely thought of as the amount of resources supplied to combat ongoing task demands, modulation of cortical neurons (resources) through tDCS may subsequently modulate operator load.

Beginning in 2005, Fregni and colleagues started examining effects of tDCS on healthy adult populations during the performance of cognitive tasks. They reported that

15 minutes of stimulation over the left dorsal lateral prefrontal cortex, an area associated with executive control and working memory, improved participants' working memory capacity. TDCS effects have now been reported on working memory (Andrews et al., 2011; Blumberg et al., 2014; Jones & Berryhill, 2012), attention (Reinhart et al., 2014, 2015; Tanoue et al., 2012; Weiss & Lavidor, 2012; Nelson et al., 2014), long-term memory (Javadi et al., 2012), and learning (Bullard et al., 2011; Falcone et al., 2013; Kincses et al., 2004) among others.

This large range of findings has generated much excitement regarding the potential usefulness of brain stimulation. However, a number of review and meta-analyses have reported inconsistent findings in the literature (Brunoni & Vanderhasselt, 2014; Horvath et al., 2014; Krause & Cohen Kadosh, 2014). They reveal that effects of tDCS on cognition are complex. There is growing evidence that the effects of tDCS are moderated by a number of individual differences such as baseline ability (Tseng et al., 2012), education (Jones & Berryhill, 2012), working memory (Berryhill & Jones, 2012), experience (Bullard et al., 2011), phenotype (Plewnia et al., 2013), and task demands such as difficulty (Berryhill & Jones, 2014). Given these findings, one could predict parietal tDCS would be most beneficial for periods of high task difficulty during the completion of tasks that require attention and spatial memory. Additionally, parietal tDCS may be most beneficial to individuals who are poorer performers (lower cognitive resources) at baseline. This baseline effect has previously been reported with parietal stimulation (Tseng et al., 2012). These two characteristics fit in very nicely with how cognitive load is operationalized, as the interaction between an individual's own abilities

and the characteristics (i.e., difficulty) of the task. Therefore, tDCS may be well suited to combat the negative effects reported under high cognitive load.

Recent work by Meinzer and colleagues (2012; 2013) extended the literature by linking the effects of tDCS (neuronal excitability) with cortical activation (i.e., changes in BOLD-fMRI signal and network connectivity). They reported two main findings: 1) tDCS decreased the BOLD signal under the *anodal* electrode and 2) tDCS decreased distributed cortical activation compared to sham. It should be noted that their participants were older adults. However, the findings are likely to still be relevant for younger adults even though older adults generally illustrate greater bi-lateral task-related activation compared to their younger counterparts (Cabeza, 2002; Cabeza et al., 2002).

Given the observation that anodal stimulation leads to excitatory neuronal effects (Antal et al., 2001), these BOLD signal findings may appear to be unexpected. However, there is considerable evidence that task practice (Chein & Schneider, 2005; Kelly & Garavan, 2005), behavioral cognitive training (Strenzoik et al., 2014) decreases BOLD signal in fronto-parietal networks, and those specifically related to task. This is in addition to evidence from the neural efficiency hypothesis (Haier et al., 1988; Haier, Siegel, Tang, Abel, & Buchsbaum, 1992). The neural efficiency hypothesis states that cortical activation (BOLD signal) and performance are inversely related; better performance being correlated with decreased BOLD signal. TDCS may then be modulating one of several potential mechanisms such as cerebral blood flow, neural metabolism, and neurotrophin release (see Kar & Wright, 2014 for a detailed explanation), each of which have been linked to changes in BOLD signal (Markham et

al., 2012). Therefore, the decrease in BOLD signal concurrent with the increase in task performance matches the expected findings within the neural efficiency hypothesis (Kar & Wright, 2014). One important note to consider is that Meinzer's task was not complex (word generation) and the more recent review by Neubauer and Fink (2009) reported that during more complex cognitive tasks such as Raven's Progressive Matrices (under time restrictions), better performance was correlated with increased cortical activation. Therefore, one might speculate that tDCS would elicit systematically different patterns of BOLD signal during the completion of complex tasks.

The Current Studies

In summary, attention is critical to general cognition and greater focused attention appears to be necessary during periods of high cognitive load. The neuroimaging literature has demonstrated that the parietal cortex plays an important role in attention and cognition (Corbetta & Shulman, 2002; Fornito et al., 2012) and that changes in task demands (e.g., attention) lead to changes in cortical activation in this area (Todd & Marois, 2004; 2005; Xu & Chun, 2006). Given the central role that attention and memory play in general cognition across a range of cognitive loads, it can be assumed that these constructs may be even more critical in high or overloaded states. Evidence from the tDCS literature also reports that stimulation of the parietal cortex can lead to significant changes in attention (Weiss & Lavidor, 2012; Jones & Berryhill, 2012) and working memory (Tseng et al., 2012). Therefore, the goal for the following experiments was to test whether parietal tDCS can be an effective intervention to reduce the detrimental effects associated with performance under high cognitive load.

Based on the previously summarized evidence, we hypothesized that anodal parietal stimulation would increase local excitatory neuronal effects thereby reducing the extent to which performance declines during periods/instances of increased cognitive load. This hypothesis was tested in three separate experiments each incorporating a different experimental paradigm with varying task characteristics and manipulating cognitive load. The experimental paradigms increased in task complexity from experiment 1 to experiment 3: 1) visual attention tracking, 2) interrupted task performance, and 3) real-time strategy simulation.

The goals for Experiment 1 were (a) to illustrate a proof of concept that parietal stimulation can improve performance in situations of cognitive overload, (b) determine whether the observed effects were due to local cortical enhancement in the parietal cortex or to global cortical enhancement, and (c) to investigate whether stimulation was more beneficial for lower performing individuals (assumed to have fewer cognitive resources).

The goals for Experiment 2 were (a) to extend the results from Experiment 1 to a different spatial paradigm, (b) to confirm that stimulation is more beneficial for lower performing individuals (assumed to have fewer cognitive resources), and (c) to also illustrate that these tDCS based effects are bi-directional (i.e., cortical excitation resulting in improved performance and cortical inhibition resulting in decreased performance).

Finally, the goals for Experiment 3 were (a) to extend the previously reported behavioral findings to a more complex cognitive paradigm and (b) to determine whether the behavioral findings are reflected in neurophysiological effects by simultaneously

assessing cerebral blood flow velocity (CBFV), a measure claimed to index cognitive resource allocation in the brain (Aaslid, 1986; Shaw et al., 2009).

Enhancing multiple object tracking performance with noninvasive brain stimulation: A causal role for the anterior intraparietal sulcus

Published in Frontiers in Systems Neuroscience – February 5th, 2015

Eric J. Blumberg, Matthew S. Peterson, Raja Parasuraman

Abstract

Multiple object tracking (MOT) is a complex task recruiting a distributed network of brain regions. There are also marked individual differences in MOT performance. A positive causal relationship between the anterior intraparietal sulcus (AIPS), an integral region in the MOT attention network and inter-individual variation in MOT performance has not been previously established. The present study used transcranial direct current stimulation (tDCS), a form of non-invasive brain stimulation, in order to examine such a causal link. Active anodal stimulation was applied to the right AIPS and the left dorsolateral prefrontal cortex (and sham stimulation), an area associated with working memory (but not MOT) while participants completed a MOT task. Stimulation to the right AIPS significantly improved MOT accuracy more than the other two conditions. The results confirm a causal role of the AIPS in the MOT task and illustrate that transcranial direct current stimulation has the ability to improve MOT performance.

Introduction

Multiple Object tracking (MOT) is a dynamic, effortful task that assesses how many moving objects a person can attend to over a short period of time (Pylyshyn, & Storm, 1988). In the traditional MOT paradigm, participants are presented with multiple objects (e.g. circles) on a monitor and are instructed to track a subset of those objects. The objects move independently and continuously around the screen, and after they stop, participants attempt to indicate which objects they had been tracking. Accuracy, or the proportion of correctly identified targets, is generally used to measure MOT performance.

MOT tasks have been used to evaluate attention capacity (Alvarez & Franconeri, 2007; Horowitz & Cohen, 2010), mechanisms of perceptual organization (Scholl et al., 2001; Yantis, 1992), and distributed attention (Sears & Pylyshyn, 2000). While MOT is a process-intensive task involving attention, object selection, object tracking, memory, and multiple types of eye movements, a number of studies (Cavanagh & Alvarez, 2005; Pylyshyn & Storm, 1988) have illustrated that on average, individuals have a tracking accuracy of 85% for 2 objects, and as the number of items to track increases, accuracy decreases sharply. In addition, there are marked inter-individual differences in MOT tracking capacity, reflecting inter-individual variation in spatial ability (Oksama & Hyönä, 2004). Given such variability, it is important to understand the underlying neural mechanisms involved in performance of dynamic attentional tasks such as the MOT.

Several researchers (Culham et al., 1998; Culham et al., 2001; Howe et al., 2009; Jovicich, 2001) have used functional magnetic resonance imaging (fMRI) to identify the brain areas associated with MOT. Given the number of perceptual and attentional processes involved in MOT, it is not surprising that the fMRI studies have implicated 12

unique brain areas recruited during MOT. Culham and colleagues (1998) concluded that 11 different brain areas were recruited during MOT whereas Jovicich and colleagues (2001) identified 12 areas, 9 of which were consistent with the previous work by Culham and colleagues. These studies identified brain regions sensitive to attention, motion, and areas involved in eye movements. However, Howe and colleagues (2009) identified a number of issues with the previous fMRI and MOT studies, the greatest of which was that the studies did not correctly differentiate brain areas specifically related to tracking objects versus attending to objects, a critical differentiation in analysis of MOT performance.

After controlling for the effects of attention, Howe and colleagues (2009) concluded that the frontal eye fields (FEF), anterior intraparietal sulcus (AIPS), the superior parietal lobule (SPL), posterior intraparietal sulcus (PIPS), and the human motion areas (MT+) were all consistently activated during MOT. The FEF and SPL are involved with the generation and execution of eye movements and spatial attention, processes clearly involved with visually tracking objects (Donner et al., 2000; Nobre et al., 1997). Area MT+ plays a critical role in motion-based tasks, and might potentially be responsible for updating location information (d'Avossa et al., 2007). Recent evidence has suggested that the PIPS plays a role in attention to both stationary and moving objects, and may be responsible for managing pointers to the spatial locations of attended objects. PIPS and MT+ may also interact to support MOT with the PIPS involved in attending to the items and MT+ associated with updating of locations (Howe et al., 2009). The AIPS was identified to be active only when objects were moving, suggesting a

dissociation between tracking moving objects and attending to stationary ones, and indicating that it plays a crucial role within the identified attention network. In addition, AIPS has been shown to be sensitive to tracking load, with greater activation associated with increased number of items to be tracked (Culham et al., 2001; Jovicich et al., 2001). Supporting this view, a lesion study conducted by Battelli and colleagues (2001) showed that individuals with a unilateral right parietal lesion were significantly worse at tracking objects in the contralateral field even when only one object was presented in each visual field. Furthermore, Battelli and colleagues (2009) provided initial evidence supporting the causal role of the AIPS in MOT performance by demonstrating that MOT performance was inhibited by transcranial magnetic stimulation (TMS) over the right and left intraparietal sulcus but not MT+.

A method that can provide evidence for a positive causal relationship between the AIPS and MOT is transcranial direct current stimulation (tDCS). It involves the application of small amounts of constant direct electric current (1 to 2 mA) with electrodes attached to the scalp. A positive polarity (anode) is typically used to stimulate neuronal function and enhance performance, while a negative polarity (cathode) is used to inhibit neuronal activity. The electric current is thought to affect the resting potential of cortical neurons (Antal et al., 2001; Bindman et al., 1964) and also synaptic efficacy (Rahman et al., 2013), which in turn increases their sensitivity, leading to an increased likelihood of firing while performing a task. (See Bikson and colleagues, 2004, for a deeper explanation on the neural affects of tDCS). The standard current values for active stimulation conditions can fluctuate up to 2 mA while control/sham levels are either 0.1

mA or a 2 mA ramp-up and immediate ramp-down (Clark et al., 2012). No serious side effects have been associated with normal tDCS operations for 30 minutes or less of prolonged stimulation (Bikson et al., 2009).

Research by Andrews and colleagues (2011) has indicated that the effects of tDCS are not global, and only occur when administered in a specific manner: the stimulation must be applied so that stimulation targets areas that are involved in the task being trained on. TDCS is thought to facilitate changes in active neurons and pathways, and those pathways must be active while the stimulation is being administered in order to show a benefit. Through the excitatory (anodal) and inhibitory (cathodal) affects on cell membranes, tDCS can improve our understanding of brain function and its corresponding behavioral correlates.

The present study used tDCS to provide a unique approach to investigating the causal role of the AIPS and of evaluating the plasticity of MOT. To demonstrate that the effects of stimulation are focal rather than global in nature both a target and a control site for stimulation were chosen. As discussed previously, the right AIPS was chosen as the targeted experimental site for potential enhancement of MOT performance. The left dorsolateral prefrontal cortex (DLPFC) was chosen as a control stimulation site because previous fMRI studies have shown that it is minimally involved, if at all, in MOT performance (Howe et al., 2009). In contrast, data from Culham et al., 2001 suggests a right lateralized recruitment in frontal brain areas during MOT. Stimulation of this area may lead to inadvertent affects on MOT performance, and because we focused on the right AIPS in the present study, we used the left DLPFC for the control stimulation

condition. In addition to the active stimulation control, we also included a sham stimulation of the left DLPFC (to control for a placebo effect). The sham condition is included to control for placebo effects as previous studies have failed to identify meaningful effects of sham stimulation on task performance (Berryhill et al., 2014). Participants were naïve as to the relationship between scalp location and its corresponding behavioral outcomes, making the sham stimulation location unimportant.

We hypothesized that tDCS would improve performance in the right AIPS stimulation condition and that there would be differences in performance between participants stimulated over the right AIPS compared to those stimulated over the left DLPFC in both active and sham conditions. To assess the possible interaction of stimulation with the processing demand associated with attentional tracking, we administered both a low and a high tracking load version of the MOT. We anticipated that an effect of tDCS would be greatest for the high tracking load and may even be absent in the low load condition due to ceiling effects for tasks already at or near ceiling in performance (Ball et al., 2007; Jaeggi et al., 2011; Schmiedek et al., 2010). In addition, previous researchers have suggested that tDCS may be more beneficial for novices/lower performers than for experts/higher performers (Blumberg et al., in press; Bullard et al., 2011; Foroughi et al., in press; Tseng et al., 2012) and that tDCS may be more effective in difficult tasks (Berryhill et al., 2014), suggesting that both task difficulty and individual abilities may play a critical role in the effectiveness of stimulation.

Methodology

Participants. Forty-eight undergraduates participated in the experiment (28 females) with an average age of 19 years (range from 18-32). Participants met the following conditions: 1) right handed, 2) normal or corrected to normal vision, and 3) English as a first language. Participants were randomly assigned to one of the three between-subject stimulation conditions while they performed the MOT task under two tracking loads. Sixteen subjects were assigned to each condition. Participants were given course credit for their participation. All participants gave written informed consent to participate in a protocol approved by the George Mason Institutional Review Board.

Tasks and equipment.

MOT task. Participants engaged in a computer-based MOT task on a Dell 15" inch LCD monitor at a distance of 40 cm from the screen. The experimental stimuli consisted of eight green circles (two or four of the circles were targets). The circles were 1° of visual angle in size. Each trial consisted of three steps. The eight circles initially appeared as static images (no movement) while the target circles flashed for one second. Then the circles moved continuously and independently for eight seconds, and could overlap as they traveled across the screen. The circles moved at a constant rate of 13 degree/sec and in constant directions (when they encountered the border of the screen they were redirected in another direction based upon the angle of impact with the border). After the circles stopped, participants selected the target circles with mouse clicks. The experimental sequence can be seen below in Figure 1. Participants tracked two circles (25% of all the circles) in the low load condition and four (50% of all the circles) in the high load condition.

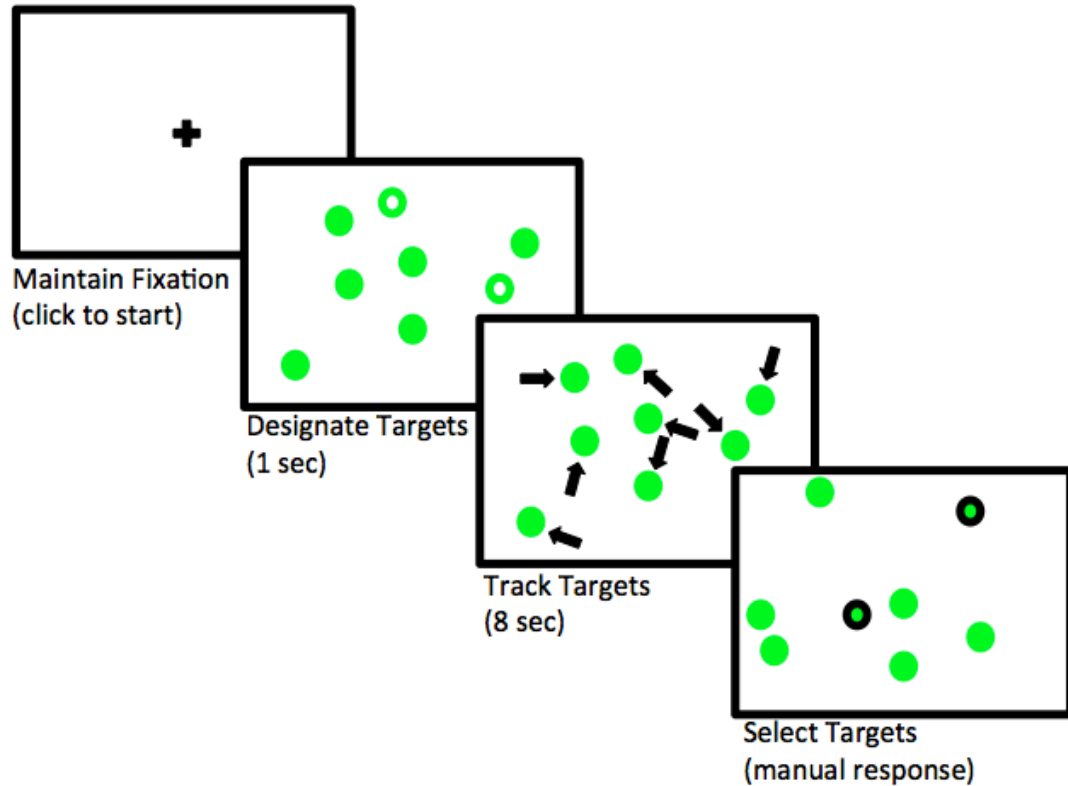


Figure 1: Sequence of actions within MOT task.

Transcranial direct current stimulation. TDCS was applied using an ActivaDose II Iontophoresis Delivery Unit. Current was constantly supplied to two electrode pads with 11cm² saline soaked sponges that were attached (with self-adhesive bandage strips) to the participant's scalp and shoulder. The anode was placed on the scalp while the cathode was placed on the contralateral upper arm, consistent with a non-cephalic montage (Falcone et al., 2012; McKinley et al., 2013). Subjects were randomly assigned to one of three stimulation conditions: AIPS active anodal stimulation, DLPFC active anodal stimulation, and DLPFC sham stimulation. In the AIPS experimental

condition the anode was placed near CP4 in the 10-20 EEG system while the cathode was placed on the contralateral upper arm. We used Soterix Medical's HDExplore software to identify an appropriate montage to best target the AIPS. A standard adult male head was incorporated for the model; therefore, a single current flow model was identified and applied for all participants. We modeled a number of different montages before identifying scalp site CP4 as the site that best activated AIPS. In both the active and sham control conditions the anode was placed near electrode site F3 in the 10-20 EEG system with the cathode placed on the contralateral upper arm (right). F3 is a commonly used site when modulating the DLPFC (Coffman et al., 2014). Participants in both experimental conditions were given 2.0 mA of stimulation for 30 minutes. Participants in the sham condition received a 2.0 mA ramp-up and immediate ramp-down to 0 mA lasting 30 seconds. The brief amount of stimulation provided participants with the full sensation of tDCS.

Design. A 3x2 mixed design was employed. The between-subjects variable (stimulation site) had the following levels: AIPS active, DLPFC active, and DLPFC sham. The within-subjects variable was tracking load (low or high). Each participant completed 6 blocks of 44 trials (three blocks during baseline testing and three blocks while stimulation was administered). The trials in each block were randomized with an equal representation of low and high tracking trials.

Procedure. Upon arrival participants were asked to read and sign the informed consent form outlining the nature of the task and any risks/benefits they may receive for participating. The Snellen near-sightedness exam was administered to test vision (20-30

or better vision required). Participants were then instructed on how to perform the MOT task. Participants completed a baseline of 3 blocks of 44 trials to test their baseline performance. The 3 blocks were completed back-to-back without any breaks.

Following baseline testing, the experimenter prepared the tDCS setup. Participants were given the DCS Sensation Questionnaire (Scheldrup et al., 2014) at three time points throughout the stimulation subsession (approximately 1-, 10-, and 30 minutes post stimulation onset) measuring how much itching, heat/burning, and tingling the participant felt at that moment. Immediately following the first administration of the sensation questionnaire participants completed a demographic and video game questionnaire. After they finished the questionnaires they completed the second sensation questionnaire. Participants then completed the final three blocks of the MOT task (132 total trials) while tDCS was being administered. After completing the trials the tDCS unit was turned off and the electrodes were removed. Finally, each participant completed the third sensation questionnaire and then was debriefed about the experiment.

Results

MOT accuracy. The primary goal of this experiment was to investigate whether a relatively short period of brain stimulation (30 minutes) could be used to improve MOT performance, thereby establishing a positive causal role of the right AIPS in MOT performance. The behavioral and dependent variable in the experiment was MOT accuracy. Accuracy was calculated by dividing the number of correctly identified targets by the total possible targets for each trial. Accuracy scores were then created for both the baseline and stimulation subsessions by averaging the accuracy scores across trials and

blocks within each subsession. Separate accuracy scores were created for both load conditions leaving each participant with four different accuracy scores (see Figure 2).

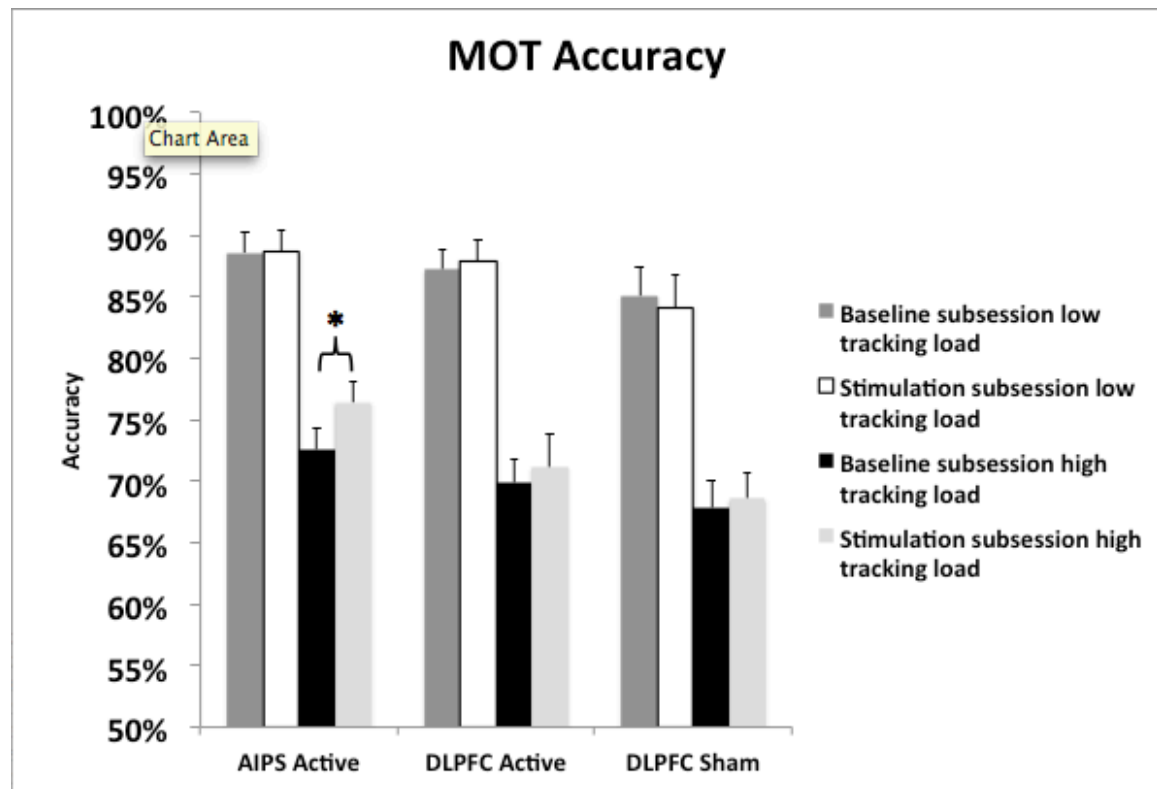


Figure 2: MOT accuracy \pm SEM (standard error of the mean) across stimulation sites broken down by time point (baseline and stimulation) and tracking load (low and high). * indicates significance at the 0.05 level.

Baseline comparison. We initially tested whether baseline performance across stimulation conditions was significantly different from one another. Two separate (low and high tracking loads) one-way analysis of variance (ANOVA) were conducted because we did not want a potential ceiling effect in the low tracking load condition (hypothesized *a priori*) to reduce the likelihood of finding an effect in the high tracking load condition. The ANOVA for the low tracking load condition failed to identify a

significant main effect of stimulation condition [$F(2,45) = 0.87, p > .20$]. The ANOVA for the high tracking load condition also did not reveal a significant main effect of stimulation condition [$F(2,45) = 1.34, p > .20$] suggesting that baseline performance was not significantly different across stimulation groups in either tracking load condition.

Condition specific stimulation effect. We then conducted a 2x2x3 mixed-design analysis of variance (ANOVA) with subsession and tracking load as the within-subjects factors, stimulation site as the between-subjects factor, and MOT accuracy as the independent variable. A self-assessment of first person shooter video game experience was initially included in the analysis as a covariate because prior research (Green & Bavelier, 2006) suggested it predicts MOT performance, however, this effect was not significant in the present study and was therefore removed from the subsequent analyses. The analysis revealed a 2-way interaction between tracking load and subsession [$F(1,45) = 5.24, p < .05, \eta^2_{\text{partial}} = 0.10$], a main effect for subsession [$F(1,45) = 351.14, p < .01$], and a main effect for tracking load [$F(1,45) = 4.34, p < .05$]. Tests of simple main effects for the two-way interaction using a Bonferroni correction ($\alpha = .05$) revealed that within the high tracking load condition, MOT performance was significantly greater in the stimulation subsession compared to baseline, [$F(1,45) = 9.5, p < .01, \eta^2_{\text{partial}} = .17$]. The three-way interaction was not significant ($p > .10$).

To better test our initial hypothesis about whether TDCS stimulation applied to the AIPS can improve MOT performance, a series of planned paired samples *t*-tests were conducted to identify if stimulation improved MOT accuracy beyond that of baseline. Six, separate paired samples *t*-test using a Šidák correction ($\alpha = .0063$, given six related

tests) were conducted comparing each baseline score to its corresponding stimulation score (low and high tracking load for each stimulation site). A significant difference in performance was identified in the high tracking load condition between AIPS baseline ($M = 76.42\%$, $SE = 1.66$) and AIPS stimulation ($M = 72.54\%$, $SE = 1.86$), $t(15) = 4.10$, $p = .00047$, $d = 1.03$ illustrating a 4% improvement in MOT accuracy, see Figure 2. No other t -test reached significance (largest $t = 1.0$; smallest $p = .33$). Given that stimulation did not affect performance in the low tracking load condition across any stimulation condition and we did not make any *a priori* predictions, the low tracking load condition was excluded from the following analyses.

Comparison of stimulation effects across conditions. In addition to testing for changes in performance due to stimulation, we also examined whether stimulation led to group differences. Given the *a priori* hypothesis that in the high tracking load condition the AIPS stimulation condition would be significantly different from the two DLPFC control conditions, the DLPFC active ($M = 71.16\%$, $SE = 2.67$) and DLPFC sham ($M = 68.56\%$, $SE = 2.12$) groups were initially compared against one another to identify any differences. An independent samples t -test using a Šidák correction ($\alpha = .025$, given two related tests) was conducted to compare performance across the two control conditions in the stimulation subsession. The analysis did not reveal a significant difference between the two control groups, $t(30) = 0.45$, $p = .41$. The two DLPFC control conditions were therefore collapsed into one control condition in the subsequent analysis, leaving two levels of the stimulation variable (AIPS active and DLPFC control).

We then tested if performance in the AIPS active and DLPFC control condition were significantly different from one another in the stimulation subsession, examining if AIPS stimulation led to better MOT performance compared to the DLPFC control. An independent samples *t*-test using a Šidák correction ($\alpha = .025$) was conducted to compare performance between the AIPS active ($M = 76.42\%$, $SE = 1.67$) and DLPFC control ($M = 69.86\%$, $SE = 1.69$) conditions. The analysis revealed a significant difference $t(46) = 2.45$, $p = .009$, $d = 0.80$. The data suggests that in the high tracking load condition, right AIPs stimulation improved MOT accuracy significantly more than in the combined control condition, see Figure 2 and Figure 3.

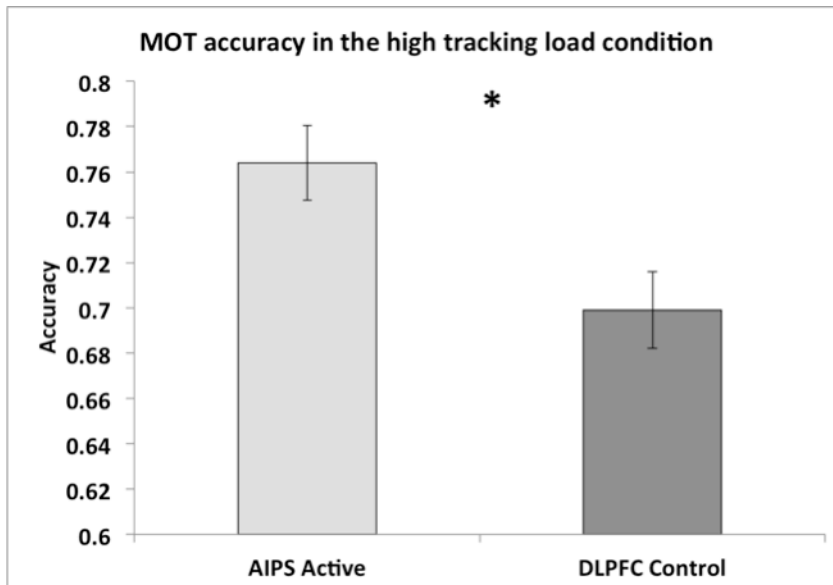


Figure 3: MOT accuracy in the high tracking load condition \pm SEM. * indicates significance at the 0.05 level.

MOT Capacity. Due to the high accuracy scores in the low tracking load condition, an important question becomes: is accuracy a sensitive enough measure to

detect performance changes close to ceiling? To answer this question, we non-linearly transformed the accuracy scores into capacity measures (k) according to Horowitz and colleagues (2007) and Scholl and colleagues (2001). The capacity measure did not lead to any significantly different outcomes compared to the accuracy measure, therefore, the analyses will not be included in this manuscript, see Table 1 for means.

Mean accuracy and capacity values					
Metric	Stimulation Condition	Low		High	
		Baseline	Stimulation	Baseline	Stimulation
Accuracy	AIPS Active	88.59	88.64	72.54	76.42
	DLPFC Active	87.26	87.97	69.89	71.16
	DLPFC Sham	85.09	84.14	67.8	68.56
Capacity	AIPS Active	1.77	1.77	2.88	3.04
	DLPFC Active	1.74	1.76	2.77	2.82
	DLPFC Sham	1.7	1.68	2.68	2.72

Table 1: Means for both accuracy and capacity measure across stimulation condition, tracking load, and subsession.

Baseline vs. change in MOT performance. We also examined whether baseline MOT accuracy predicted the amount of improvement exhibited in the right AIPS stimulation condition (high tracking load trials). To accomplish this we compared participants' baseline MOT accuracy to their change in MOT accuracy (stimulation minus baseline). The two scores were negatively correlated, $r(16) = -0.45$, $p < .05$, see Figure 4. This significant association suggests that tDCS may be more beneficial to individuals with lower baseline MOT abilities. Note also, that all but two of the

participants, irrespective of their baseline performance, showed improvement in MOT accuracy with tDCS.

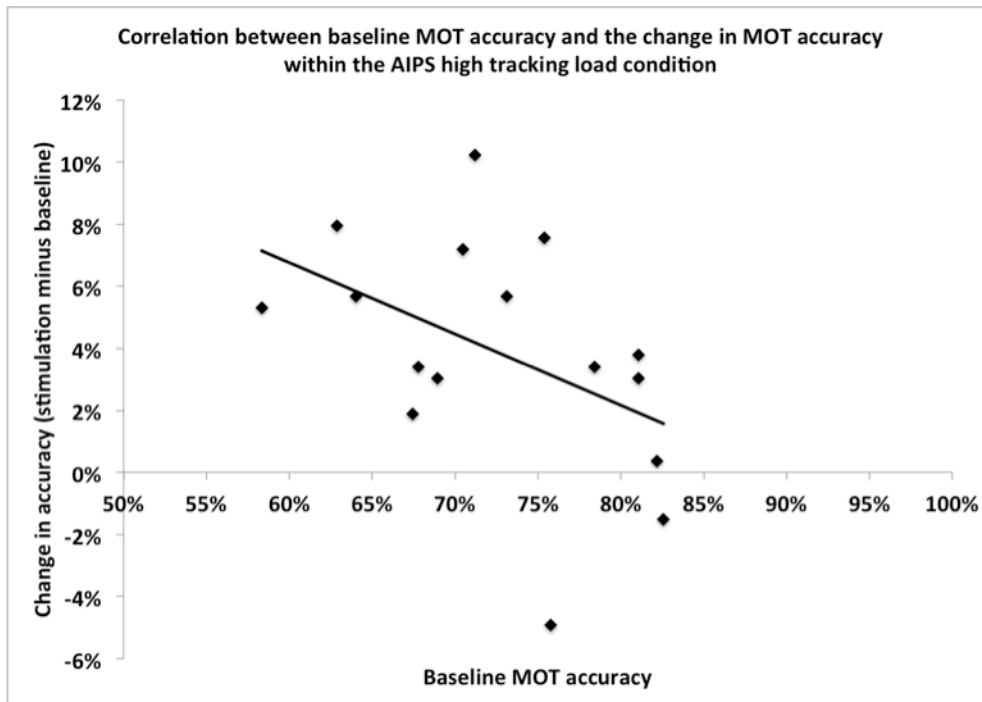


Figure 4: Correlation between baseline MOT accuracy and the change in MOT accuracy within the AIPS high tracking load condition.

Rate of MOT improvement. Additionally, we examined the rate at which stimulation impacted MOT performance in the AIPS stimulation high tracking load condition (Figure 5). We ran a repeated measure ANOVA with block (only in the stimulation subsession) as the within-subjects factor. Block was not significant [$F(2,30) = 0.04, p > .10$] indicating that stimulation led to an immediate boost in MOT performance that was sustained across the three blocks (blocks 4,5,6).

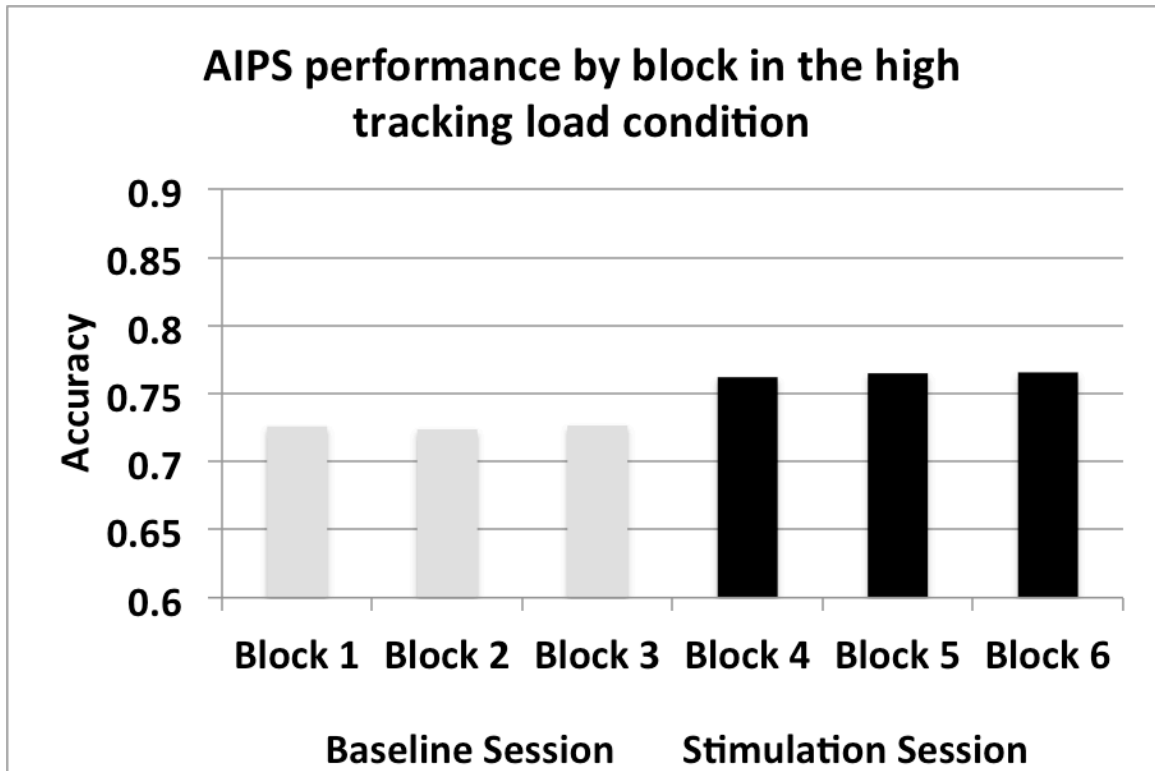


Figure 5: Accuracy per block in the AIPS stimulation high tracking load condition, subsession differentiated by bar color.

Discussion

The present study evaluated the efficacy of using targeted non-invasive brain stimulation to improve understanding of the causal role of the right AIPS in MOT performance through improved learning and skill acquisition of MOT. TDCS was targeted to the right AIPS, a brain area that plays a unique and integral role for tracking multiple objects (Howe et al., 2009). Active anodal stimulation to the right AIPS improved MOT performance in the high tracking load condition but not in the low tracking load condition. Active and sham stimulation of the left DLPFC had no effect in either tracking load condition. This finding suggests that: 1) the right AIPS plays an

active role in MOT, 2) modulation of this area by tDCS directly leads to changes in MOT performance, and 3) the effects of the tDCS were focal in nature and not a global enhancement due to stimulation of the entire cortex.

Right AIPS stimulation improved performance in the more difficult tracking load condition where participants' accuracy was relatively low (~70%) whereas stimulation did not affect performance in the easier tracking load condition (85-90%) where participants were performing at or close to ceiling. These results are consistent with the *a priori* hypotheses and are in line with the previous literature that suggests that tDCS is more beneficial to novices (Bullard et al., 2011) and lower performers (Blumberg et al., in press; Foroughi et al., in press; Tseng et al., 2012) and may be more effective when paired with difficult tasks (Berryhill et al., 2014; Jones & Berryhill, 2012). Additionally, cognitive training is not beneficial for individuals already performing at ceiling (Ball et al., 2007; Jaeggi et al., 2011; Schmiedek et al., 2010).

We also identified that in the high tracking load condition, the amount of improvement in MOT was negatively correlated with a participant's baseline MOT ability. On average, individuals with lower baseline MOT accuracies exhibited greater increases in accuracy compared to those with higher baseline abilities. Tseng and colleagues (2012) found a similar inverse effect in change-detection ability stimulating a posterior parietal location.

Additionally, we identified that stimulation had an immediate effect on MOT performance in the right AIPS high tracking load condition. Performances across the three blocks in the stimulation subsession were similar, illustrating a constant positive

impact of stimulation. We believe this is due to the fact that MOT is very simple task with little to no learning curve, therefore, stimulation immediately modulated the relationship between the right AIPS and MOT performance.

While research (Boot et al., 2008; Green & Bavelier, 2006) has previously shown that specific types of training such as playing action video games can improve MOT performance, this is the first study to show that brain stimulation can do so too, but in a much shorter time. If used as a tool for accelerated training, tDCS may offer a number of benefits compared to traditional training paradigms. Video game training can take extended periods of time (Basak et al., 2008; Feng et al., 2007; Green & Bavelier, 2006), whereas in this study, tDCS immediately improved spatial tracking performance. Also, specific subsets of the population cannot or do not enjoy playing video games because the games can be difficult to learn, can cause frustration, and can require fine motor control. On the other hand, tDCS requires little or no additional effort from the user apart from the task being performed, making it ideally suited to a larger segment of the population. TDCS focused on the right AIPS, a brain area integral to the attention network (Howe et al., 2009) immediately improved MOT performance, this transient improvement was accomplished in a substantially shorter amount of time than through traditional training programs, however, the effects may not be as significant or as long lasting. While this study provides initial evidence that tDCS can rapidly improve MOT performance, further research should identify if these effects are transferable to other spatial tracking tasks in both basic and complex settings. Brain stimulation over the right AIPS offers a unique method to better understand the function of this area as it relates to MOT. This study adds

to the existing literature that the right AIPS plays an active role in MOT and that the neural substrates recruited for MOT exhibit significant plasticity.

Our findings mirror previous TDCS studies that have found effects on perception, attention, and memory abilities (Coffman et al., 2014). For example, Clark and colleagues (2012) showed increased perceptual learning when tDCS electrodes were targeted to brain areas related to perceptual learning, with the benefit of tDCS being retained for at least 24 hour (Falcone et al., 2012). Of particular note is the study by Moos and colleagues (2012), in which they observed that cathodal stimulation over the right AIPS increased top-down attentional selection. While they applied cathodal stimulation to the same area we did, the two studies measured different aspects of attentional selection. Additionally, transcranial magnetic stimulation (TMS) has previously been applied to support a causal mechanism between modulation of the IPS and MOT (Battelli et al., 2009). They inhibited IPS function, leading to decreased MOT accuracy. However, our study is the first to illustrate that the causal mechanism is in the positive direction as well. We used tDCS to illustrate the facilitative effects of AIPS stimulation on MOT ability, finding increased MOT accuracy. TDCS is also less invasive and more easily applied making it a more practical tool to accelerate MOT abilities.

This study had some limitations. Although current modeling was used to identify the electrode montage that would best lead to stimulation of AIPS, such modeling involves a number of assumptions that may not always be met, and modeling must be considered as a hypothesis to be tested rather than definitive. That the empirical evidence confirmed the hypothesis and showed that other stimulation sites did not lead to

improvement in MOT performance is consistent with the predicted results. Furthermore, we did not directly measure cortical activation in AIPS or other parietal regions as a result of tDCS. However, previous research has illustrated that tDCS does affect neuronal firing (Radman et al., 2009). Additionally, the tDCS electrode montage used in the experiment may have resulted in stimulation of the posterior parietal cortex in general.

Another possible concern involves the baseline performance of the different stimulation/sham groups. While statistically significant differences between groups in MOT baseline performance were not found, one could argue that individuals in the AIPS condition were somewhat better to begin with, so that the difference identified in the stimulation subsession could just reflect these initial differences in performance and random variation or potentially a small tDCS effect. However, it would be highly unlikely that random noise would increase performance in individuals that were already performing at high levels and not for individuals performing poorly. Additionally, it is unlikely given that individuals with the lowest baseline MOT abilities saw the largest increases in MOT performance. If baseline averages were identical (decreasing initial AIPS accuracy) potentially more individuals would see greater benefits in their MOT performance. Task difficulty can also modulate the beneficial effects of tDCS (Berryhill et al., 2014; Jones & Berryhill, 2012). While AIPS stimulation significantly improved MOT accuracy in the four ball tracking condition (an amount at or close to our attention capacity) and not the two ball tracking condition, an even more difficult MOT condition (i.e., tracking six objects) may have resulted in larger effects. Therefore, the findings in this paper may be underestimating the beneficial effect of tDCS on MOT performance.

Future research should investigate the limitations of applying tDCS to the intraparietal sulcus, how cathodal stimulation may affect spatial tracking performance, and how tDCS could be used in conjunction with other training programs to improve spatial tracking beyond that of just video game play or tDCS alone. Additionally, it will be very important to identify how long the tDCS effects last, especially if tDCS is used for long-term enhancement of spatial abilities.

The current study is the first to illustrate that brain stimulation can improve MOT accuracy. Stimulation to the AIPS, a central location in the attention network improved MOT accuracy while stimulation to the DLPFC did not. Accelerated training techniques like tDCS can be used to improve perceptual, attention, and memory training programs and to identify the causal relationships between brain and behavior.

Activation and inhibition of posterior parietal cortex have bi-directional effects on spatial errors following interruptions

Published in Frontiers in Systems Neuroscience - January 12, 2015

Cyrus K. Foroughi[#], Eric J. Blumberg[#], and Raja Parasuraman

[#] denotes co-first authors, order determined by coin flip

Abstract

Interruptions to ongoing mental activities are omnipresent in our modern digital world, but the brain networks involved in interrupted performance are not known, nor have the activation of those networks been modulated. Errors following interruptions reflect failures in spatial memory, whose maintenance is supported by a brain network including the right posterior parietal cortex (PPC). The present study therefore used bi-directional transcranial Direct Current Stimulation (tDCS) of right PPC to examine the neuromodulation of spatial errors following interruptions, as well as performance on another PPC-dependent task, mental rotation. Anodal stimulation significantly reduced the number of interruption-based errors and increased mental rotation accuracy whereas cathodal stimulation significantly increased errors and reduced mental rotation accuracy. The results provide evidence for a causal role of the PPC in the maintenance of spatial representations during interrupted task performance.

Introduction

Interruptions to our ongoing mental activities are omnipresent in modern life—whether from cell phones, emails, navigation devices, alarms, etc. An observational study found that people are interrupted an average of 12 times per hour at work in our increasingly digital world (Cades et al., 2010), with such interruptions often leading to errors. Another study of nurses from two hospitals showed that interruptions increased both procedural (e.g., fail to check patient identification) and clinical judgment errors (e.g., give the wrong drug or wrong dose), with potentially life threatening consequences (Westbrook et al., 2010). Interruption-related errors are ubiquitous and appear to be unrelated to individual expertise (e.g., Dismukes et al., 2012; Prakash et al., 2014).

Ratwani and Trafton (2008) used eye-tracking to investigate visual search patterns of the resumption process in a simple data entry task following an interruption. The primary task required participants to place randomly generated numbers into one of fifteen different locations on a computer display following preset rules. The interruption task involved either solving math problems or performing mental rotation. Both interruption tasks impaired resumption accuracy; compared to a non-interrupted condition, individuals fixated on a location following an interruption that was further away from the correct location. However this effect was significantly larger when the interruption involved mental rotation, suggesting that the same visuo-spatial processes involved in mental rotation are important for the resumption process. Shen and Jiang (2006) also showed that an interruption involving a spatial search significantly decreased

memory accuracy in a change detection search task. Both findings suggest that spatial representation may play an important role in guiding resumption after an interruption.

Despite the importance of interruptions in everyday life, the brain networks involved in interrupted performance are not known, nor have the activation of those networks been modulated. The present study used the latter strategy to better understand the neuromodulation of interruption performance. Active modulation of brain networks involved in spatial memory can provide direct evidence for the causal role of transient disruption of spatial representation in resumption performance following an interruption. There is considerable evidence that the posterior parietal cortex (PPC), and more specifically the intraparietal sulcus (IPS), is implicated in the maintenance of spatial representations (Cabeza and Nyberg, 2000; Champod and Petrides, 2007; Cohen and Andersen, 2002; Jonides et al., 2005).

These findings suggest that active stimulation or inhibition of the right PPC should respectively decrease or increase spatial errors during resumption after an interruption. We tested this hypothesis in the present study using transcranial Direct Current Stimulation (tDCS), which provides a method for non-invasive, bi-directional modulation of brain function (Antal et al., 2001; Nitsche and Paulus, 2000). The polarity of stimulation plays a critical role in how tDCS affects performance; typically anodal (positive) stimulation over a particular cortical site increases cortical excitability and can improve performance (Coffman et al., 2014; Cohen Kadosh et al., 2010; Parasuraman and McKinley, 2014), whereas cathodal (negative) stimulation over the cortical area inhibits excitability and may lead to decrements in task performance (Bikson et al., 2004;

Coffman et al., 2014). We therefore hypothesized that anodal stimulation of the right PPC would reduce spatial errors following an interruption, whereas cathodal stimulation of the same brain region would increase errors. For the primary task, we used the *Financial Management Task*, a complex computer-based task (Trafton et al., 2011; see Figure 1) commonly used in studies of interrupted task performance and the resumption process (Brumby et al., 2013; Trafton et al., 2003). The task requires participants to store information in memory and then place that information into different locations on the computer screen, either uninterrupted or following an interruption. The interruption task required participants to solve math problems.

Our main hypothesis was that compared to a sham (placebo) group, anodal stimulation of right PPC would reduce spatial errors following an interruption, whereas cathodal stimulation would increase errors. Additionally, as a manipulation check, we also used a mental rotation task, given the causal role of the PPC in mental rotation has been previously established in a repetitive transcranial magnetic stimulation (rTMS) study (Harris and Miniussi, 2003). We hypothesized that compared to a sham (placebo) group, anodal stimulation of the right PPC would improve mental rotation accuracy, whereas cathodal stimulation would decrease accuracy. A final hypothesis, based on previous findings (e.g., Blumberg et al., in press; Tseng et al., 2012), was that lower performing individuals (those with more interruption-related errors and lower mental rotation scores) receiving anodal stimulation of the right PPC would exhibit the greatest improvements in resumption performance compared to higher performing individuals.

Methods

Participants. The George Mason University Institutional Review Board (IRB) approved this study. Forty-six right-handed students ($M = 19.74$ years, $SD = 2.2$, 35 females, 11 males) from George Mason University participated for course credit. One participant was excused from the study because of problems with the stimulation delivery device and the data were excluded from all analyses. Participants were randomly assigned to one of three groups: anodal stimulation ($n = 15$), cathodal stimulation ($n = 15$), and sham stimulation ($n = 15$) to the posterior parietal cortex. Sample size was determined based on effect sizes reported in previous modulation studies using tDCS over the PPC (e.g., Sparing et al., 2009; Stone and Tesche, 2009). Thus, the group size was set *a priori* at 15 resulting in a total sample size of 45.

Transcranial Direct Current Stimulation. An ActivaDose II Iontophoresis Delivery Unit was used to deliver constant current via two electrode pads housing saline-soaked sponges with an 11cm^2 contact area. One electrode was placed on the scalp (directly between sites CP4 and P4, identified as CPP4 of the 10-5 EEG Scalp Recording System; Oostenveld and Praamstra, 2001)—this is the same right parietal site previously found to decrease mental rotation performance in an rTMS study (Harris and Miniussi, 2003). The reference electrode was placed on the contralateral (left) upper arm. The electrodes were attached to each participant using velcro wraps. Participants received 2 mA of current for 30 minutes in the active stimulation group, an amount found to be safe in a number of previous studies (Coffman et al., 2014). Participants in the sham group received a 2 mA ramp up (30 sec) and then immediate ramp down (6 sec) of current,

receiving the full 2 mA for a very short period of time (< 5 sec). This short stimulation duration (applied prior to the beginning of the experimental tasks) is enough to cause similar skin sensations compared to the active stimulation group, but is generally insufficient to produce lasting causal effects on cortical excitability (Coffman et al., 2014).

Financial Management Task. The goal of this task was to successfully complete a client stock order as quickly and accurately as possible. To do this, participants first selected a stock order to buy or sell and then filled in twelve pieces of information relevant to that order. This information was placed, one component at a time, in one of twelve different boxes located throughout the computer screen. Importantly, participants had to place this information in order starting with the upper left box (labeled 1 in Figure 6), then the upper right box (labeled 2 in Figure 6), and so on, until all twelve pieces of information were correctly placed. If a participant went to the wrong box (i.e., made an error), the participant was unable to fill in the information. Instead, the box that the participant was supposed to go to would turn red. This indicated that an error was made and that the participant would need to place information in the red box before moving on.

The screenshot displays a financial management application with the following components and numbered callouts:

- 1**: Stock Symbol input field (Symbol: dropdown)
- 2**: Client input field (Client: dropdown)
- 3**: Quantity input field (Quantity: 7700)
- 4**: Current Stock Price input field (Current Stock Price: dropdown)
- 5**: Requested Price input field (Requested Price: \$9.93)
- 6**: Associate input field (Associate: dropdown)
- 7**: Order Info input field (Order #: dropdown)
- 8**: Margin input field (Margin: Yes)
- 9**: Margin Rate input field (Margin Rate: dropdown)
- 10**: Stock Exchanges input field (Exchange: dropdown)
- 11**: Transaction input field (Buy or Sell: dropdown)
- 12**: Review input field (Review: dropdown)

Stock Information Panel (Center):

- Macrohard MCH**: Associate: Fred McTavish, Margin Rate: 12%, Current Price: \$10.18
- Gentech GNT**: Associate: Stephen Smith, Margin Rate: 5.5%, Current Price: \$48.86
- Technonics TTN**: Associate: Fran Mabel, Margin Rate: 15%, Current Price: \$101.24

Performance Bar: Time Elapsed: 00:00:06, Avg Time Per Transaction: 00:00:00

Order Ticker (Bottom):

- Macrohard**: \$9.88 | North American | Sam Spade | Sell | Shares: 7700 | Margin: Yes | Order: 1 | Alert Manager
- Gentech**: \$50.32 | Middle Eastern | John Doran | Buy | Shares: 3000 | Margin: Yes | Order: 2 | Alert Manager
- Technonics**: \$100.98 | Asian | Susan Quince | Sell | Shares: 8400 | Margin: Yes | Order: 3 | Alert Manager
- Macrohard**: \$9.93 | Asian | Roger Waters | Sell | Shares: 9000 | Margin: Yes | Order: 4 | Alert Manager

Active Order:

- Macrohard**: \$9.88 | North American | Sam Spade | Sell | Shares: 7700 | Margin: Yes | Order: 1 | Alert Manager

Figure 6: The Financial Management Task.

Interruptions occurred randomly throughout the duration of the financial management task. The interruption task, which replaced the primary task screen, required participants to answer multiple choice addition (math) problems that were located on the bottom, center of the computer screen for the entire duration of the 15 sec interruption (see Figure 7). Participants answered the problems at their own pace. Immediately following the interruption, the primary task screen reappeared and participants were able to continue the primary task. Importantly, when returning to the primary task following an interruption, all of the information that was on the screen before the interruption occurred was gone. Therefore, participants needed to remember

where they left off to successfully re-engage the task without making an error (see Trafton et al., 2011 for more information about the Financial Management task).

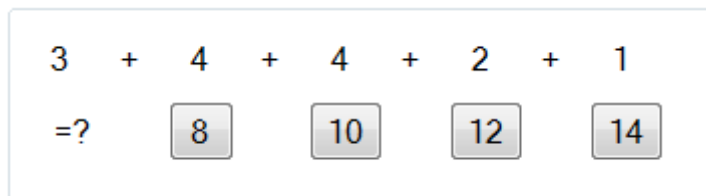


Figure 7: The interruption task. The interruption task replaced the screen for the duration of each interruption.

Mental Rotation Task. The Vandenberg and Kuse Mental Rotation Test, Version C (MRT-C; Peters et al., 1995; Shepard and Metzler, 1978; Vandenberg and Kuse, 1978) was used to assess mental rotation ability. This version, unlike versions A and B, and most other mental rotation tests, rotates objects around both the vertical and horizontal axes, thereby increasing the difficulty of the test. The use of this version of a mental rotation task made it less likely that individuals would be at ceiling levels of performance at baseline, thus allowing for assessment of potential improvement with anodal tDCS.

In this version, each question has one template and four possible answers (i.e., objects that when rotated match the base stimuli or objects that when rotated do not match the base stimuli). For every question, there are exactly two correct matching answers. To successfully answer the question, you must correctly identify both of the matching stimuli.

Design and procedure. Participants first signed a consent form and were then instructed on how to complete the mental rotation task (MRT-C). Each participant

completed all four practice problems with the experimenter. Following practice, participants completed the first half of the test (i.e., problems 1-12). Participants were given five minutes to complete the problems. Participants were then trained on the Financial Management task to ensure that they were familiar with the task and minimize potential learning effects. Participants were instructed to complete both tasks (primary and interruption) as quickly and accurately as possible. The trials took approximately 75 seconds each to complete with interruption time removed. During baseline, participants completed 9 total trials with 27 total interruptions. Interruptions occurred randomly after the successful completion of any one box. Researchers ensured the participants were actively completing the interruption task.

Following the baseline block, the tDCS unit was set up and stimulation was applied. The DCS Sensation Questionnaire (Scheldrup et al., 2014) was administered at three time points throughout the stimulation block. This questionnaire is used to gauge the amount of itching, heat/burning, and tingling each participant felt as a result of the stimulation; participants responded by selecting their perceived sensations on a 11-point Likert scale where 0 represented no sensation at all and 10 represented the most intense sensation imaginable. This questionnaire is required by the George Mason University IRB to ensure participants safety during the experiment; thus, the data were not analyzed post-hoc. Once the current value reached 2.0 mA, the DCS Sensation Questionnaire was administered. Afterwards, participants completed the stimulation block of the Financial Management task, which was identical to the design of the baseline block (i.e., 9 trials with 27 random interruptions). The DCS Sensation Questionnaire was then administered

a second time. Next, participants completed the second half (i.e, problems 13-24) of the mental rotation task (MRT-C). Once complete, the final DCS Sensation Questionnaire was administered. The tDCS unit was turned off and detached from the participant. They were thanked for their participation, given a short debrief about the experiment, and then left.

Measures. An error occurred when a participant attempted to place information in an incorrect box following an interruption; therefore, a maximum of 27 errors could be committed. Average trial completion time was computed in seconds for each participant. Performance on the interruption task was scored. Lastly, the mental rotation test (MRT-C) was scored for accuracy.

Results

Manipulation verification. We initially examined participants' engagement in the interruption task. Participants successfully answered 83% ($SD = 5.1$, range: 74-96%) of the multiple choice math problems, suggesting they were actively engaged in the interruption task and not rehearsing the primary task.

To determine if interruptions affected performance on the primary task, we compared the number of errors a participant made when completing the task without interruptions ($M = .47$, $SD = .66$) to the number of errors a participant made following an interruption ($M = 12.71$, $SD = 2.81$) in the baseline trials. A paired samples t -test confirmed that the interruptions negatively affected performance, $t(44) = 27.51$, $p < .001$, $d = 4.10$.

Before determining if tDCS affected performance, we needed to ensure that no baseline differences existed between the three stimulation groups (anodal, cathodal, and sham). A one-way analysis of variance (ANOVA) revealed no differences existed in the number of errors made during the baseline trials between groups, $F(2,42) = 0.076, p > .250, \eta^2_{\text{partial}} = .004$, see Figure 8A. A separate one-way ANOVA of the MRT-C revealed no differences existed in baseline scores (i.e., problems 1-12) between groups as well, $F(2,42) = .056, p > .250, \eta^2_{\text{partial}} = .003$, see Figure 8B.

Interruption-related errors. A mixed-design ANOVA was performed to determine whether tDCS affected the number of errors participants made following an interruption. The within-subject factor was block (baseline and stimulation) and the between-subject factor was stimulation group (anodal, cathodal, and sham). Levene's test indicated equal error variances in both the baseline ($F = .09, p > .250$) and stimulation ($F = .84, p > .250$) data. There was a significant main effect of block, $F(1,42) = 8.68, p = .005, \eta^2_{\text{partial}} = 0.17$ and a significant interaction between block and stimulation group, $F(2,42) = 26.93, p < .001, \eta^2_{\text{partial}} = 0.56$, see Figure 8A.

Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the anodal stimulation group revealed that significant differences existed between the number of errors in baseline ($M = 12.67, 95\% \text{ CI } [11.17, 14.16]$) and stimulation ($M = 9.8, 95\% \text{ CI } [8.35, 11.25]$), $t(14) = 7.56, p < .001, d = 1.95$. Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the cathodal stimulation group revealed that significant differences existed between the number of errors made at baseline ($M = 12.93, 95\% \text{ CI } [11.44, 14.43]$) and during stimulation ($M = 13.8, 95\% \text{ CI } [12.35, 15.25]$), $t(14) =$

2.29, $p = .027$, $d = .59$. No differences existed within the sham group ($p > .250$). On average anodal stimulation resulted in three fewer spatial errors (i.e., 23% reduction), whereas cathodal stimulation increased spatial errors by one (i.e., 7% increase), and sham did not change performance.

Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the stimulation block revealed that significant differences existed between the number of errors committed in the anodal stimulation group ($M = 9.8$, 95% CI [8.35, 11.25]) compared to both the cathodal stimulation group ($M = 13.8$, 95% CI [12.35, 15.25]), $t(28) = 3.94$, $p = .001$, $d = 1.49$) and sham stimulation group ($M = 12.6$, 95% CI [11.15, 14.05], $t(28) = p = .026$, $d = 1.04$), but not between the cathodal and sham stimulation groups ($p > .250$; see Figure 2A). On average individuals receiving anodal stimulation made three fewer errors (i.e., 22% reduction) in the stimulation block compared to individuals in the sham stimulation group and four fewer errors (i.e., 29% reduction) compared to individuals in the cathodal stimulation group.

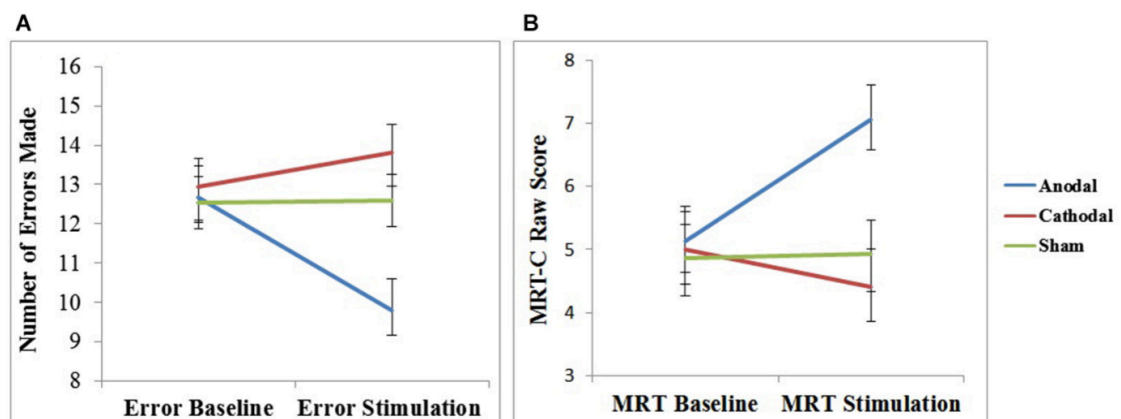


Figure 8: The mean number of errors made (fewer errors represent improved performance) following an interruption (A) and the mean raw scores (higher scores represent improved performance) on the mental rotation task (B) during baseline and stimulation blocks.

We also correlated the number of errors each participant in the anodal stimulation group made at baseline to their change in errors (stimulation minus baseline), revealing a significant correlation, $r(14) = -.61, p = .016, R^2 = .37$. This suggests that individuals with worse initial performance (i.e., more errors in baseline) benefitted the most from anodal stimulation, see Figure 9A.

Mental Rotation Task (MRT-C). A mixed-design ANOVA was performed to determine whether tDCS affected performance on the mental rotation task. The within-subject factor was block (baseline and stimulation) and the between-subject factor was stimulation group (anodal, cathodal, and sham). Levene's test indicated equal error variances in both the baseline ($F = .218, p > .250$) and stimulation ($F = .074, p > .250$) data. There was a significant main effect of block, $F(1,42) = 8.32, p = .006, \eta^2_{\text{partial}} = .17$ and a significant interaction between block and stimulation group, $F(2,42) = 21.96, p < .001, \eta^2_{\text{partial}} = .51$, see Figure 9B.

Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the anodal stimulation group revealed that significant differences existed between mental rotation accuracy during baseline ($M = 5.133, 95\% \text{ CI } [4.00, 6.27]$) and in stimulation ($M = 7.07, 95\% \text{ CI } [5.96, 8.17]$), $t(14) = 6.90, p < .001, d = 1.78$. Tests of simple main using a Bonferroni correction ($\alpha = .05$) effects within the cathodal stimulation group revealed that significant differences existed between mental rotation accuracy at baseline ($M = 5.00, 95\% \text{ CI } [3.86, 6.14]$) and during stimulation ($M = 4.40, 95\% \text{ CI } [3.29, 5.51]$), $t(14) = 2.14, p = .038, d = .55$. No differences existed within the sham group ($p > .250$). On average participants in the anodal stimulation group improved mental rotation score by

two (i.e., 27% improvement), cathodal stimulation decreased mental rotation score by half a point (i.e., 12% reduction), and sham did not change performance.

Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the stimulation block revealed that significant differences existed between MRT-C scores in the anodal stimulation group ($M = 7.07$, 95% CI [5.96, 8.17]) compared to both the cathodal stimulation group ($M = 4.40$, 95% CI [3.29, 5.51], $t(28) = 3.44$, $p = .004$, $d = .89$) and sham stimulation group ($M = 4.93$, 95% CI [3.83, 6.04], $t(28) = 2.75$, $p = .026$, $d = .71$). Scores in the cathodal stimulation group were not significantly different from sham ($p > .250$; see Figure 9B). On average individuals receiving anodal stimulation scored two points higher (i.e., 30% improvement) on the mental rotation task compared to individuals in the sham stimulation group and two and a half points higher (i.e., 38% improvement) than individuals in the cathodal stimulation group.

Additionally, we correlated each participants MRT-C score in the anodal stimulation group at baseline to their change in MRT-C score (stimulation minus baseline), revealing a significant correlation, $r(14) = -.47$, $p = .04$, $R^2 = .22$, however this effect is largely driven by one participant given the relatively low amount of variability ($s^2 = 4.5$) in MRT-C scores at baseline, see Figure 9B.

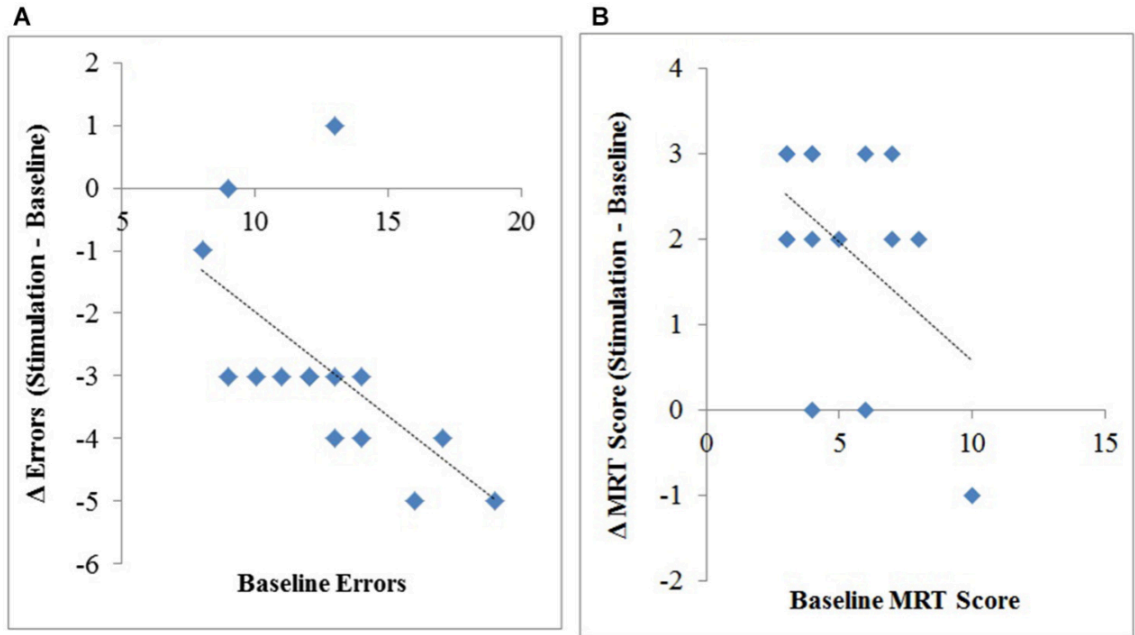


Figure 9: Change (stimulation - baseline) in interruption related errors (A) and MRT scores (B) plotted against the number of errors (A) and mean mental rotation scores (B) at baseline.

Completion time. To determine whether tDCS affected average trial completion time, a mixed-design ANOVA was performed to determine whether tDCS affected average trial completion time across all three groups, with the within-subject factor being block (baseline and stimulation) and the between-subject factor being stimulation group (anodal, cathodal, and sham). Levene's test indicated equal error variances in both the baseline ($F = .859, p > .250$) and stimulation ($F = .331, p > .250$) data. There was a main effect of block, $F(1,42) = 7.69, p = .008, \eta^2_{partial} = 0.16$ and a significant interaction between block and stimulation group, $F(2,42) = 7.169, p = .002, \eta^2_{partial} = 0.25$.

Tests of simple main effects using a Bonferroni correction ($\alpha = .05$) within the anodal stimulation group revealed that a significant difference existed ($p < .001$) between average trial completion time in baseline ($M = 77.07s, 95\% CI [72.69, 81.45]$) and

average trial completion time in stimulation ($M = 72.13s$, 95% CI [67.93, 76.34]). No differences existed between baseline and stimulation average completion time in the cathodal or sham stimulation groups ($p > .250$ for both). That is, individuals in the anodal stimulation group completed the task more quickly while stimulated compared to baseline. This may not be a surprise as these same individuals made fewer errors and making an error would result in more time spent on that trial.

Mental rotation and errors. Given that the processes that guide resumption after an interruption may recruit the same neural substrates as mental rotation, it is likely that changes in one (mental rotation) may be reflected in changes in the other (resumption process, i.e., errors). To examine the extent to which they are related, we correlated the difference scores (stimulation minus baseline) for both measures, including all three stimulation groups. The analysis revealed a significant correlation, $r(45) = -.72, p < .001$, $R^2 = .52$, see Figure 10. The magnitudes of the changes in performance for each measure were significantly related.

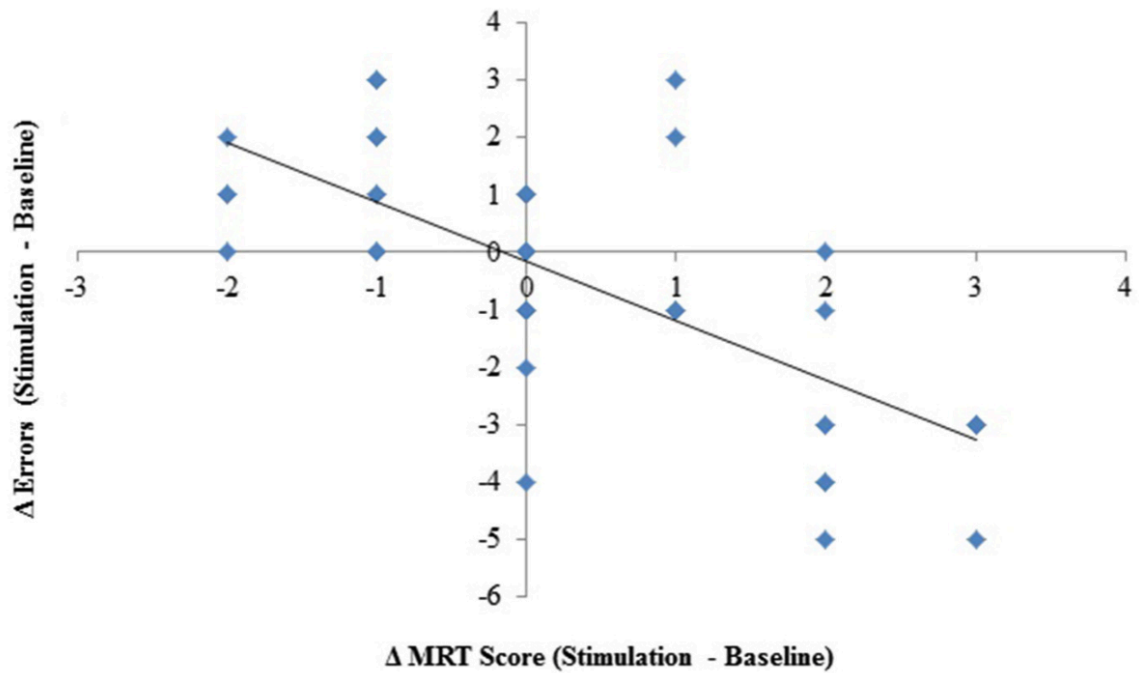


Figure 10: Change (stimulation - baseline) in interruption related errors plotted against change in mental rotation scores.

Discussion

The brain networks involved in the interruption process are not known and the neuromodulation of those networks has not been previously been examined. Given that spatial representations aid in the resumption process after an interruption (Ratwani and Trafton, 2008) and that the right posterior parietal cortex is activated during the maintenance of spatial representations (Cabeza and Nyberg, 2000; Cohen and Andersen, 2002), we hypothesized that anodal stimulation of this region would reduce the number of errors by enhancing memory for spatial information. Additionally, we hypothesized that cathodal stimulation applied to the PPC would increase the number of errors by diminishing spatial representation ability. The results supported these hypotheses: anodal stimulation of right PPC significantly reduced the number of interruption-related errors

while increasing mental rotation accuracy, whereas cathodal stimulation of the same region had the opposite effects, and sham stimulation did not affect either performance measure.

To our knowledge, this is the first demonstration of bi-directional effects of activation and inhibition of PPC on spatial errors following interruptions and on mental rotation performance. The results provide evidence for a causal role for the PPC in the maintenance of spatial representations during interrupted task performance. We also found that the magnitude of the changes in interruption-related errors with tDCS was significantly related to changes in mental rotation performance, as measured by the MRT-C. Specifically, individuals who improved in mental rotation accuracy exhibited a reduction in the number of interruption errors to a similar degree. This finding supports the idea that spatial representation ability, as assessed using the MRT-C, guides resumption after an interruption. The findings are unlikely to reflect a placebo effect given that sham stimulation did not affect performance.

Additionally, we found that lower performing individuals at baseline testing, measured by both the number of interruption errors and MRT-C, showed the greatest improvements in performance following anodal stimulation of PPC. This result suggests that individual differences in baseline ability may modulate the behavioral effects of tDCS. Such “cognitive equalizing” due to tDCS was also previously reported in a study of change detection (Tseng et al., 2012). Our finding that lower-performing individuals showed greater benefits of tDCS than higher-performing ones diminishes concerns that tDCS and other non-invasive brain stimulation techniques may widen or exacerbate

ability differences in the population, thereby leading to greater social inequality (Cohen Kadosh et al., 2012).

During stimulation, performance in both the interruption and mental rotation tasks was significantly greater in the anodal group than in the cathodal and sham groups. However, whereas cathodal stimulation significantly reduced performance on both tasks compared to baseline, the cathodal and sham groups did not differ significantly following stimulation. Some other previous tDCS studies have also found that effects of cathodal stimulation are often less pronounced than anodal effects (Coffman et al., 2014; Fregni et al., 2005; Tseng et al., 2012). Another limitation in the present study is that although we designed the tDCS montage to target the IPS based on current modeling (Datta et al., 2009) and previous literature (Harris and Miniussi, 2003), the relatively non-focal nature of tDCS means that other brain regions could also have been stimulated and could have played a role in the effects. In addition, each participant received only one type of stimulation; therefore it is possible that other individual differences that were not assessed in this study could have been responsible for the differential effects of anodal and cathodal stimulation on interruption errors and mental rotation performance. Additionally, math problems were included as the interruption task in the present study even though mental rotation has been shown to interfere with the resumption process to a greater extent (Ratwani and Trafton, 2008). Given that tDCS produced significant effects in resumption performance in the less interfering task (math problems), potentially greater effects may be found with mental rotation. Finally, many tasks that can be interrupted exist (e.g., giving verbal commands) that many not benefit from anodal

stimulation of the PPC when interrupted because the task is not spatial in nature.

Therefore, we cannot generalize our results to all tasks and forms of interruption.

This is the first study to show how noninvasive brain stimulation can reduce human error following interruptions. Interruptions are unavoidable, and while many only cause delays or reduce efficiency, they can also lead to serious errors (Prakash et al., 2014; Westbrook et al., 2010). Importantly, tDCS offers a safe, inexpensive, and easy to administer method to reduce errors during the resumption process. This study offers bi-directional causal support for the role of PPC in mental rotation ability and in the resumption process. Important issues that need to be addressed in future research include retention of tDCS-induced benefits on interruption performance and their transfer to other tasks (Parasuraman and McKinley, 2014).

Anodal stimulation reduces complex task performance: The importance of evaluating individual differences in tDCS research

Abstract

Objective: We investigated how transcranial direct current stimulation impacts neurophysiological function in the performance of a complex task where task load was systematically manipulated. **Method:** Participants were randomly assigned to one of three right parietal stimulation conditions: anodal, cathodal or sham. They completed a set of cognitive batteries prior to stimulation. Participants then completed a real-time strategy simulation while simultaneously being stimulated and cerebral blood flow velocities being recorded. **Results:** Cathodal stimulation significantly improved performance compared to anodal and sham. We then categorized participants using a cluster analysis to control for individual differences in baseline abilities. The subsequent results revealed that anodal stimulation significantly reduced performance for the high ability individuals. There were no differences in cerebral blood flow velocities between stimulation conditions. **Conclusions:** Anodal stimulation decreased performance potentially by increasing neural noise, thus reducing executive control abilities. The results highlight a need in this field to measure and control for individual differences in cognitive abilities and baseline task performance as both can moderate tDCS-based effects.

Introduction

Transcranial Direct Current Stimulation. Transcranial electrical stimulation has risen in popularity over the past decade as an increasing number of studies report facilitatory effects across a wide range of tasks (Coffman, Clark, & Parasurman, 2014; Nitsche & Paulus, 2000). Transcranial direct current stimulation (tDCS), a form of non-invasive brain stimulation has been at the center of this revival due to its portability, inexpensiveness, and ease of use. tDCS is an electrically based stimulation technique that typically includes one positive and one negative electrode. The electrodes are placed in a montage on the skull and body and are typically aimed to target a specific cortical region. Current flows from the anodal (positive) electrode through skull and brain to the cathodal (negative) electrode. tDCS has been reported to be a safe way to modulate both motor and cognitive abilities (Bikson Datta, & Elwassif, 2009).

tDCS-based behavioral effects have been reported in tasks ranging from working memory (Andrews Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Brunoni & Vanderhasselt, 2014) and cued attention (Tanoue, Jones, Peterson, & Berryhill, 2012; Weiss & Lavidor, 2012) to attention tracking (Blumberg, Peterson, & Parasuraman, 2015) and multi-tasking (Blumberg et al., 2014; Scheldrup et al., 2014). Although the list of reported findings continues to increase (over 3000 tDCS studies published in 2015-Google Scholar Search), there is strong evidence suggesting that these effects are more complex in nature than initially thought (Brunoni & Vanderhasselt, 2014; Horvath, Forte, & Carter, 2014; Krause & Cohen Kadosh, 2014).

Cognitive effects of tDCS appear to be modulated by two inter-individual difference factors, those stemming from general differences in cognitive task performance along with specific individual differences that appear to be mediated by the stimulation itself. Regarding individual differences in performance, such differences have been observed in a wide range of tasks and jobs (Humphreys & Revelle, 1984; Malinowski & Gillespie, 2001; Motowildo, Borman, & Schmit, 1997). The individual differences appear to be both task-specific and trait-based, highlighting the importance of capturing such information. Importantly, individual differences appear to be related to underlying differences in neurophysiological function, such as the activation of specific brain regions or networks. As examples, evidence from fMRI studies demonstrate that individual cognitive abilities in spatial memory and attention can be closely linked to activation in the parietal cortex (Colby & Goldberg, 1999; Culham & Kanwisher, 2001; Todd & Marois, 2004) while response inhibition can be measured through activation in the lateral prefrontal cortices (Konishi et al., 1999; Liddle, Kiehl, & Smith, 2001).

There are also individual differences in how tDCS affects cognition. Individual differences that have a reported effect include baseline task-related ability (Blumberg et al., 2014; Blumberg et al., 2015; Tseng et al., 2012), experience (Bullard et al., 2011), and task difficulty (Berryhill & Jones, 2014; Blumberg et al., 2015). Additionally education level (Jones & Berryhill, 2012), working memory capacity (Berryhill & Jones, 2012), and genotype (Plewnia et al., 2013) have all been reported to moderate tDCS-based effects. TDCS has been reported to provide the greatest behavioral benefit to individuals who were lower baseline performers prior to the stimulation.

Given that tDCS-based cognitive effects appear to be modulated by task difficulty (Berryhill & Jones, 2014; Blumberg et al., 2015) and individual differences in baseline ability (Blumberg et al., 2014; 2015; Tseng et al., 2012), an effective approach in designing a study may be to include a task that directly modulates task load. In this way as task load is modulated, simultaneous recordings of cortical activation can be mapped on, providing robust findings relating task load, performance, and neurological function in the performance of a complex task.

Unfortunately, relatively little is known about how direct current stimulation impacts the underlying neurological function in humans. Evidence from single cell animal studies illustrated that cell membranes under the anode depolarize while cell membranes under the cathode hyperpolarize. Anodal stimulation is generally thought to decrease resting membrane potentials leading to excitatory effects while cathodal stimulation is thought to increase resting membrane potentials leading to inhibitory effects (Antal, Nitsche, & Paulus, 2001; Bindman, Lippold, & Redfearn, 1964). The electric current is also thought to impact synaptic efficacy (Rahman et al., 2013), in turn increasing the neurons sensitivity, leading to an increased likelihood of firing while performing a task. (See Bikson and colleagues, 2004, for a deeper explanation on the neural affects of tDCS). However, none of this evidence addresses how tDCS modulates activity in brain regions mediating a given cognitive function.

Recent research has used magnetic resonance imaging to measure the effects of tDCS (local neuronal excitability) on both cortical activity (i.e., changes in BOLD-fMRI signal and network connectivity) and performance (Alekseichuk, Diers, Paulus, & Antal,

2015; Callan, Falcone, Wada, & Parasuraman, 2016; Meinzer et al., 2012; Meinzer, Lindenberg, Antonenko, Flaisch, & Flöel, 2013). Alekseichuk and colleagues identified that tDCS applied over the occipital cortex induced increased BOLD signals in the occipital cortex during the presentation of visual stimuli (2015). The reported BOLD signal changes occurred in occipital areas theorized to be along the path of current flow. It should be noted that the task used in their experiment was purely perceptual, so it should not be inferred that their results would directly transfer to more cognitively demanding tasks.

Callan and colleagues reported an increase in resting state functional connectivity during and following right parietal anodal stimulation during a visual search task (2016). Anodal stimulation was found to significantly modulate spontaneous brain activity in an area around the anodal electrode (i.e., precuneus) while also increasing resting state functional connectivity between the precuneus and a cluster related to visuospatial processing. The authors interpreted their findings to mean that anodal stimulation increased spontaneous neuronal firing as a result of the anodal stimulation.

In a series of experiments, Meinzer and colleagues reported that tDCS decreased the BOLD signal under the anodal electrode but also increased distributed cortical activation compared to sham in a word generation task (2012; 2013). Their neurophysiological effects appear to be consistent with those reporting decreased BOLD signal in fronto-parietal networks following cognitive practice and training (Chein & Schneider, 2005; Kelly & Garavan, 2005) and decreased functional connectivity following cognitive training (Strenziok et al., 2014).

Evidence from the neural efficiency hypothesis also supports these findings. The neural efficiency hypothesis suggests that cortical activation (BOLD signal) and performance are inversely related; better performance being correlated with decreased BOLD signal (Haier et al., 1988). TDCS may then be modulating one of several potential mechanisms such as cerebral blood flow, neural metabolism, and neurotrophin release, each of which have been linked to changes in BOLD signal (Markham & Greenough, 2004). However, a recent review by Neubauer and Fink (2009) reported that during more complex/difficult tasks (e.g., Raven's Progressive Matrices under time restrictions), better performance was correlated with increased cortical activation. Therefore, one might speculate that tDCS would elicit systematically different patterns of BOLD signal during the completion of complex tasks compared to visual perception or word generation.

Transcranial Doppler Sonography. We examined the underlying neurophysiological characteristics by which tDCS improves performance by using Transcranial Doppler Sonography (TCD). TCD is a noninvasive ultrasound device used to measure cerebral blood flow velocity (CBFV) changes in the brain (Aaslid, 1986; Shaw et al., 2009). The CBFV method is based upon the principle that the brain becomes more metabolically active in response to mental or physical activities. A by-product of metabolic activity in the brain is carbon dioxide, which is removed by oxygenated blood pumped to the metabolically active areas (Aaslid, 1986). Therefore, the more the brain works (high metabolic activity) the greater the blood flow velocity to remove the carbon dioxide. Given that both CBFV and the BOLD signal are related to blood oxygenation, changes seen in one may be similar to changes in the other. Hattemer and colleagues

reported that fMRI data and fTCD data correlated well during the completion of a mental rotation task (2011), therefore, it could be inferred that TCD could be able to measure tDCS-induced brain based changes.

TCD has primarily been used in the study of vigilance, or sustained attention. These studies revealed that the absolute level of blood flow velocity is directly related to increases in task difficulty (Hitchcock et al. 2003; Shaw, Finomore, Warm, & Matthew, 2012, Shaw et al. 2010; Warm, Matthew, & Parasuraman, 2009), and the vigilance decrement is paralleled by a temporal decline in cerebral hemovelocity (Shaw et al. 2009). In addition, several studies have shown that this time-on-task CBFV effect only occurs when observers are actively engaged in the task. When compared to observers performing the task, there is no decrement in CBFV in control observers who are exposed to an identical vigilance task without a work imperative (Shaw et al. 2009, Shaw et al. 2010). In all of these previous vigilance studies, CBFV recordings were taken from the middle cerebral artery (MCA), since the MCA carries about 80% of the blood within each cerebral hemisphere and can provide a global index of CBFV changes (Warm et al. 2009). Thus, one conclusion that can be drawn from these studies is that CBFV can index changes in the amount of resources needed by the brain (Shaw et al., 2012).

As mentioned previously, CBFV has traditionally been used to study resource changes in the completion of sustained attention tasks, with consistent decreases in CBFV with time on task (e.g., Helton et al., 2010). Recently, TCD has been successfully used to measure CBFV changes during task load transitions in a different context, a real-time strategy simulation (Satterfield, Ramirez, & Shaw, 2012). The researchers reported

that task performance and CBFV changed in response to changes in task load, such that as task load increased, CBFV increased. Satterfield and colleagues also noted a right lateralized effect during the high load period, such that there was greater CBFV in the right compared to the left hemisphere (2012).

TCD has the advantage of being more compatible with tDCS than other neurophysiological measures of brain activity such as electroencephalography. TDCS does not interfere with CBFV recording, as the methods work through different mechanisms (direct current and Doppler sonography, respectively). Also, functional TCD is less expensive to operate and is relatively easier to set up and administer compared to magnetic resonance imaging. In contrast, TCD is less spatially precise when compared to magnetic resonance imaging, as blood flow is measured through single arteries in each hemisphere. TCD has previously been successfully used in conjunction with tDCS in a vigilance paradigm (Nelson, McKinley, Golob, Warm, & Parasuraman, 2014). Those authors reported that tDCS decreased the rate of CBFV decline as time on task increased, a phenomenon typically found in sustained attention paradigms. Thus, CBFV was sensitive to tDCS.

Current study. Use of TCD allowed us to relate effects of tDCS to changes in CBFV during task performance under varying levels of task load. Further, by using a task in which task load was systematically varied, we assessed changes in effects of tDCS on both performance and CBFV during a transition from low to high task load. We simultaneously recorded participant CBFV to measure tDCS-induced brain-based changes during the completion of a real-time strategy simulation. The Dynamic

Distributed Decision-making simulation (DDD) was used to manipulate task load (McKendrick et al., 2013; Satterfield et al., 2012). Task load manipulations in this simulation have led to reported effects through objective, subjective, and neurophysiological measures (McKendrick et al., 2013; Satterfield, Ramirez, & Shaw, 2012).

The DDD simulation is complex and requires many different cognitive processes including spatial attention, procedural memory, executive control, attention tracking, task-switching and others. Therefore, we independently tested participants' visual attention tracking, response inhibition, and working memory capacities to better understand the extent to which these information processes contribute to DDD performance.

Given the particular cognitive processes proposed to be involved with the DDD simulation (e.g., MOT) and evidence that a similar DDD task load manipulation induced a larger right hemisphere CBFV compared to left (Satterfield et al., 2012), the right parietal cortex was targeted for stimulation. The right parietal cortex is associated with spatial processing and memory along with exogenously directed attention (Cabeza & Nyberg, 2000; Champod & Petrides, 2007; Cohen & Andersen, 2002; Jonides, Lacey, & Nee, 2005). Also, tDCS studies have reported facilitatory effects from right anodal parietal stimulation on working memory (Tseng et al., 2012) and on MOT (Blumberg et al., 2015) among others.

We hypothesized that right anodal parietal stimulation would improve performance on the DDD simulation through excitatory neuronal effects in the parietal

cortex, leading to increased right hemisphere CBFV. Conversely, we hypothesized that cathodal stimulation would reduce performance through inhibitory neuronal effects and decreased right hemisphere CBFV. Importantly, the polarity specific nature of tDCS suggests that we would expect the greatest differences in performance and CBFV between the anodal and cathodal groups, as they are theorized to induce opposite effects on cortical neurons. Although anodal and cathodal stimulation operate through the same mechanism but in functionally opposite directions, the literature reports that when compared against one another, anodal stimulation leads to larger effect sizes (Jacobson, Koslowsky, & Lavidor, 2012). Therefore, we expect the next largest difference would be between the anodal and sham conditions, followed by cathodal and sham. See Figure 11 for an illustration of the expected differences.

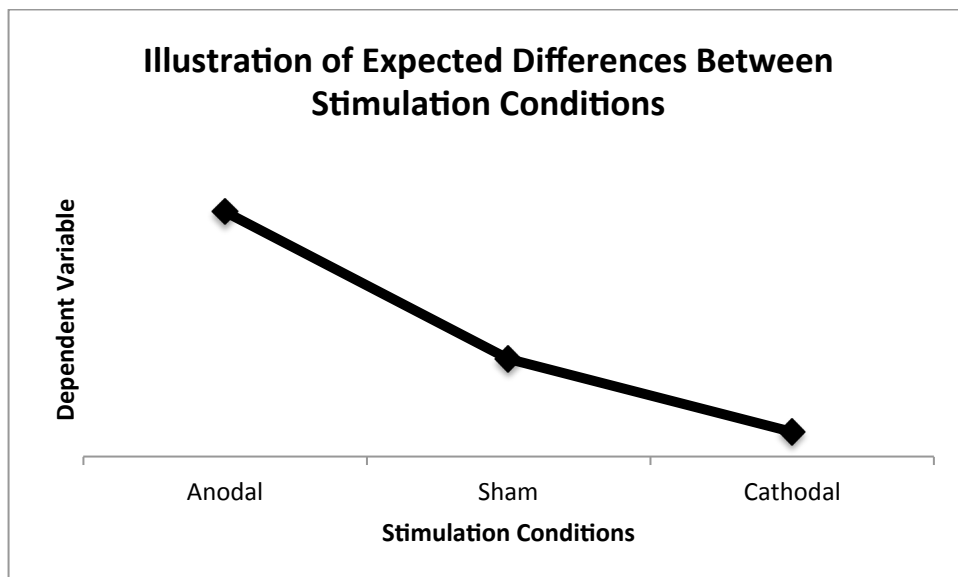


Figure 11: Illustration of expected differences between stimulation conditions. For effect, should not be interpreted literally.

Secondly, we predicted that anodal stimulation would improve MOT performance compared to cathodal and sham stimulation, a finding that was previously reported by our group (Blumberg et al., 2015). We also hypothesized that cathodal stimulation would significantly reduce the flanker conflict cost compared to the anodal and sham conditions. The flanker conflict cost is a way to measure participant's attentional control/executive control. This would be consistent with research by Weiss and Lavidor (2012) reporting that cathodal parietal stimulation reduced the flanker conflict cost. Weiss and Lavidor interpreted their findings as cathodal stimulation increased attentional capacity resources by reducing the relative level of neural noise while performing the task (please see the **Discussion** section for a fuller description of this theorized effect).

Methods

Participants. Forty-five undergraduate students (26 females) participated for course credit. All participants met the inclusionary criteria: 1) right handed, 2) normal or corrected to normal vision, 3) no history of head injuries, 4) no history of seizures, 5) no history of migraines, 6) are not taking any central nervous system affecting drugs, 7) and had not participated in a brain stimulation study within the past week. The George Mason University Internal Review Board (IRB) approved this study.

Design. Participants were randomly assigned to one of three parietal stimulation conditions; anodal, cathodal, or sham. Fifteen participants were assigned to each condition.

Tasks and Equipment.

Computer. The experimental tasks were completed on a Dell 15" inch LCD monitor. Participants were positioned approximately 40 cm from the screen.

Dynamic Distributed Decision-making simulation. The DDD simulation is a real-time strategy simulation in which a human operator controls multiple vehicles in an effort to destroy incoming enemy vehicles while protecting their red zone (home base). In order for successful performance, participants needed to continuously re-prioritize the most eminent threats to the red zone and then act to destroy those vehicles. In this manner, the DDD simulation requires a high degree of task-switching or cognitive control. Participants controlled six vehicles using the mouse and enemy vehicles were programmed to fly from off-screen and through the red zone, see Figure 12. Enemy vehicles could also attack the participants' vehicles if they crossed flight paths.

The primary goal for the participants was to prevent enemy vehicles from entering the red zone. The participants' secondary goals were to destroy all enemy vehicles and protect your own vehicles from being attacked.

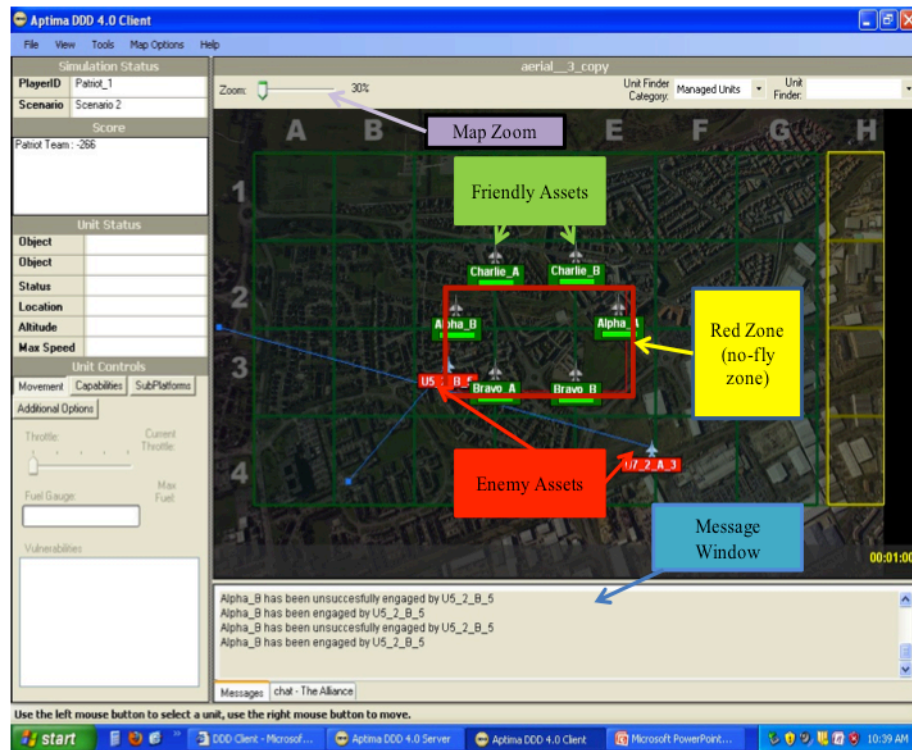


Figure 12. The DDD simulation map.

Participants completed a 20-minute DDD scenario in which task load was systematically manipulated. Task load was manipulated through pre-programmed changes in the distribution and density of incoming enemy vehicles (40 total enemies), Figure 13.

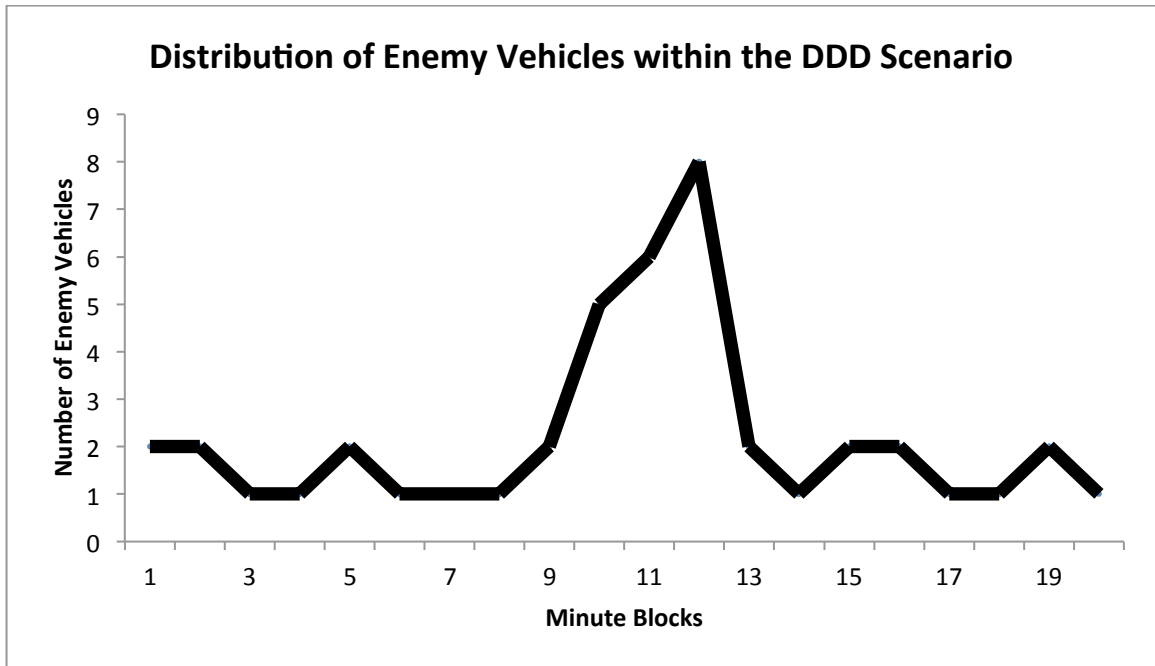


Figure 13. Distribution of enemy vehicles within the DDD scenario.

Multiple object tracking. Multiple object tracking (MOT) tasks are used to measure distributed attention (Sears & Pylyshyn, 2000). These tasks require individuals to keep track of a specific subset of items on a screen as the entire set of items move around.

Participants completed an Adobe-Flash based MOT task while seated approximately 48 cm's away from the screen. The stimuli consisted of eight green circles, each 1° of visual angle in size. At the beginning of each trial, the eight circles appeared as static images (no movement) and the target circles flashed for one second. Then all of the circles moved continuously and independently. The circles overlapped as they traveled across the screen moving at a constant rate of 13 degree/sec. The circles moved in constant directions (when they encountered the border of the screen they were

redirected in another direction based upon the angle of impact with the border). After eight seconds the circles stopped, participants then selected the target circles using the mouse. Participants tracked two circles (low task load condition) or four circles (high task load condition). Each participant completed 44 trials prior to and after stimulation. Half of the trials at each time period consisted of low and high task load trials. The trials were randomly presented within the 44 trial set.

Flanker. The Eriksen Flanker task is used to measure response inhibition and executive control (Eriksen & Eriksen, 1974). The flanker task requires participants to discriminate the direction a central arrowhead pointed arrayed in a centerline while ignoring the direction of adjacent distractor arrowheads peripheral to the centered target arrowhead. Participants completed a variation of the traditional Eriksen Flanker Task (Eriksen & Eriksen, 1974) that also included neutral trials. The version was programmed in PEBL and contained 40 congruent trials, 40 incongruent trials, and 40 neutral trials (Mueller & Piper, 2014).

Operation Span. The Operation Span is widely used to quantify working memory capacity (Conway et al., 2005; Engle, 2002). Participants completed the Shortened Operation Span task (Foster et al., 2015). The task required individuals to remember sequentially presented lists of letters (list lengths of 3, 4, 5, 6, 7) while also completing math problems during the retention interval. Participants completed one trial for each list length with a total possible score out of 25.

NASA-TLX. The NASA-TLX is a tool used to assess the amount of workload an individual experienced (Hart & Staveland, 1988). This subjective measure requires

participants to rate their perceived workload on six scales: mental demand, physical demand, temporal demand, performance, effort, and frustration.

tDCS. A MultiChannel Systems STG-4002 stimulator device delivered a constant current to two 11cm² electrode pad housing saline soaked sponges. Five mL of saline were applied to each sponge. The target electrode was placed on scalp site CP4 (10-20 EEG system) while the reference electrode was placed on the participant's contralateral shoulder (left). Scalp site CP4 is located over the right parietal cortex, and the electrode was placed over this site because previous studies have reported successful modulation of spatial attention and memory (Blumberg et al., 2015; Foroughi, Blumberg, & Parasuraman, 2015). The electrodes were secured by Surgilast tubular elastic dressing. Participants in the anodal and cathodal conditions received 1.5 mA for 20 minutes (duration of the DDD scenario). Participants in the sham stimulation condition received a 1.5mA ramp up and then immediate ramp down to 0mA at the beginning of the experiment. The ramp up/ramp down period lasted 15 seconds.

TCD. A DWL/Multi-Dop X4 TCD unit with two 2-MHz ultrasound transducers, one over the left and one over the right side of the head was used to measure CBFV through the middle cerebral arteries (MCAs). The MCAs carry approximately 80% of the blood within each hemisphere so they provide a good index of overall CBFV (Tripp & Warm, 2006).

Procedure. Upon arrival, participants read and signed the informed consent. They were each screened for the inclusionary criteria. Participants completed one block of the MOT task, followed by one block of the flanker task, and then the Operation Span.

Participants were then trained through an in-depth tutorial on how to perform the DDD task. The researcher directed participants in the simulation until they illustrated basic operational proficiency (i.e., select and move vehicles along with firing missiles).

The researcher set up the tDCS and TCD (and turned on) devices. Participants completed a two-minute CBFV resting baseline measurement while staring at a white screen. The resting baseline is common practice in TCD studies (Shaw et al., 2009; Warm & Parasuraman, 2007). Each participant then completed a five-minute low difficulty and a five-minute high difficulty practice scenario. Following the practice scenarios the participant completed a second two-minute CBFV resting baseline.

Then, the tDCS unit was turned on. The participants completed the DCS Sensation Questionnaire (Scheldrup et al., 2014) after the current reached 1.5 mA. They then completed the 20-minute DDD scenario. Following the scenario they completed the NASA-TLX. The researcher then removed the tDCS and TCD equipment. Participants filled out the DCS Sensation Questionnaire for a second time.

Each participant then completed the MOT and flanker tasks once more. The researcher administered a demographic questionnaire along with a Video Game Experience Questionnaire (Blumberg et al., 2015). Finally, the researcher read the debriefing statement to the participant.

Analysis. We conducted planned comparisons instead of omnibus tests in order to test our specific hypotheses. Planned comparisons were conducted to identify whether performance and CBFV changed in relation to the DDD task load manipulations across periods. Additional planned comparisons were conducted to identify whether stimulation

impacted performance and CBFV. We also conducted a cluster analysis to identify commonalities in participant abilities across a number of baseline factors. These analyses included a subset of the entire sample, and information about the specific group sizes can be found in Table 2. We subsequently conducted separate planned comparisons that examined the effect of stimulation on the individual clusters that were created from the analysis. More information regarding this analysis can be found below under the heading, “*Red zone incursions examining individual differences*”. We used Bonferroni corrections to adjust for multiple comparisons for each set of analyses. We chose to not do an experiment-wise correction because we were testing independent hypotheses.

Results

Following initial data inspection, two participants’ (one participant from the anodal condition and one from the cathodal condition) data were removed from the study in a family-wise manner. Their data fell below three standard deviations of the CBFV mean.

DDD. The primary performance metric for the DDD simulation was ‘red zone incursions’ as preventing enemy vehicles from entering the red zone was the primary goal during DDD gameplay. Four additional metrics were recorded and analyzed in an exploratory manner to capture potential differences in gameplay behavior. The metrics included ‘percentage of enemies destroyed’, ‘number of enemy attacks’, ‘attack efficiency’, and ‘vehicle engagement’ which is the number of moves each participant made with their own vehicles. However, the stimulation conditions did not significantly

differ along any of the metrics. The results from each of these analyses can be found in Appendix A.

Red zone incursions. The DDD performance data was segmented into three contiguous time periods of the task that varied in load. These are referred to as follows: low task load 1 (minutes 1-8), high task load (minutes 9-13), and low task load 2 (minutes 14-20). The low task load 1 and 2 periods were considered low task load periods because each minute within those periods averaged approximately one enemy vehicle. The high task load period was considered a high task load period because each minute within that period averaged approximately 4.5 enemy vehicles.

‘Red zone incursions’ occurred when a participant failed to intercept and destroy an enemy vehicle prior to the vehicle entering into the red zone. The percentage of enemy incursions into the red zone was calculated for each period by dividing the number of enemy incursions into the red zone by the total possible number of incursions (Satterfield et al., 2012). Percentage of red zone incursions have previously been used as the primary dependent outcome for DDD gameplay (McKendrick et al., 2013; Satterfield et al., 2012). Higher percentages of red zone incursions therefore indicate worse performance. Based on our hypotheses we conducted two sets of Bonferroni adjusted ($\alpha = .05$) planned comparisons.

Comparisons between periods. The first set of comparisons was done to confirm that the manipulation in DDD task load modulated performance across the periods (see Figure 14). The Bonferroni adjusted ($\alpha = .05$) comparison revealed that there were significantly more ‘red zone incursions’ during the high task load period compared to the

low task load 1 period ($p < 0.01$). There were also significantly greater ‘red zone incursions’ during high task load period compared to the low task load 2 period ($p < 0.01$). There was not a significant difference in ‘red zone incursions’ between the two low task load periods ($p = 1.00$).

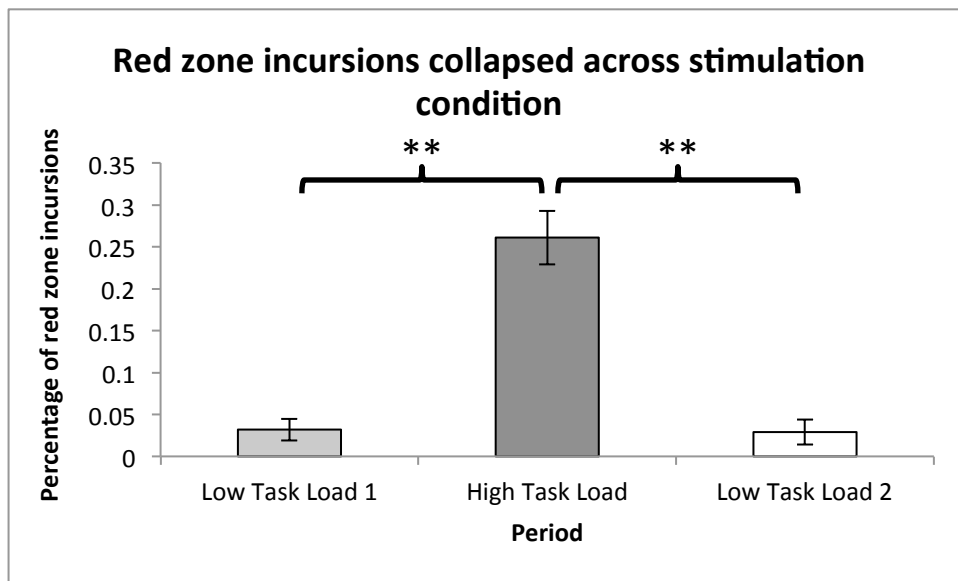


Figure 14: Red zone incursions collapsed across stimulation conditions. Significant difference in red zone incursions between high and low task load periods. Plotted with standard error of the mean. * $p < 0.05$, ** $p < 0.01$.

Comparisons between stimulation conditions. The second set of Bonferroni adjusted ($\alpha = .05$) planned comparisons were run to test whether there were significant differences in ‘red zone incursions’ between stimulation conditions, Figure 15. The comparison revealed that cathodal stimulation significantly reduced ‘red zone incursions’ compared to anodal stimulation, $p = 0.01$, as well as to sham stimulation, $p = 0.05$. There

was no difference in ‘red zone incursions’ between the anodal and sham conditions, $p = 1.00$.

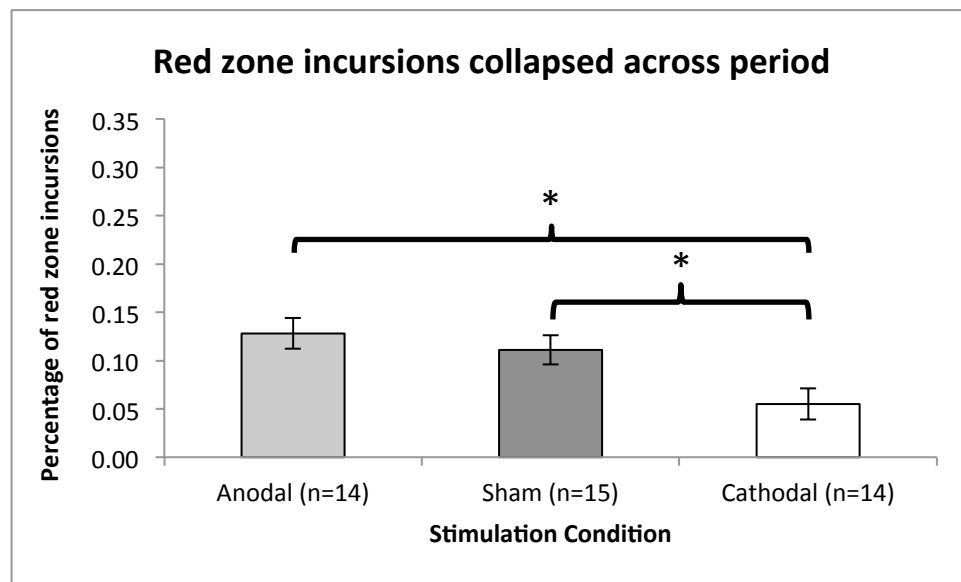


Figure 15: Red zone incursions collapsed across period. Significant difference in red zone incursions between cathodal stimulation and both anodal and sham stimulation. Plotted with standard error of the mean. * $p < 0.05$, ** $p < 0.01$.

Exploratory comparisons were also conducted between stimulation conditions, but separately for the low and high task load periods. The two low task load periods were combined into a single low task load period for the analysis, Figure 16. The Bonferroni adjusted ($\alpha = .05$) comparison during the low task load period revealed that cathodal stimulation significantly reduced ‘red zone incursions’ compared to anodal stimulation, $p = 0.04$. However, there was not a significant difference between cathodal and sham stimulation, $p = 0.17$. The comparison also did not reveal a significant difference between anodal stimulation and sham stimulation, $p = 1.00$.

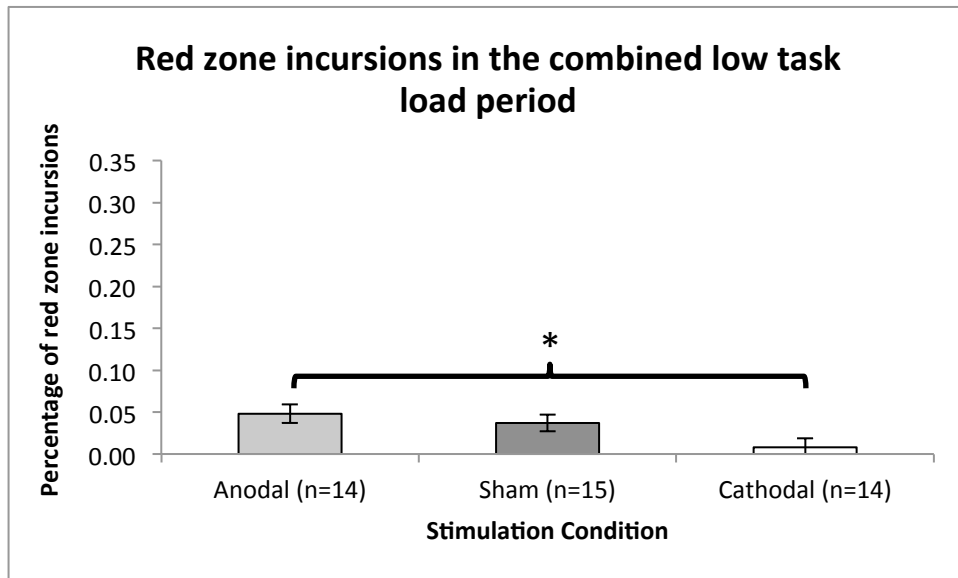


Figure 16: Red zone incursions during the combined low task load period. Significant difference between the anodal and cathodal conditions. Plotted with standard error of the mean. * $p < 0.05$.

Bonferroni adjusted ($\alpha = .05$) comparisons were also conducted for the high task load period, Figure 17. The comparisons revealed that cathodal stimulation significantly reduced ‘red zone incursions’ compared to anodal stimulation, $p = 0.05$, during periods of high task load. None of the other comparisons revealed a difference, smallest $p = 0.34$.

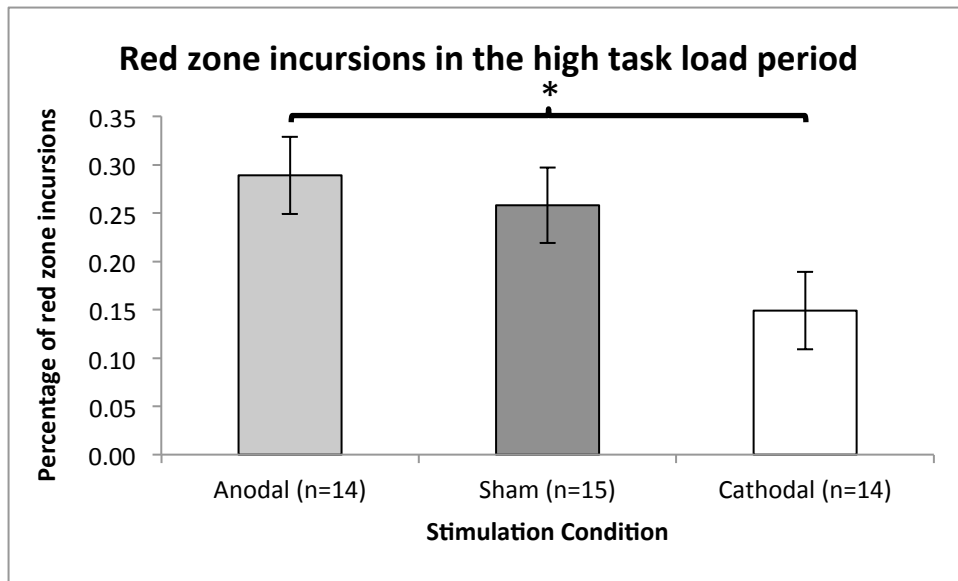


Figure 17: Red zone incursions during the high task load period. Significant difference between the anodal and cathodal conditions. Plotted with standard error of the mean. * $p < 0.05$.

Summary. The results revealed that the changes in DDD task load led to significant differences in ‘red zone incursions’ between the high and low task load periods such that performance was worse during the high task load period compared to either low task load period. We also identified that cathodal stimulation significantly decreased ‘red zone incursions’ (improved performance) compared to both anodal and sham stimulation, when collapsing across periods. However, when we examined the low and high task load periods separately, cathodal stimulation was only significantly different from anodal stimulation. The smaller group sizes for these comparisons may have contributed to the null finding between the cathodal and sham conditions. The set of findings fit with our hypothesis that the greatest difference in performance would be between the anodal and cathodal conditions, just in the direction opposite to our hypothesis.

Red zone incursions examining individual differences. Given that we were also interested in understanding how individual differences in both task specific gameplay and general cognitive abilities impact performance, we conducted follow up exploratory analyses. The comparisons were conducted with subsets of participants with low sample sizes. Because we predicted individual differences in performance might predict DDD performance, we recorded videos of the participants while they completed the practice scenarios. In viewing those videos, researchers identified a specific behavioral pattern in how participants organized and controlled their own vehicles. Participants either maintained an active spatial organization of their vehicles (i.e., a formation) around the red zone or they did not. Given that enemy vehicles could attack from any point from off the screen, maintaining a strategy provided an advantage for intercepting and destroying the enemy vehicles. Participants were categorized (post-hoc) as either being organized or unorganized. It must be noted that participants were identified as having an organized or unorganized strategy in using their vehicles during the practice scenarios that took place prior to stimulation. Therefore, stimulation cannot account for observed differences in gameplay ‘organization’.

In addition, we conducted an exploratory 2-Step Cluster Analysis in SPSS to identify commonalities in participant abilities across a number of factors. The cluster analysis classified data values into “clusters” based upon relationships between the variables. The analysis was initially performed using each participant’s baseline flanker conflict cost, baseline MOT accuracy (under both low and high task load), Operation Span score, self-report of First Person Shooter Experience, ‘red zone incursions’ during

the high task load practice, and ‘organization’. The most parsimonious cluster analysis included baseline flanker conflict cost, baseline MOT accuracy under low task load, Operation Span score, and the subjective judgment of ‘organization’.

The cluster analysis produced two clusters. The first cluster included participants who exhibited lower flanker conflict costs ($m = 50.24$, $SD = 23.92$), higher MOT accuracies under low task load ($m = 0.92$, $SD = 0.05$), higher Operation Span scores ($m = 16.62$, $SD = 5.15$), and those who maintained a spatial organization of their vehicles. The second cluster included participants who exhibited higher flanker conflict costs ($m = 69.82$, $SD = 22.89$), lower MOT accuracies under low task load ($m = 0.82$, $SD = 0.12$), lower Operation Span scores ($m = 15.22$, $SD = 6.0$), and those who did not maintain a spatial organization of their vehicles.

Given the behavioral characteristics described by each cluster, a potentially shared cognitive process may be the basis of the differences between them. The flanker and MOT tasks both require participants to attend to specific visuospatial components on the screen while ignoring other sources of visual distraction. The Operation Span requires participants to rehearse information in memory while simultaneously performing a secondary visual task. The cognitive process common to these tasks appears to be the ability to suppress processing of distractions, also known as executive control. Such ability is fundamental to cognition (Berry, Zanto, Rutman, Clapp, & Gazzaley, 2009; Gazzaley, Cooney, Rissman, & D’Esposito, 2005; Hillyard & Anllo-Vento, 1998; Luck & Hillyard, 1994; reviewed in Greenwood & Parasuraman, 2015). Additionally, the flanker task and the Operation Span are commonly used to measure executive control

function (Engle, 2002; Kane & Engle, 2002; Kopp, Rist, & Mattler, 1996). The underlying difference between the two clusters may be related to levels of executive control. Therefore, the overall cluster variable will be referred to as ‘executive control’ and cluster 1 will be referred to as high executive control (EC) and cluster 2 will be referred to as low EC.

There was an uneven distribution of high EC and low EC participants regarding stimulation conditions, shown in Table 2. In the anodal condition, 12 participants were categorized as high EC while 2 were categorized as low EC. In the cathodal condition, 13 participants were categorized as high EC while only 1 was categorized as low EC. In the sham condition, nine participants were categorized as high EC while six were categorized as low EC.

Distribution of high and low executive control individuals across stimulation conditions

<u>Cluster</u>	<u>Stimulation Condition</u>			<u>Total</u>
	<u>Anodal</u>	<u>Sham</u>	<u>Cathodal</u>	
High EC	12	9	13	34
Low EC	2	6	1	9
Total	14	15	14	43

Table 2: Distribution of high EC and low EC participants in each stimulation condition. Participants were categorized as being high EC or low EC through a cluster analysis.

Using ‘executive control’ from the output of the cluster analysis as a factor, a second analysis was conducted. Exploratory planned comparisons between the high and low EC clusters were conducted for the sham condition because there were relatively

even numbers of high and low EC individuals, nine and six, respectively. This analysis allowed us to test the extent to which the high and low EC categorization actually impacted DDD performance.

Planned comparisons confined to the high EC cluster were also conducted between the stimulation conditions. Planned comparisons for the low EC cluster could not be conducted between the stimulation conditions because of the small samples of low EC individuals in each condition. Conducting separate comparisons for each EC cluster allowed us to compare groups that were more homogeneous in nature.

Comparisons between cluster levels. The first set of planned comparisons tested whether there were differences in ‘red zone incursions’ between the high and low EC clusters. However, given the small sample of low EC individuals categorized in the anodal and cathodal stimulation conditions, a comparison could only be tested for the sham condition. The comparison revealed that high EC individuals ($M = 0.08$, $SE = 0.02$) had significantly fewer ‘red zone incursions’ compared to the low EC individuals ($M = 0.15$, $SE = 0.02$), $p = 0.02$.

Comparisons between stimulation conditions. Two sets of Bonferroni adjusted ($\alpha = .05$) planned comparisons were conducted to test specific differences within the high EC cluster between stimulation conditions. The first comparison tested whether there were significant differences in ‘red zone incursions’ between stimulation conditions but only for the high EC cluster ($n = 34$), Figure 18. The Bonferroni adjusted ($\alpha = .05$) comparison revealed that anodal stimulation significantly increased ‘red zone incursions’ (worse performance) compared to cathodal stimulation, $p = 0.01$. There were no

differences in ‘red zone incursions’ between anodal and sham stimulation, $p = 0.34$, or between cathodal and sham stimulation, $p = 0.79$.

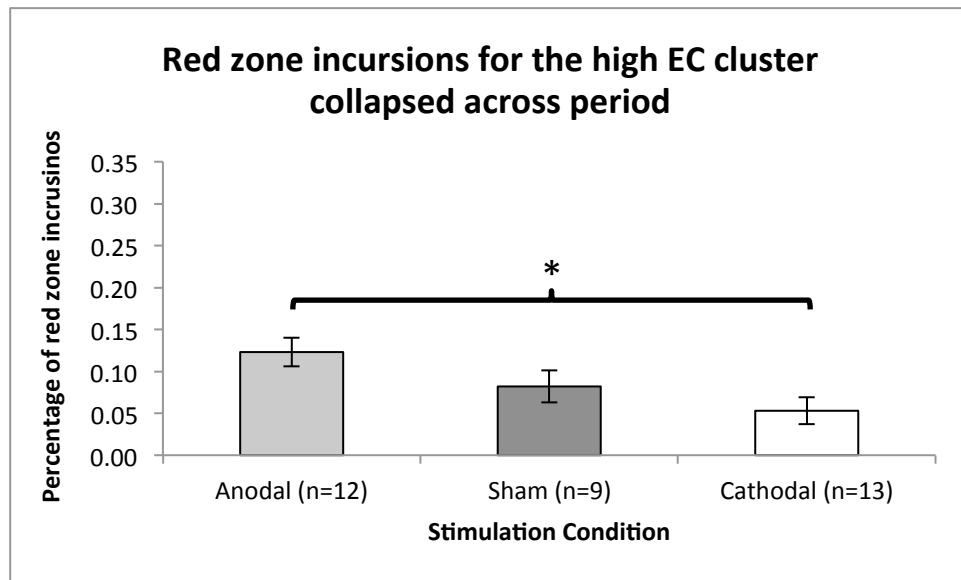


Figure 18: Red zone incursions for the high EC cluster collapsed across period. Significant difference between the anodal and cathodal conditions. Plotted with standard error of the mean. * $p < 0.05$.

Exploratory comparisons were also conducted between stimulation conditions, but separately for the low and high task load periods. The two low task load periods were combined into a single low task load period for the analysis, Figure 19. The Bonferroni adjusted ($\alpha = .05$) comparison during the low task load period revealed a marginally significant difference between cathodal and anodal stimulation, $p = 0.07$. None of the other comparisons revealed a difference, smallest $p = 0.31$.

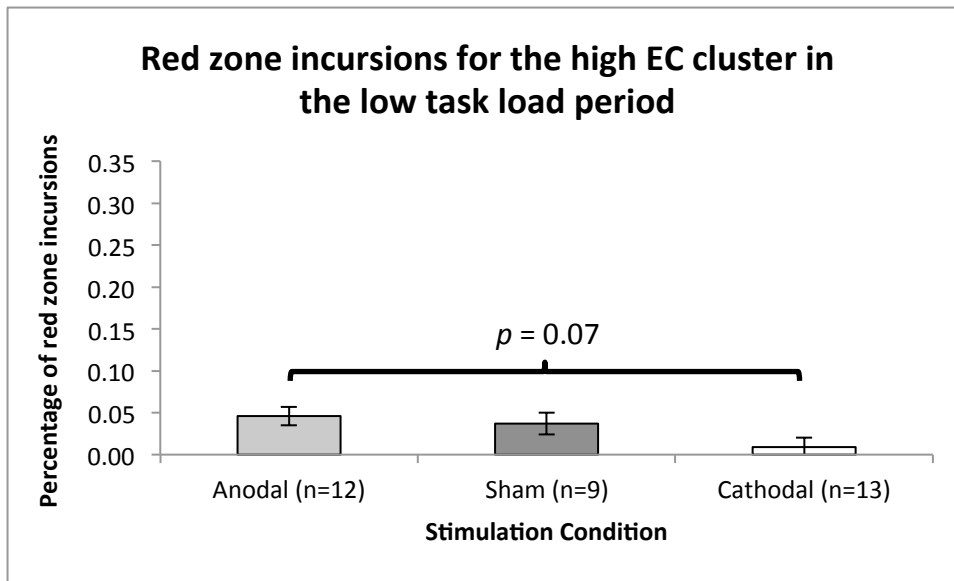


Figure 19: Red zone incursions for the high EC cluster during the low task load period. Marginal difference between the anodal and cathodal conditions. Plotted with standard error of the mean.

Bonferroni adjusted ($\alpha = .05$) comparisons were also conducted for the high task load period, Figure 20. The comparison revealed a marginally significant difference between cathodal and anodal stimulation, $p = 0.07$. None of the other comparisons revealed a difference, smallest $p = 0.30$.

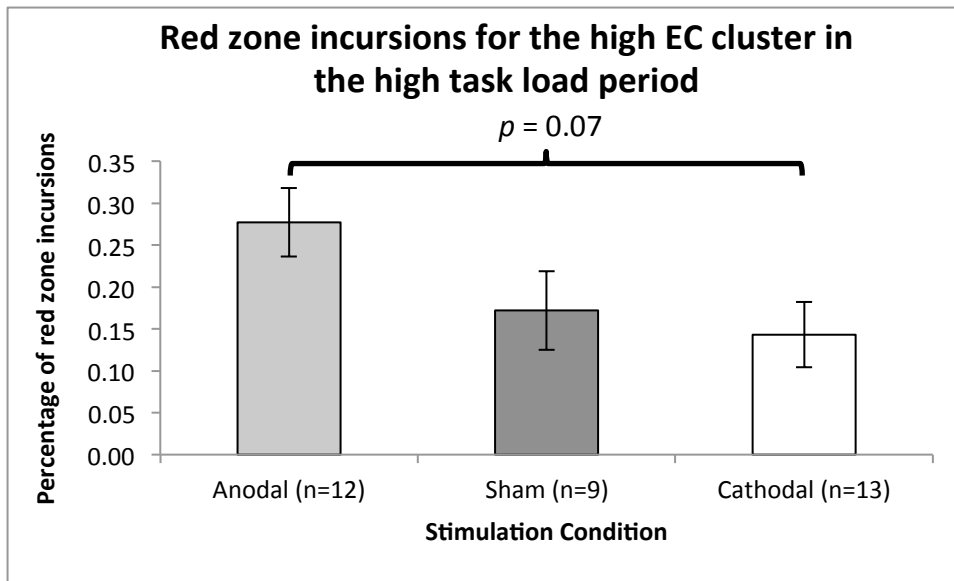


Figure 20: Red zone incursions for the high EC cluster during the high task load period. Marginal difference between the anodal and cathodal conditions. Plotted with standard error of the mean.

Summary. For the sham condition, participants categorized in the high EC cluster had significantly fewer ‘red zone incursions’ (better performance) compared to participants categorized in the low EC cluster suggesting that baseline ‘executive control’ predicted performance. Therefore, categorizing participants into high and low EC groups are beneficial to our analysis. It should be noted that groups in this comparison had small sizes (9 and 6, respectively).

The results only incorporating the high EC cluster revealed a pattern of findings that differed from the analysis that collapsed across clusters. For the high EC cluster, anodal stimulation increased ‘red zone incursions’ (decreasing performance) compared to the cathodal stimulation condition. Neither the anodal nor cathodal groups differed from the sham group. However, we also examined the low and high task load periods separately. For the low task load period, cathodal stimulation led to marginally fewer ‘red

zone incursions' compared to anodal stimulation. During the high task load period, anodal stimulation appeared to increase 'red zone incursions' compared to cathodal stimulation, indicating that anodal stimulation was actually more detrimental to performance during the more difficult task load period. Therefore, anodal stimulation made participants in the high EC cluster worse, and this effect was seen specifically during the high task load period.

Cerebral blood flow velocity. The CBFV data was segmented into the same three periods as the 'red zone incursions' data, corresponding to minutes 1-8, 9-13, and 14-20. The CBFV data was also separated based upon hemisphere.

CBFV values were calculated by dividing the mean CBFV values (calculated at 1 Hz) for each period by the mean CBFV value during the last one-minute of the Resting Baseline period. In this way, CBFVs could be interpreted in relation to a resting state of comparatively low metabolic activity. The procedure is commonly used in the analysis of CBFV data (Shaw et al., 2009; Warm & Parasuraman, 2007). Six unique CBFV values were created for each participant corresponding to the three periods and two hemispheres. The CBFV groups are referred to as: left low task load 1, left high task load, left low task load 2, right low task load 1, right high task load, and right low task load 2.

Magnitude of CBFV. One of the main research questions was whether right parietal anodal or cathodal stimulation modulated right hemisphere CBFV. In addition, previous work supports the idea that individual differences in cognitive performance, including Gf, are related to the recruitment of different and diverse cortical regions, such that lower cognitive performers recruit more bi-laterally to the detriment of overall

performance (Haier et al., 1988; Haier, Siegel, Tang, Abel, & Buchsbaum, 1992; Jaeggi et al., 2007). Therefore, specific comparisons between the high and low EC clusters were carried out to help identify unaccounted variance.

Similar to our analysis of ‘red zone incursions’, we initially conducted two separate analyses, one with and one without the cluster analysis factor ‘executive control’. However, there were no meaningful differences in the results of the data between the two analyses, therefore, we have excluded the analyses that did not include ‘executive control’. Four sets of Bonferroni adjusted ($\alpha = .05$) planned comparisons were conducted to test for specific differences between task conditions.

Comparisons between periods. The first set was conducted to identify whether the DDD task load manipulation led to differences in CBFV during each period, Figure 21. The Bonferroni adjusted ($\alpha = .05$) comparisons revealed that CBFV was significantly higher during the high task load period compared to the low task load 1 period, $p < 0.01$, and the low task load 2 period, $p < 0.01$. The comparison also revealed that CBFV was significantly higher during the low task load 1 period compared to the low task load 2 period, $p = 0.02$.

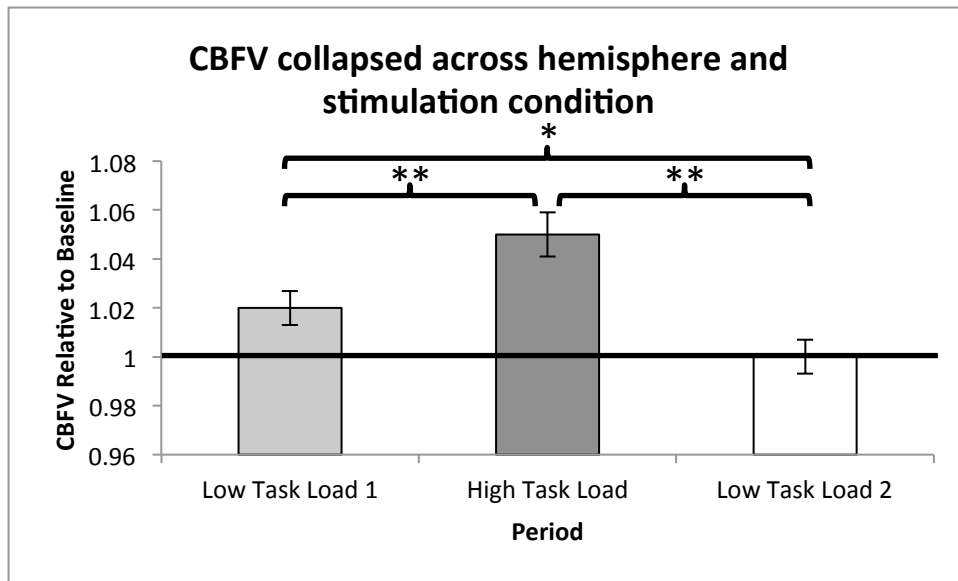


Figure 21: CBFV collapsed across hemispheres and stimulation conditions. CBFV was significantly greater during the high task load period compared to either low task load period. Plotted with standard error of the mean. * $p < 0.05$, ** $p < 0.01$.

Comparisons between clusters. A series of planned comparison were also conducted to determine whether there were hemisphere differences in CBFV between the high EC and low EC clusters for the sham condition, Figure 22. In this way, we can identify whether individual differences in ‘executive control’ are directly related to specific patterns of CBFV. The Bonferroni adjusted ($\alpha = .05$) comparison did not reveal a difference in left hemisphere CBFV or right hemisphere CBFV between the high and low EC clusters, smallest $p = 0.34$.

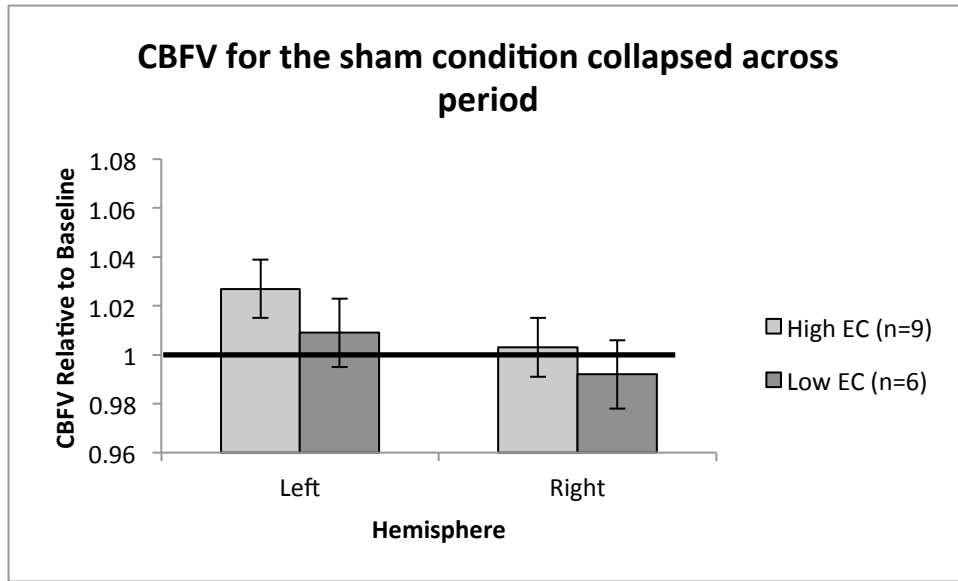


Figure 22: CBFV for the sham condition collapsed across period. There were no differences in CBFV between the high EC and low EC clusters within the left or right hemispheres.

Comparisons between hemispheric CBFV. A set of Bonferroni adjusted ($\alpha = .05$) planned comparisons was conducted to evaluate whether there were differences in CBFV between the left and right hemispheres for individuals categorized as high EC. A comparison between hemispheric CBFV for the high EC cluster ($n = 34$) revealed that left hemisphere ($M = 1.03$, $SE = 0.01$) was significantly greater than right hemisphere ($M = 1.01$, $SE = 0.01$), $p = 0.01$. We next conducted comparisons for each stimulation group. However, due to smaller sample sizes, comparisons at this level only reached marginal levels of significance, Figure 23. Each of the comparisons reached marginal significance, largest $p = 0.12$.

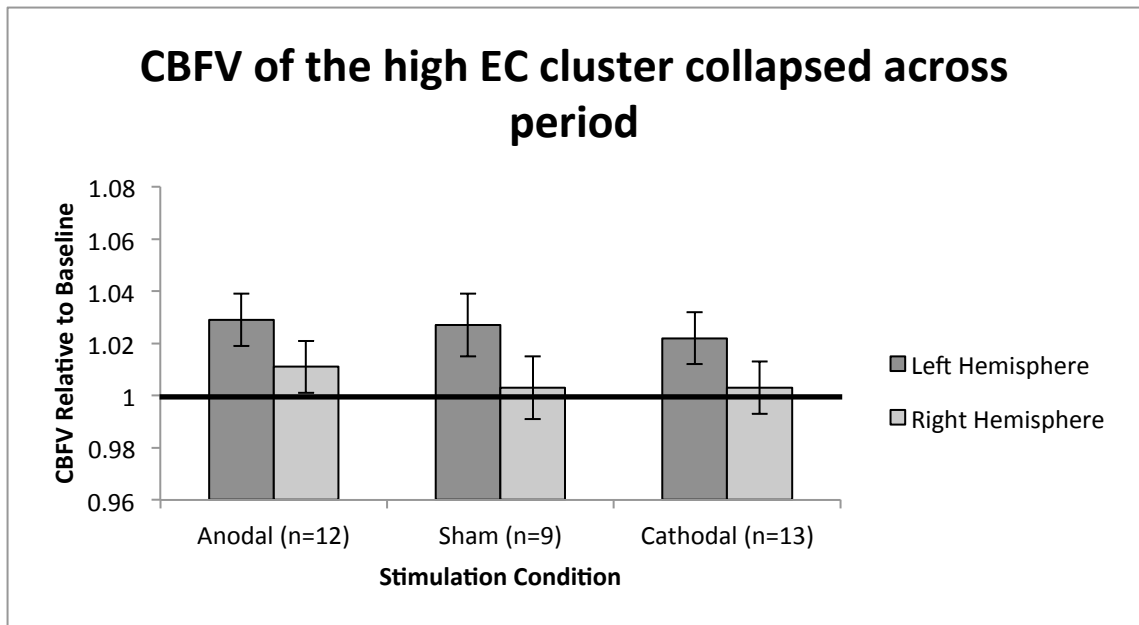


Figure 23: CBFV of the high EC cluster collapsed across periods. There were marginally significant differences in CBFV between the left and right hemisphere for the cathodal and sham conditions.

Comparisons between stimulation conditions. The third set of planned comparisons was conducted to test our hypothesis that stimulation would affect right hemisphere CBFV. These comparisons were only conducted for the high EC cluster, Figure 24. The Bonferroni adjusted ($\alpha = .05$) comparisons failed to identify differences in right hemisphere CBFV between any of the stimulation conditions, smallest $p = 1.00$.

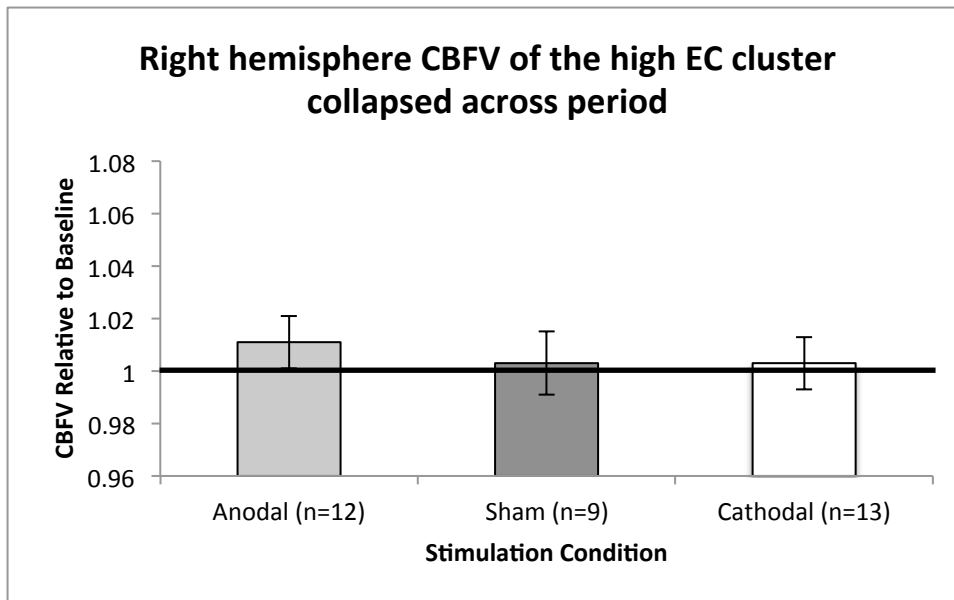


Figure 24: Right hemisphere CBFV of the high EC cluster collapsed across periods.
No differences in right hemisphere CBFV were identified between stimulation conditions.

Comparisons between clusters. A series of planned comparison were also conducted to determine whether there were hemisphere differences in CBFV between the high EC and low EC clusters for the sham condition, Figure 22. In this way, we can identify whether individual differences in ‘executive control’ are directly related to specific patterns of CBFV. The Bonferroni adjusted ($\alpha = .05$) comparison did not reveal a difference in left hemisphere CBFV or right hemisphere CBFV between the high and low EC clusters, smallest $p = 0.34$.

Summary. The CBFV results indicated that the task load manipulation led to significantly different levels of CBFV during each period. CBFV during the high task load period was higher than during either of the low task load periods. Also, there were no differences in CBFV between the high EC and low EC clusters in either hemisphere for the sham condition (small group sizes notwithstanding). This is particularly

noteworthy because it suggests that between the two clusters, CBFV was similar regardless of hemisphere. Left hemisphere CBFV was generally greater than right hemisphere CBFV for the high EC individuals, however, comparisons at the group level only reach marginal significance due to smaller group sizes. Surprisingly, there was no difference in right hemisphere CBFV between any of the stimulation conditions.

Transitions in cerebral blood flow velocity. Beyond general differences in the magnitude of CBFV during any one period, another important factor to consider is whether stimulation modulated the relative increase or decrease in CBFV during the low-to-high and high-to-low task load transitions. Therefore, the change in CBFV during each task load transition (i.e., from low to high and from high to low) was calculated. Values for transition 1 were calculated for each participant by subtracting the mean CBFV in the high task load period by the mean CBFV for the low task load 1 period within each hemisphere. The process was repeated for transition 2 by subtracting the mean CBFV in the low task load 2 period by the mean CBFV for the high task load period. Therefore, each participant ended up with four transition scores, two for each hemisphere.

Similar to our analysis of the magnitude of CBFV, we initially conducted two separate analyses; one with and one without the ‘executive control’ factor that was created from the cluster analysis. However, there were no meaningful differences in the results of the data between the two analyses, therefore, we have excluded the analysis that did not include the ‘executive control’ factor.

Comparisons between stimulation conditions. A set of planned comparisons was conducted to test whether there were significant differences between stimulation

conditions in transitions for right hemisphere CBFV. The comparisons were only run for the high EC cluster and separate comparisons were run for transition 1 (Figure 25 Top) and transition 2 (Figure 25 Bottom). The Bonferroni adjusted ($\alpha = .05$) comparisons failed to identify differences between stimulation conditions for either transition, smallest $p = 0.58$.

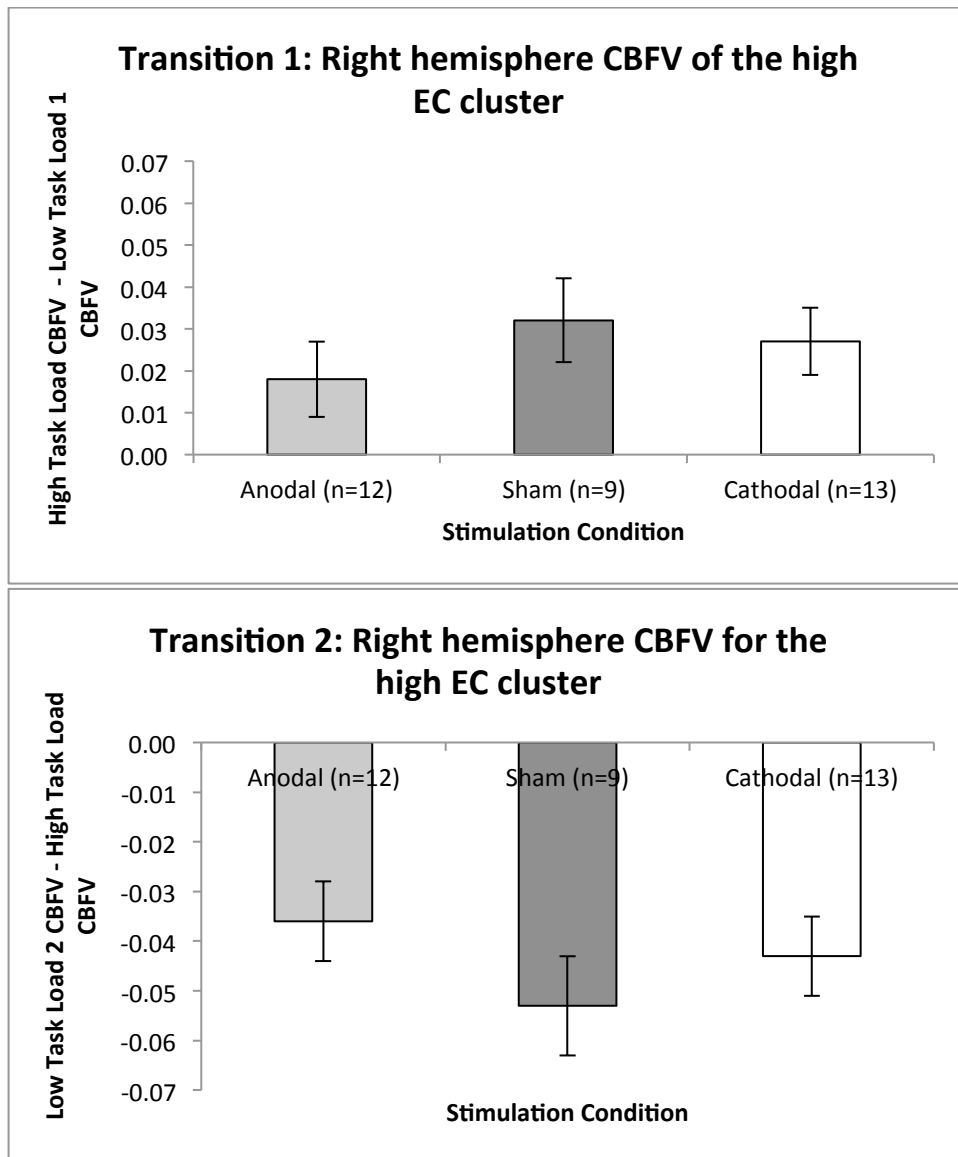


Figure 25: Top – Transition 1 right hemisphere CBFV for the high EC cluster. There were no differences between stimulation conditions. Bottom - Transition 2 right hemisphere CBFV for the high EC cluster. There were no differences between stimulation conditions. Plotted with standard error of the mean.

Summary. Transition 1 right hemisphere CBFV was not significantly different between stimulation conditions. Transition 2 right hemisphere CBFV was not significantly different between stimulation conditions.

Correlations between ‘red zone incursions’ and CBFV. Our hypotheses predicted a specific framework by which tDCS would modulate both DDD performance and CBFV. We expected changes in performance to be met with changes in CBFV. To test our assumptions, we conducted a series of correlations. Correlations were run between ‘red zone incursions’ and two sets of CBFV data. Given that the high EC cluster illustrated significantly greater left hemisphere CBFV compared to the right hemisphere and the high EC cluster had significantly fewer ‘red zone incursions’ than the low EC cluster (for sham condition), there may be fundamental differences in the magnitude of CBFV and/or the differences in hemispheric CBFV that predict performance.

Therefore, CBFV difference values were calculated by subtracting right hemisphere CBFV from left hemisphere CBFV. To better understand these results, separate analyses were conducted for the high and low EC clusters during the high task load period only. The correlations were conducted for the high task load period because there was greater variability in ‘red zone incursions’ during this period compared to the low task load periods. Each set of correlations was independently adjusted for multiple comparisons using a Bonferroni correction.

High executive control cluster.

Magnitude of CBFV. Alpha was adjusted to equal 0.017, however, none of the correlations were significant, smallest $p = 0.05$.

Hemispheric differences in CBFV. Alpha was adjusted to 0.017 for the following correlations. For the anodal condition, a significant correlation was identified between the CBFV difference value and ‘red zone incursions’, [$r = 0.71$, $n = 12$, $p = 0.01$]. No other correlation was significant, smallest $p = 0.09$.

Summary. Only one significant relationship was detected. For the anodal stimulation condition, there was a positive correlation between the CBFV difference value and ‘red zone incursions’. The finding suggests that for individuals in the high EC cluster that received anodal stimulation, greater similarity in CBFV between the left and right hemispheres was related to fewer ‘red zone incursions’ (better performance).

Low executive control cluster (sham condition only).

Magnitude of CBFV. For participants in the sham condition, the correlations were not significant, smallest $p = 0.15$

Hemispheric differences in CBFV. For the sham stimulation condition, the correlation was not significant, $p = 0.14$.

Summary. The results indicate that for the low EC individuals, neither the magnitude of CBFV nor the hemispheric difference in CBFV were significantly related to ‘red zone incursions’. However, the sample sizes were small.

Subjective workload. NASA-TLX scores were analyzed and then compared to determine whether stimulation impacted overall subjective ratings of workload, Figure 26. A one-way ANOVA revealed a marginally significant main effect of stimulation condition, $F(2, 40) = 2.71, p = 0.08$.

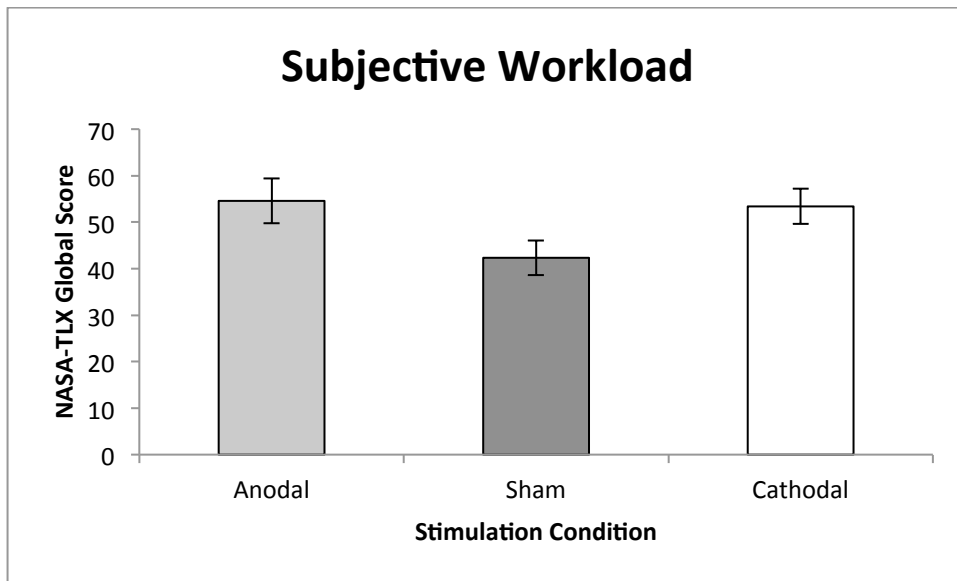


Figure 26: Subjective mental workload. Plotted with standard error of the mean.

A Pearson one-way correlation was run to confirm that the subjective measure of workload (NASA-TLX) was related to the objective measure of task performance ('red zone incursions'; Figure 27). The correlation was only run for the high task load period as this period-involved the highest level of task load within the scenario. The correlation between NASA-TLX score and 'red zone incursions' was significant, [$r = 0.30$, $n = 43$, $p = 0.03$], suggesting that participants who performed worse also rated the task as inducing higher levels of overall workload.

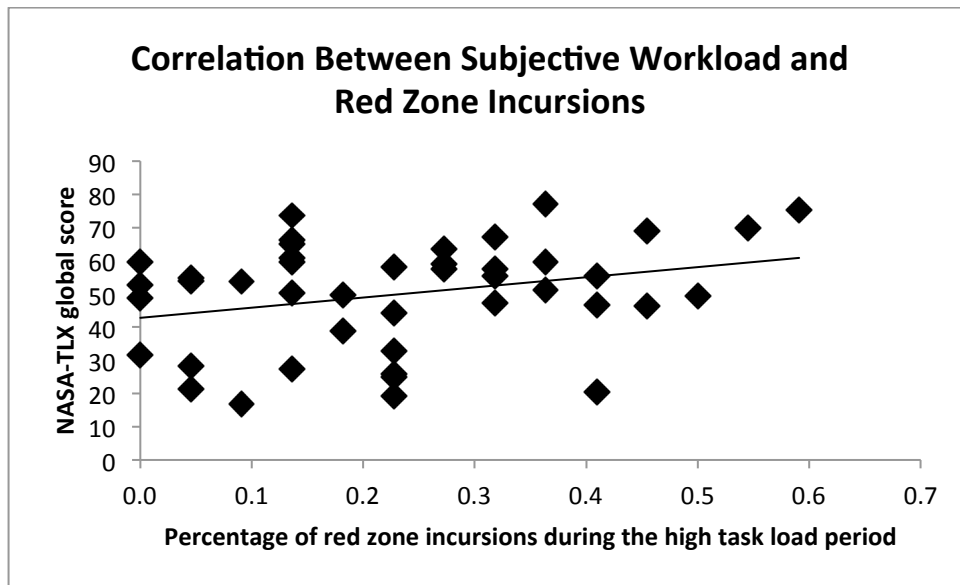


Figure 27: Correlation between subjective workload and red zone incursions. A significant positive correlation was identified.

Two Pearson two-way correlations were run to determine whether the subjective measure of workload (NASA-TLX) was related to CBFV during the high task load period. Separate correlations were run for each hemisphere. The correlation between NASA-TLX global score and left hemisphere CBFV was significant, [$r = 0.37$, $n = 43$, $p = 0.01$]. The correlation between NASA-TLX score and right hemisphere CBFV was not significant, $p = 0.35$. The results suggest that participants with greater left hemisphere CBFV also reported the task as inducing a greater level of workload.

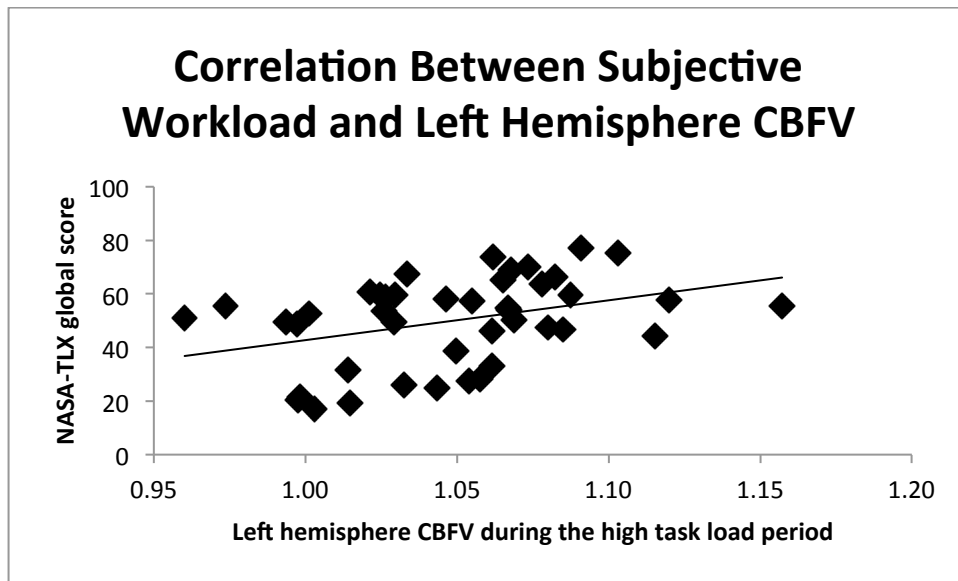


Figure 28: Correlation between subjective workload and left hemisphere CBFV. A significant positive correlation was identified.

Working memory capacity. Operation Span scores were calculated by summing up the total number of correctly recalled letters. Operation Span scores were correlated with ‘red zone incursions’ on the high task load period. The Pearson one-way correlation revealed a marginally significant correlation, [$r = -0.24$, $n = 43$, $p = 0.06$], indicating that higher Operation Span scores tended to be associated with fewer ‘red zone incursions’.

Visual attention tracking. Separate accuracy scores were calculated for each tracking load for each subsession (pre- and post-stimulation). The accuracy scores were calculated by dividing the number of correctly identified targets for each trial by the total number of targets for each trial. A separate analysis of variance (ANOVA) was run for each tracking load as we hypothesized that anodal stimulation would only be beneficial for the high tracking load trials.

A one-way mixed design ANOVA for low tracking load MOT accuracy failed to reveal a significant interaction, $p = 0.17$, nor a main effect of stimulation, $p = 0.12$, or subsession, $p = 0.13$, (Figure 29).

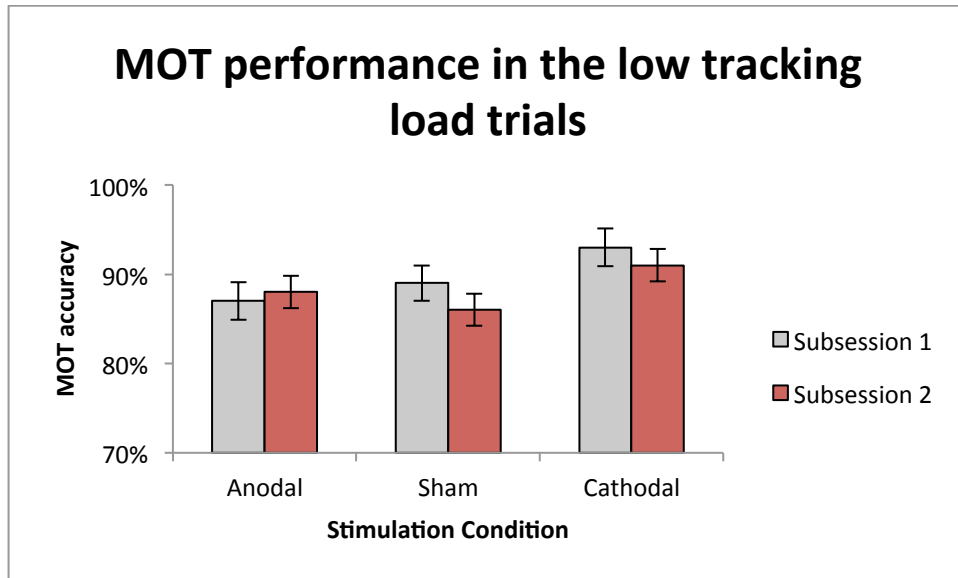


Figure 29: MOT performance in the low tracking load trials. Plotted with standard error of the mean.

A one-way mixed design ANOVA for high tracking load MOT accuracy failed to reveal a significant interaction, $p = 0.60$, nor a main effect of stimulation, $p = 0.11$. The ANOVA revealed a significant main effect of subsession, $F(2,40) = 14.58$, $p < .01$, $\eta^2_{partial} = 0.27$, (Figure 30).

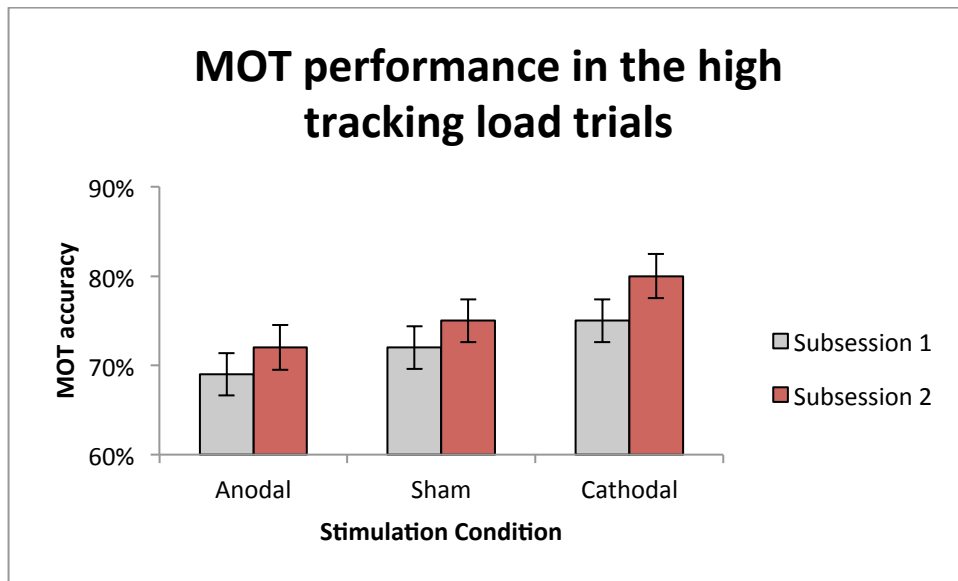


Figure 30: MOT performance in the high tracking load trials. Plotted with standard error of the mean.

Response inhibition. The flanker conflict cost was calculated by subtracting the average response time for congruent trials from the average response time for incongruent trials during both subsessions. A one-way ANOVA was run to explore whether stimulation affected flanker performance, Figure 31. The ANOVA failed to identify a significant stimulation by subsession interaction, $p = 0.93$, nor significant main effects of stimulation or subsession, smallest $p = 0.59$.

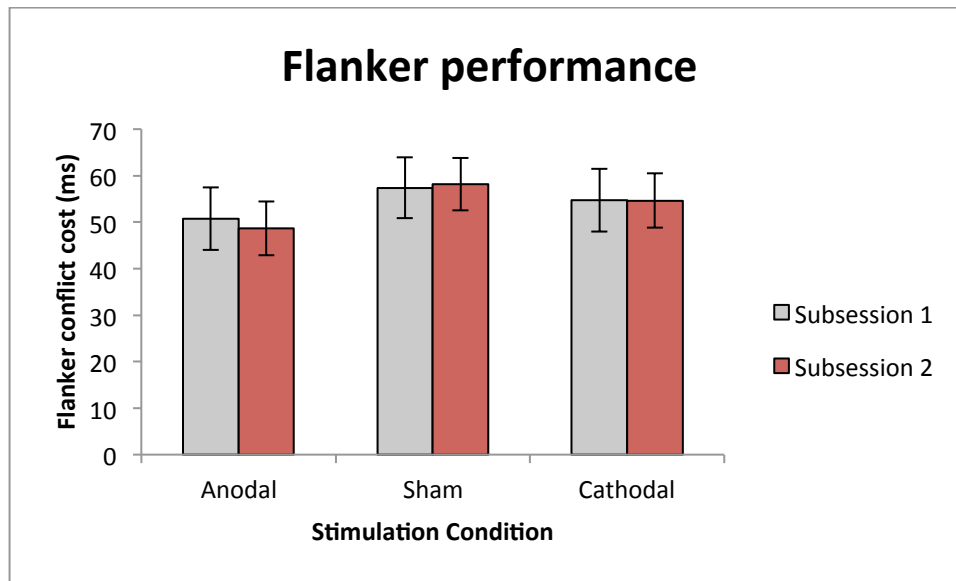


Figure 31: Flanker performance plotted with standard error of the mean.

Discussion

The goal for this experiment was to determine whether direct current stimulation of the parietal cortex can modulate the functioning of that cortex, as manifested in both complex task performance and in cerebral blood flow velocity. We hypothesized that right anodal parietal stimulation would improve performance (i.e., decrease ‘red zone incursions’) through excitatory neuronal effects in the right parietal cortex leading to increased right hemisphere CBFV. We also hypothesized that right cathodal parietal stimulation would impair performance (i.e., increase ‘red zone incursions’) through inhibitory neuronal effects that also decreased right hemisphere CBFV. The main findings from the study will be discussed below.

DDD task load manipulation. The manipulation in DDD task load between periods modulated both ‘red zone incursions’ and CBFV. Therefore, changes in task load

could be indexed by changes in the percentage of ‘red zone incursions’ and by CBFV. It is important to note that ‘red zone incursions’ and CBFV were not significantly correlated, leading us to speculate that they may be illustrative of different underlying processes.

The manipulation of DDD task load between periods led to differences in ‘red zone incursions’. Specifically, performance decreased during the high task load period reflecting an increase in task difficulty. The manipulation of DDD task load also induced changes in CBFV between periods, with CBFV being the highest during the high task load period. Taken together, there is converging evidence that the manipulation in task load induced changes in cognitive load. Cognitive load is often considered as the relationship between task load and operator abilities; therefore, changes in performance and in resource allotment (CBFV) are suggestive of a change in cognitive load. In addition, the subjective rating of workload (NASA-TLX) was positively correlated with both ‘red zone incursions’ and left hemisphere CBFV indicating that the participants were sensitive to the level of workload they experienced.

Individual differences. Inter-individual differences played a significant role in the experiment. We ran an exploratory cluster analysis to detect the natural individual differences in abilities between participants. The cluster analysis categorized two clusters of participants, characterized by differences in executive control. In particular, the cluster variable may be related to differences in visuospatial executive control as the flanker task, MOT task, and DDD vehicle organization variable are all visuospatial in nature.

The exploratory categorization of participants by ‘executive control in the cluster analysis also added an additional layer of difficulty for interpreting the entirety of the results. The cluster analysis created clusters of unequal group sizes. The number of high EC and low EC individuals within each stimulation condition was widely different; in particular, there were few low EC individuals in the anodal and cathodal conditions. Due to this skewed distribution, comparisons involving low EC individuals (e.g., asking whether stimulation affects high EC and low EC individuals differently) could not be tested leaving us unable to make conclusions about the impact stimulation may have had on them.

However, a comparison between the high and low EC clusters for the sham condition illustrated that the high EC individuals had significantly fewer ‘red zone incursions’ compared to the low EC individuals. The finding suggests that the underlying difference between the clusters (level of executive control) significantly predicted DDD performance. In particular, greater executive control would be beneficial to DDD performance because participants needed to continuously up-date or switch their actions depending upon the most pressing enemy threat, and this flexibility may be associated with levels executive control. Specific individual differences in cognitive abilities have also been previously reported to be advantageous to task performance in a wide range of tasks (Berry et al., 2009; Engle & Kane, 2004; Gazzaley et al., 2005; Humphreys & Revelle, 1984; Malinowski & Gillespie, 2001).

We also conducted analyses examining the effect of stimulation with and without the cluster factor. Collapsing across the cluster factor revealed a fundamentally different

behavioral finding compared to when we examined performance for the high EC cluster only. When we combined both the high and low EC clusters, the comparisons revealed that cathodal stimulation led to significantly fewer ‘red zone incursions’ (better performance) compared to both the anodal and sham conditions. This was inconsistent with our hypothesis.

However, when we limited our comparisons to individuals in the high EC cluster only, the results revealed that anodal stimulation led to significantly worse performance compared to cathodal stimulation. This was most evident when the comparison was conducted on the high task load period. The finding that anodal stimulation increased ‘red zone incursions’ (reducing performance) in the high EC participants was inconsistent with our hypothesis, which predicted that anodal stimulation would improve performance. There were also no differences in performance between anodal and sham nor between cathodal and sham conditions. However, it should be noted that most participants in the anode and cathode groups were categorized as ‘high executive control’. Since these participants were homogeneous (relative to baseline factors), the difference in ‘red zone incursions’ between the conditions can most likely be attributed to the effect of the stimulation.

Although the direction of the behavioral findings was unexpected, the fact that the difference in performance was reported between the anodal and cathodal conditions still fit our hypothesis. We expected the largest difference to occur between the anodal and cathodal conditions, as they should exert similar but opposite effects on cortical neurons and subsequent behavior.

Inclusion of the cluster factor changed the direction of the findings. Without its inclusion, we would have reached the misleading conclusion that cathodal stimulation improved performance overall. Rather, the overall finding was distorted by underlying individual differences in “executive control”. In most participants, anodal stimulation actually increased ‘red zone incursions’ and hurt performance. Negative effects resulting from anodal stimulation have not been frequently reported. In a change detection paradigm, Jones and Berryhill reported that anodal stimulation reduced N-back working memory performance for low education participants (2012). However, they were unsure of the cause of this effect.

In addition, some studies report facilitatory cathodal effects for tasks with complex perceptual and visual noise. Although we reported an inhibitory anodal effect, a facilitatory cathodal effect and an inhibitory anodal effect are opposite ends of the same spectrum; therefore, a mechanism responsible for facilitatory cathodal effects may also be responsible for inhibitory anodal effects. The mechanism proposed to be responsible for such facilitatory cathodal effects is that cathodal stimulation decreases neural “noise” thereby, increasing the signal-to-noise ratio (Antal et al., 2004; Weiss & Lavidor, 2012). This makes sense given the evidence that cathodal stimulation increases membrane resting potential leading to a decreased likelihood of neural firing. Specifically, since complex environments already lead to increased neural activity, reducing the overall neural firing through cathodal stimulation would functionally increase the signal-to-noise ratio leading to improved ability to discern “targets” from “distractors”. Therefore, increased overall neural firing through anodal stimulation would functionally decrease

the signal-to-noise ratio leading to decreased ability to discern “targets” from “distractors”.

For the DDD simulation, participants needed to move their vehicles in response to the movements of the enemy vehicles. In addition, a critical component is the ability to re-prioritize actions in relation to how the enemy vehicles are behaving. Therefore, identifying and modifying your actions relative to the most pertinent threat in any one moment of time is critical to successful game-play. Given that the DDD simulation is visually and cognitively noisy with lots of task-relevant information, increasing the neural activity (through anodal stimulation) would theoretically hurt performance by making it more difficult for participants to correctly identify the most relevant action to take at any one moment in time. This would fall in line with evidence that the parietal cortex supports the network that is responsible for executive and cognitive control (Desimone & Duncan, 1995; Kane & Engle, 2002; Yantis, 1998).

Given that anodal stimulation induced worse performance, one might expect to find a similar change in CBFV, however, that was not the case. For the high EC individuals, right hemisphere CBFV did not differ significantly between stimulation conditions. Without observing a direct physiological change or difference, it is difficult to explain how anodal stimulation affected the brain leading to reduced performance.

Although this was disappointing, other researchers have also failed to identify neurophysiological changes in concert with tDCS-based behavioral effects. Jones, Gözenman, and Berryhill using functional near infrared spectroscopy (fNIRS) reported significant changes in oxygenated blood for participants with low but not high working

memory capacities even though both groups showed behavioral effects from tDCS (2015). One reason for these findings could be the fact that both fNIRS and TCD have lower spatial resolution compared to fMRI. Particularly with TCD, CBFV was measured from the middle cerebral arteries, leaving open the possibility that CBFV could have remained the same even though CBFV increased in one area (e.g., parietal cortex) while simultaneously decreasing in another (e.g., pre-frontal). Therefore, potential effects could have been washed out. Even so, we still explored potential theoretical frameworks for our findings.

Balance in hemispheric CBFV. The analysis examining hemispheric CBFV for the stimulation conditions of only the high EC individuals illustrated greater left hemisphere CBFV compared to right hemisphere. Since this was also observed within the sham condition, this suggests that there is a natural difference in CBFV between hemispheres. Interestingly, for participants in the anodal stimulation condition only, greater similarity between the hemispheres in CBFV was correlated with better performance. Therefore, anodal stimulation may have impacted CBFV in such a way that fundamentally changed the relationship between blood flow velocity and performance, without producing significantly different levels of CBFV compared to the other conditions.

Network Dynamics. An alternative explanation stems from research reporting that general cognition is organized into two large-scale networks. The two networks are the default mode network (DMN) and the dorsal attention network (DAN), with each mediating a specific cognitive state, internally and externally directed attention,

respectively (Fornito, Harrison, Zalesky, & Simons, 2012; Fox et al., 2005; Spreng, Sepulcre, Turner, Stevens, & Schacter, 2013). Activation of the DMN is related to good memory retrieval, self-referential processing, and goal-directed behavior (Fornito et al., 2012; Ullsperger, Crone, & Nieuwenhuis, 2004) while activation of the DAN is related to good memory encoding such as the processing of external events (Corbetta & Shulman, 2002).

Given the variety of cognitive processes necessary to complete the DDD simulation, activation of both the DMN and DAN are important. However, given that individuals categorized as “high executive control” performed better than those categorized as “low executive control”, the DMN may be more relevant to DDD performance.

The DMN and the DAN both engage regions of the frontal and parietal cortices, however, they do so in functionally different ways based upon a hierarchical organization. Nodes in the prefrontal cortex are believed to drive the entire DMN (Di & Biswal, 2014; Uddin, Clare Kelly, Biswal, Xavier Castellanos, & Milham, 2009; Jiao et al., 2011; Zhou et al., 2011) while nodes in the parietal cortex are thought to drive the DAN (Bressler, 1995; Vossel, Weidner, Driver, Friston, & Fink, 2012). The networks also appear to be anti-correlated, whereby DAN activation results in decreased DMN activation and vice versa (Fox et al., 2005; Singh & Fawcett, 2008).

Therefore, the preferential enhancement of the DAN network could lead to a detrimental effect on overall DDD performance. In this manner, right anodal parietal stimulation could have then selectively enhanced the activation of the DAN while

simultaneously suppressing activation of the DMN. Thereby, increasing the processing of external events during gameplay at the expense of accessing items in memory and goal-directed behaviors. Recent research has also provided evidence supporting such an idea. Direct current stimulation has been reported to modulate network dynamics such as functional connectivity and resting state behavior, measured by fMRI (Alekseichuk et al., 2015; Callan et al., 2016; Meinzer et al., 2012; 2013). Although we did not report any modulations in CBFV within either hemisphere, changes in functional connectivity and network activation may not have been detected by TCD given its relatively low spatial resolution.

Additional findings. Stimulation did not impact MOT accuracy under either task load. This was a surprising finding as our research group and another had previously reported modulatory tDCS-based effects on MOT accuracy (Blumberg et al., 2015; Roe et al., 2016). In particular, our group reported a facilitatory effect from anodal stimulation in high tracking load trials and that this effect was larger for individuals with lower baseline MOT accuracies. Since participant's baseline MOT accuracies were relatively similar between the present study and the one published in 2015, we would have expected to find similar beneficial effects. However, the null finding may be attributed to the time-on-task effect, which is also referred to as fatigue (Mackworth, 1948). This experiment took on average two and a half hours to complete and participants were performing cognitively challenging tasks throughout. Therefore, it is reasonable to assume that general cognitive performance may have declined over the course of the experiment.

Stimulation also did not affect flanker conflict cost, something we had predicted since previous research reported a facilitatory effect from cathodal stimulation (Weiss & Lavidor, 2012). The discrepant results may be due to two different things, the time-on-task effect mentioned earlier and differences in the flanker tasks. Weiss and Lavidor used a non-traditional flanker task where the stimuli were presented in a circular arrangement instead of the classic horizontal line arrangement. Their task may have required different cognitive skills compared to the task used in our experiment.

Limitations. We acknowledge a number of experimental limitations that may have contributed to the somewhat puzzling results. The between-subjects design limited our ability to account for individual differences specifically related to baseline DDD gameplay performance. A second limitation was that there was a small sample and an uneven distribution of low EC individuals across stimulation conditions. This was unfortunate because individuals in the low EC cluster also performed worse than individuals in the high EC cluster and the literature has reported that tDCS is more beneficial for lower skilled individuals (Blumberg et al., 2014; Blumberg et al., 2015; Tseng et al., 2012). Therefore, stimulation may have been more effective for the low EC cluster leading to larger behavioral and neurophysiological effects.

In addition, we selected the right parietal cortex as the target for stimulation by systematically breaking down the operations involved with the DDD stimulation. We then identified the cortical area that we believed would be involved with those specific processes. Although this was a thorough process, it may have led us to stimulate a brain region and network that was not directly responsible for some of the critical cognitive

processes necessary to complete the DDD simulation. Prefrontal cortex stimulation may have been more beneficial as this area is associated with executive control (Duncan & Owen, 2000; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Wagner, Maril, Bjork, & Schacter, 2001).

We used TCD to measure the neurophysiological changes in the brain induced by tDCS. Although TCD is an attractive tool to combine with tDCS because the mechanisms of action (blood flow & direct current) are compatible and TCD is relatively easy to use and administer, TCD has low spatial resolution. Therefore TCD may have not been able to detect tDCS-induced CBFV changes within each hemisphere.

One additional limitation was our relatively low sample size. Specifically, examining individual differences in our participants through the exploratory cluster analysis further reduced the group sizes.

Conclusions. To our knowledge, this is the first tDCS study to directly manipulate task load while simultaneously recording cortical activation. Not common in the tDCS literature, we reported a performance decline resulting from anodal stimulation. Specifically, anodal stimulation decreased performance in the real-time strategy simulation compared to cathodal stimulation, potentially through an effect on executive control.

The results from this study provide a strong framework for designing future tDCS research. Studies should have sufficiently large sample sizes to allow assessment of individual differences in both task-specific and general cognitive abilities. It will be particularly important to quasi-randomize participants into experimental conditions to

maintain even samples of individuals exhibiting specific individual difference characteristics. In addition future studies should leverage fMRI to guide the placement of electrodes for stimulation (Clark et al., 2012). This is especially important for researchers exploring the effects of brain stimulation on the completion of complex tasks.

General Conclusion

Across three experiments we examined the extent to which direct current stimulation applied over the right parietal cortex can reduce the negative effects associated with performance under high load. Experiments 1 and 2 illustrated that anodal stimulation can successfully reduce performance declines during periods of increased task load. This was reflected in better MOT accuracy and fewer spatial errors for experiments 1 and 2, respectively. Both experiments reported that tDCS was more beneficial for lower baseline performing individuals compared to higher baseline performing individuals, categorized by task performance. Experiment 1 also reported that the stimulation-based effect was due to focal (parietal) stimulation and not a global cortical enhancement. Experiment 2 reported a bi-directional effect such that cathodal stimulation increased the number of spatial errors participants committed.

It is important to note that cognitive load was not assessed by a neurophysiological measure in either experiment 1 or 2. However, the behavioral evidence suggests that anodal stimulation decreased cognitive load. This inference relies heavily on the understanding that cognitive load is related to task load and individual abilities. In both experiments, performance was measured prior to and concurrent with stimulation using the same task load manipulations at each subsession. Given that performance improved with anodal stimulation while task load remained constant, it can

be inferred that stimulation modulated individual cognitive abilities, allowing them to perform better. The behavioral results provide compelling evidence that tDCS enhanced participants' ability to deal with the overloaded cognitive state.

Experiment 3 reported an inhibitory effect from anodal stimulation on task performance. We interpret this effect as anodal stimulation increased neuronal activity in the parietal cortex leading to a decrease in signal-to-noise ratio, therefore, it was more difficult for participants to discern between goal and task-irrelevant information. In addition, we used TCD to directly measure tDCS-induced CBFV changes during the completion of a task where task load was explicitly manipulated, however, we did not detect differences in CBFV between the stimulation conditions. The exploratory cluster analysis revealed two populations of participants; presumably one high and one low in "executive control". Individuals categorized in the high executive control cluster had significantly better performance on the subsequent DDD task compared to those categorized in the low executive control cluster. Analyzing the data with and without the exploratory cluster factor led to different sets of conclusions about how stimulation impacted DDD performance.

In total, direct current stimulation over the parietal cortex modulated task performance in three different tasks and in varying behavioral directions. We reported both facilitatory and inhibitory effects from anodal stimulation. Although the reason for these differential effects is unclear, they may be related to the nature and complexity of the tasks themselves. The tasks used in experiments 1 and 2 were relatively basic in both cognitive architecture and the amount of perceptual noise on the screen. The DDD

simulation in experiment 3 was much more complex, requiring participants to multi-task in a dynamic complex environment. The large differences in the make-up and complexity of the tasks may account for the differential effects from anodal stimulation. However, further research is necessary.

In sum, the findings demonstrate that tDCS can modulate performance in cognitively challenging situations. Finally, individual differences in baseline task ability and cognitive processes such as executive control can also moderate tDCS-based effects.

Appendix A

Percentage of enemies destroyed. The Percentage of enemies destroyed was calculated by dividing the total number of enemy vehicles destroyed by the total number of enemy vehicles, Figure 32. An exploratory one-way analysis of variance (ANOVA) was run to test whether stimulation impacted the ‘percentage of enemies destroyed’. The ANOVA failed to identify a significant main effect of stimulation condition ($p = 0.31$).

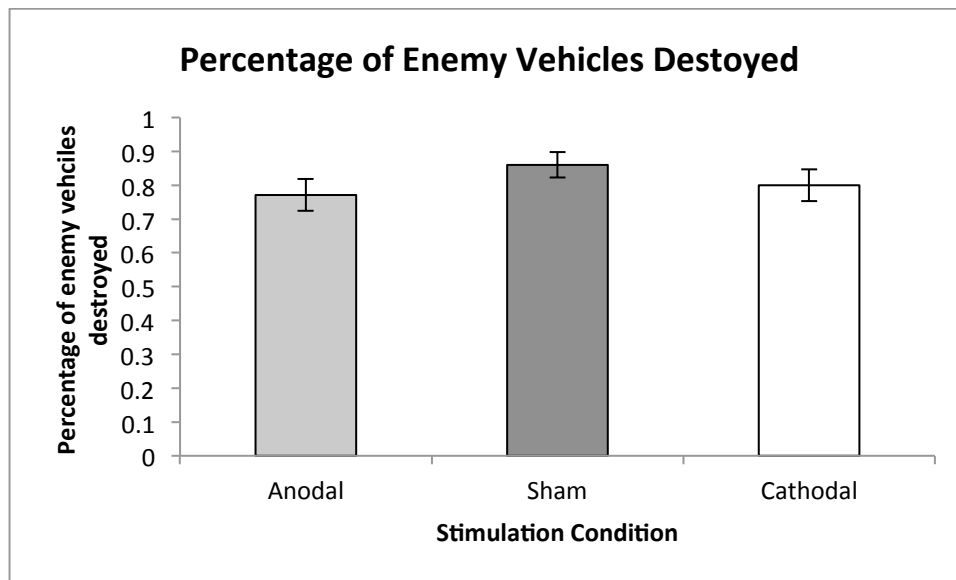


Figure 32: Percentage of enemy vehicles destroyed across stimulation conditions. There were no differences between stimulation conditions. Plotted with standard error of the mean.

Enemy attacks. Enemy attacks was calculated by summing up the number of times an enemy vehicle shot and hit a participant’s own vehicle, Figure 33. The

exploratory one-way ANOVA failed to identify a significant main effect of stimulation condition ($p = 0.38$).

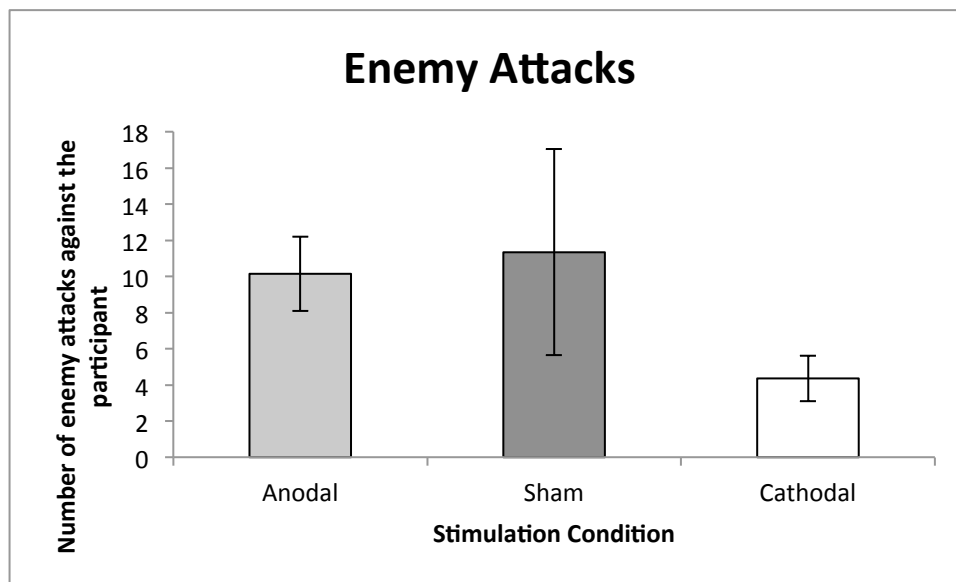


Figure 33: The number of enemy attacks across stimulation conditions. There were no differences between stimulation conditions. Plotted with standard error of the mean.

Attack efficiency. Attack efficiency was calculated by summing the total number of enemies that were destroyed by the total number of missiles each participant used (Saquer & Parasuraman, 2014). The exploratory one-way ANOVA failed to identify a significant main effect of stimulation condition ($p = 0.53$), Figure 34.

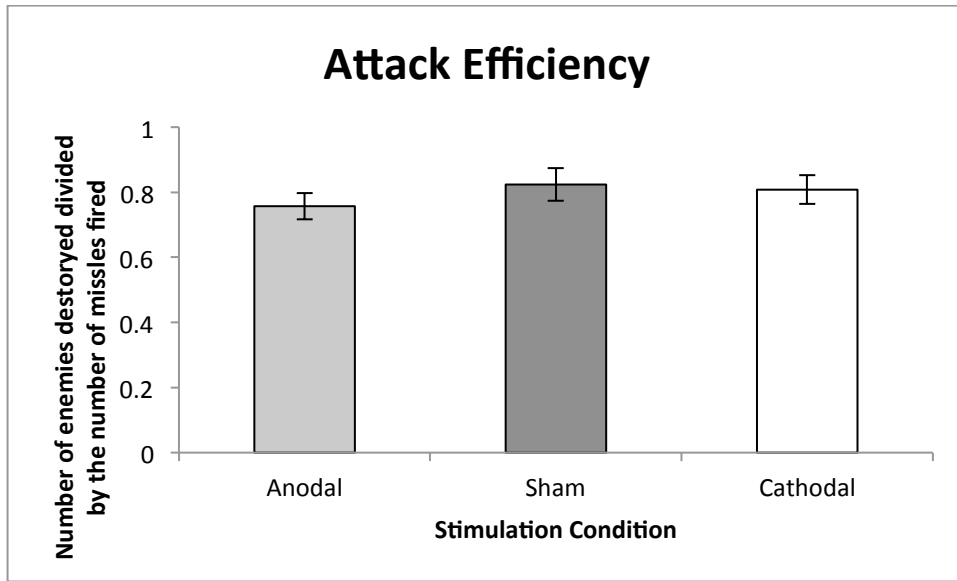


Figure 34: Attack efficiency across stimulation conditions.
There were no differences between stimulation conditions. Plotted with standard error of the mean.

Vehicle engagement. ‘Vehicle engagement’ was calculated by summing up the number of individual movements each participant made with their vehicles, Figure 35. The exploratory one-way ANOVA revealed a marginally significant main effect of stimulation condition, $F(2, 40) = 3.05, p = 0.06, \eta^2_{\text{partial}} = 0.13$.

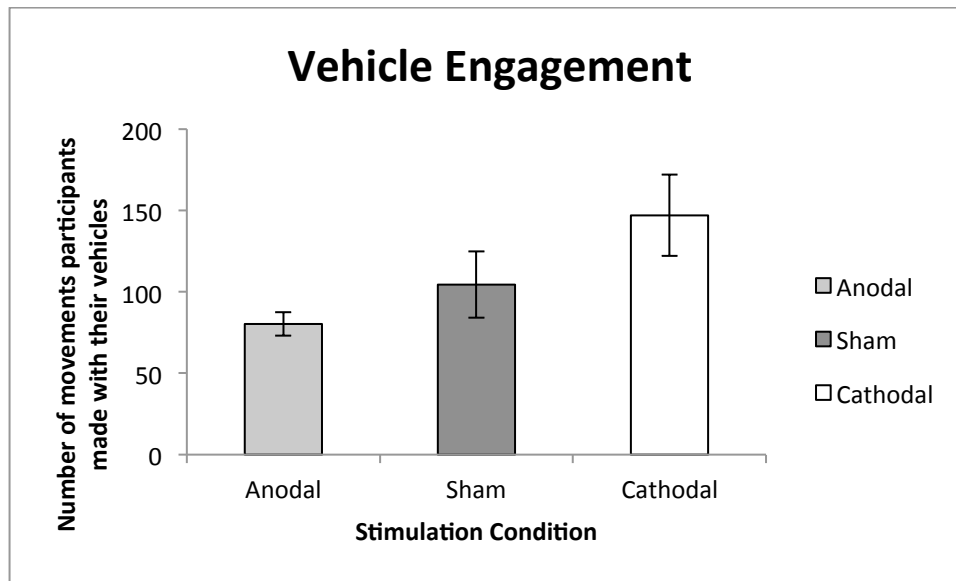


Figure 35: The number of individual vehicle movements across stimulation conditions. There was a marginally significant difference between the anodal and cathodal conditions. Plotted with standard error of the mean.

References

- Aaslid, R. (1986). Transcranial Doppler examination techniques. *Transcranial doppler sonography*, 39-59.
- Alekseichuk, I., Diers, K., Paulus, W., & Antal, A. (2015). Transcranial electrical stimulation of the occipital cortex during visual perception modifies the magnitude of BOLD activity: A combined tES–fMRI approach. *NeuroImage*.
- Alvarez, G. A., & Franconeri, S. L. "How many objects can you track?: Evidence for a resource-limited attentive tracking mechanism." *Journal of Vision* 7, no. 13 (2007): 14.
- Andrews, S. C., Hoy, K. E., Enticott, P. G., Daskalakis, Z. J., & Fitzgerald, P. B. (2011). Improving working memory: the effect of combining cognitive activity and anodal transcranial direct current stimulation to the left dorsolateral prefrontal cortex. *Brain stimulation*, 4(2), 84-89.
- Antal, A., Nitsche, M. A., Kruse, W., Kincses, T. Z., Hoffmann, K. P., & Paulus, W. (2004). Direct current stimulation over V5 enhances visuomotor coordination by improving motion perception in humans. *Journal of Cognitive Neuroscience*, 16(4), 521-527.
- Antal, A., Nitsche, M. A., & Paulus, W. (2001). External modulation of visual perception in humans. *Neuroreport*, 12(16), 3553-3555.

- Awh, E., Barton, B., & Vogel, E. K. (2007). Visual working memory represents a fixed number of items regardless of complexity. *Psychological science*, 18(7), 622-628.
- Bailey, B. P., Konstan, J. A., & Carlis, J. V. (2001, July). The effects of interruptions on task performance, annoyance, and anxiety in the user interface. In *Proceedings of INTERACT* (Vol. 1, pp. 593-601).
- Ball, K., Edwards, J. D., & Ross, L. A. "The impact of speed of processing training on cognitive and everyday functions." *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences* 62, no. Special Issue 1 (2007): 19-31.
- Basak, C., Boot, W. R., Voss, M. W., & Kramer, A. F. "Can training in a real-time strategy video game attenuate cognitive decline in older adults?." *Psychology and aging* 23, no. 4 (2008): 765.
- Battelli, L., Alvarez, G. A., Carlson, T., & Pascual-Leone, A. "The role of the parietal lobe in visual extinction studied with transcranial magnetic stimulation." *Journal of Cognitive Neuroscience* 21, no. 10 (2009): 1946-1955.
- Battelli, L., Cavanagh, P., Intriligator, J., Tramo, M. J., Hénaff, M., Michèl, F., & Barton, J. S. "Unilateral right parietal damage leads to bilateral deficit for high-level motion." *Neuron* 32, no. 6 (2001): 985-995.
- Bavelier, D., Green, C. S., Pouget, A., & Schrater, P. "Brain plasticity through the life span: learning to learn and action video games." *Annual review of neuroscience* 35 (2012): 391-416.
- Bays, P. M., & Husain, M. (2008). Dynamic shifts of limited working memory resources in human vision. *Science*, 321(5890), 851-854.

- Beeli, G., Koeneke, S., Gasser, K., & Jancke, L. "Brain stimulation modulates driving behavior." *Behav. Brain Funct* 4 (2008): 34.
- Berry, A. S., Zanto, T. P., Rutman, A. M., Clapp, W. C., & Gazzaley, A. (2009). Practice-related improvement in working memory is modulated by changes in processing external interference. *Journal of neurophysiology*, 102(3), 1779-1789.
- Berryhill, M. E., & Jones, K. T. (2012). tDCS selectively improves working memory in older adults with more education. *Neuroscience letters*, 521(2), 148-151.
- Berryhill, M. E., Peterson, D. J., Jones, K. T., & Stephens, J. A. (2014). Hits and misses: leveraging tDCS to advance cognitive research. *Frontiers in psychology*, 5.
- Bikson, M., Datta, A., & Elwassif, M. (2009). Establishing safety limits for transcranial direct current stimulation. *Clinical neurophysiology: official journal of the International Federation of Clinical Neurophysiology*, 120(6), 1033.
- Bikson, M., Inoue, M., Akiyama, H., Deans, J. K., Fox, J. E., Miyakawa, H., & Jefferys, J. G. (2004). Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro. *The Journal of physiology*, 557(1), 175-190.
- Bindman, L. J., Lippold, O. C. J., & Redfearn, J. W. T. (1964). The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. *The Journal of physiology*, 172(3), 369.
- Blumberg, E. J., Foroughi, C. K., Scheldrup, M. R., Peterson, M. S., Boehm-Davis, D. A., & Parasuraman, R. (2014). Reducing the disruptive effects of interruptions

- with noninvasive brain stimulation. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 0018720814565189.
- Blumberg, E. J., Peterson, M. S., & Parasuraman, R. (2015). Enhancing multiple object tracking performance with noninvasive brain stimulation: a causal role for the anterior intraparietal sulcus. *Frontiers in systems neuroscience*, 9.
- Boot, W. R., Kramer, A. F., Simons, D. J., Fabiani, M., & Gratton, G. "The effects of video game playing on attention, memory, and executive control." *Acta psychologica* 129, no. 3 (2008): 387-398.
- Bressler, S. L. (1995). Large-scale cortical networks and cognition. *Brain Research Reviews*, 20(3), 288-304.
- Brumby, D. P., Cox, A. L., Back, J., & Gould, S. J. (2013). Recovering from an interruption: Investigating speed– accuracy trade-offs in task resumption behavior. *Journal of Experimental Psychology: Applied*, 19(2), 95.
- Brunoni, A. R., & Vanderhasselt, M. A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: a systematic review and meta-analysis. *Brain and cognition*, 86, 1-9.
- 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.
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychology and aging*, 17(1), 85.

- Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: compensatory brain activity in high-performing older adults. *Neuroimage*, 17(3), 1394-1402.
- Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of cognitive neuroscience*, 12(1), 1-47.
- Cades, D. M., Werner, N. E., Boehm-Davis, D. A., & Arshad, Z. (2010). Interruptions are disruptive in the real world: Evidence from an office setting. In *54th annual human factors and ergonomics society conference. San Francisco, California: Human Factors and Ergonomics Society*.
- Callan, D., Falcone, B., Wada, A., & Parasuraman, R. (2016). Simultaneous tDCS-fMRI Identifies Resting State Networks Correlated with Visual Search Enhancement. *Frontiers in Human Neuroscience*, 10, 72.
- Callejas, A., Lupiáñez, J., & Tudela, P. (2004). The three attentional networks: On their independence and interactions. *Brain and cognition*, 54(3), 225-227.
- Cavanagh, P., & Alvarez, G. A. (2005). Tracking multiple targets with multifocal attention. *Trends in cognitive sciences*, 9(7), 349-354.
- Champod, A. S., & Petrides, M. (2007). Dissociable roles of the posterior parietal and the prefrontal cortex in manipulation and monitoring processes. *Proceedings of the National Academy of Sciences*, 104(37), 14837-14842.
- Chein, J. M., & Schneider, W. (2005). Neuroimaging studies of practice-related change: fMRI and meta-analytic evidence of a domain-general control network for learning. *Cognitive Brain Research*, 25(3), 607-623.

- Clark, V. P., Coffman, B. A., Mayer, A. R., Weisend, M. P., Lane, T. D., Calhoun, V. D., & Wassermann, E. M. (2012). TDCS guided using fMRI significantly accelerates learning to identify concealed objects. *Neuroimage*, 59(1), 117-128.
- 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.
- Cohen, Y. E., & Andersen, R. A. (2002). A common reference frame for movement plans in the posterior parietal cortex. *Nature Reviews Neuroscience*, 3(7), 553-562.
- Colby, C. L., & Goldberg, M. E. (1999). Space and attention in parietal cortex. *Annual review of neuroscience*, 22(1), 319-349.
- Conway, A. R., Kane, M. J., Bunting, M. F., Hambrick, D. Z., Wilhelm, O., & Engle, R. W. (2005). Working memory span tasks: A methodological review and user's guide. *Psychonomic bulletin & review*, 12(5), 769-786.
- Cordes, C. (1983, May). Human factors and nuclear safety: Grudging respect for a growing field. *APA Monitor*, p. 1.
- 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.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature reviews neuroscience*, 3(3), 201-215.
- Cowan, N. (2001). Metatheory of storage capacity limits. *Behavioral and brain sciences*, 24(01), 154-176.

- Culham, J. C., & Kanwisher, N. G. (2001). Neuroimaging of cognitive functions in human parietal cortex. *Current opinion in neurobiology*, 11(2), 157-163.
- Culham, J. C., Brandt, S. A., Cavanagh, P., Kanwisher, N. G., Dale, A. M., & Tootell, R. B. "Cortical fMRI activation produced by attentive tracking of moving targets." *Journal of Neurophysiology* 80, no. 5 (1998): 2657-2670.
- Culham, J. C., Cavanagh, P., & Kanwisher, N. G. "Attention response functions: characterizing brain areas using fMRI activation during parametric variations of attentional load." *Neuron* 32, no. 4 (2001): 737-745.
- d'Avossa, G., Tosetti, M., Crespi, S., Biagi, L., Burr, D. C., & Morrone, M. C. (2007). Spatiotopic selectivity of BOLD responses to visual motion in human area MT. *Nature neuroscience*, 10(2), 249-255.
- Datta, A., Bansal, V., Diaz, J., Patel, J., Reato, D., & Bikson, M. (2009). Gyri-precise head model of transcranial direct current stimulation: improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain stimulation*, 2(4), 201-207.
- Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual review of neuroscience*, 18(1), 193-222.
- Di, X., & Biswal, B. B. (2014). Identifying the default mode network structure using dynamic causal modeling on resting-state functional magnetic resonance imaging. *Neuroimage*, 86, 53-59.

- Dismukes, K., Berman, B. A., & Loukopoulos, L. D. (2007). *The limits of expertise: Rethinking pilot error and the causes of airline accidents*. Ashgate Publishing, Ltd..
- Ditunno, P. L., & Mann, V. A. (1990). Right hemisphere specialization for mental rotation in normals and brain damaged subjects. *Cortex*, 26(2), 177-188.
- Donner, T., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., & Brandt, S. A. (2000). Involvement of the human frontal eye field and multiple parietal areas in covert visual selection during conjunction search. *European Journal of Neuroscience*, 12(9), 3407-3414.
- Duncan, J. (1980). The locus of interference in the perception of simultaneous stimuli. *Psychological review*, 87(3), 272.
- Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in neurosciences*, 23(10), 475-483.
- Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. *Neuron*, 52(6), 1109-1120.
- Endsley, M. R., & Rodgers, M. D. (1997). *Distribution of attention, situation awareness, and workload in a passive air traffic control task: Implications for operational errors and automation* (No. DOT/FAA/AM-97/13). Federal Aviation Administration Washington DC Office of Aviation Medicine.
- Engle, R. W. (2002). Working memory capacity as executive attention. *Current directions in psychological science*, 11(1), 19-23.

- Engle, R. W., & Kane, M. J. (2004). Executive attention, working memory capacity, and a two-factor theory of cognitive control. *Psychology of learning and motivation, 44*, 145-200.
- Erickson, K. I., Colcombe, S. J., Wadhwa, R., Bherer, L., Peterson, M. S., Scalf, P. E., & Kramer, A. F. (2007). Training-induced plasticity in older adults: effects of training on hemispheric asymmetry. *Neurobiology of aging, 28*(2), 272-283.
- Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & psychophysics, 16*(1), 143-149.
- 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.
- Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I., & Posner, M. I. (2005). The activation of attentional networks. *Neuroimage, 26*(2), 471-479.
- Fehd, H. M., & Seiffert, A. E. (2008). Eye movements during multiple object tracking: Where do participants look?. *Cognition, 108*(1), 201-209.
- Feng, J., Spence, I., & Pratt, J. (2007). Playing an action video game reduces gender differences in spatial cognition. *Psychological science, 18*(10), 850-855.
- Fornito, A., Harrison, B. J., Zalesky, A., & Simons, J. S. (2012). Competitive and cooperative dynamics of large-scale brain functional networks supporting recollection. *Proceedings of the National Academy of Sciences, 109*(31), 12788-12793.

- Foroughi, C. K., Blumberg, E. J., & Parasuraman, R. (2014). Activation and inhibition of posterior parietal cortex have bi-directional effects on spatial errors following interruptions. *Frontiers in systems neuroscience*, 8.
- Foroughi, C. K., Werner, N. E., Nelson, E. T., & Boehm-Davis, D. A. (2014). Do interruptions affect quality of work?. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 56(7), 1262-1271.
- Foster, J. L., Shipstead, Z., Harrison, T. L., Hicks, K. L., Redick, T. S., & Engle, R. W. (2014). Shortened complex span tasks can reliably measure working memory capacity. *Memory & cognition*, 43(2), 226-236.
- Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America*, 102(27), 9673-9678.
- Fregni, F., Boggio, P. S., Nitsche, M., Bermanpohl, F., Antal, A., Feredoes, E., & Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental brain research*, 166(1), 23-30.
- Fukuda, K., Awh, E., & Vogel, E. K. (2010). Discrete capacity limits in visual working memory. *Current opinion in neurobiology*, 20(2), 177-182.
- Gazzaley, A., Cooney, J. W., McEvoy, K., Knight, R. T., & D'esposito, M. (2005). Top-down enhancement and suppression of the magnitude and speed of neural activity. *Journal of cognitive neuroscience*, 17(3), 507-517.

- Gevins, A., & Smith, M. E. (2000). Neurophysiological measures of working memory and individual differences in cognitive ability and cognitive style. *Cerebral Cortex*, 10(9), 829-839.
- Green, C. S., & Bavelier, D. (2006). Enumeration versus multiple object tracking: the case of action video game players. *Cognition*, 101(1), 217-245.
- Green, C. S., & Bavelier, D. (2006). Effect of action video games on the spatial distribution of visuospatial attention. *Journal of experimental psychology: Human perception and performance*, 32(6), 1465.
- Greenwood, P. M., & Parasuraman, R. (2015). The Mechanisms of Far Transfer From Cognitive Training: Review and Hypothesis.
- Haier, R. J., Siegel, B. V., Nuechterlein, K. H., Hazlett, E., Wu, J. C., Paek, J., & Buchsbaum, M. S. (1988). Cortical glucose metabolic rate correlates of abstract reasoning and attention studied with positron emission tomography. *Intelligence*, 12(2), 199-217.
- Haier, R. J., Siegel, B., Tang, C., Abel, L., & Buchsbaum, M. S. (1992). Intelligence and changes in regional cerebral glucose metabolic rate following learning. *Intelligence*, 16(3), 415-426.
- Harris, I. M., & Miniussi, C. (2003). Parietal lobe contribution to mental rotation demonstrated with rTMS. *Journal of Cognitive Neuroscience*, 15(3), 315-323.
- Hart, S. G., & Staveland, L. E. (1988). Development of NASA-TLX (Task Load Index): Results of empirical and theoretical research. *Advances in psychology*, 52, 139-183.

- Hattermer, K., Plate, A., Heverhagen, J. T., Haag, A., Keil, B., Klein, K. M., & Knake, S. (2011). Determination of hemispheric dominance with mental rotation using functional transcranial Doppler sonography and FMRI. *Journal of Neuroimaging*, 21(1), 16-23.
- Helmreich, R. L., Merritt, A. C., & Wilhelm, J. A. (1999). The evolution of crew resource management training in commercial aviation. *The international journal of aviation psychology*, 9(1), 19-32.
- Helton, W. S., Warm, J. S., Tripp, L. D., Matthews, G., Parasuraman, R., & Hancock, P. A. (2010). Cerebral lateralization of vigilance: a function of task difficulty. *Neuropsychologia*, 48(6), 1683-1688.
- Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences*, 95(3), 781-787.
- 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.
- Horowitz, T. S., & Cohen, M. A. (2010). Direction information in multiple object tracking is limited by a graded resource. *Attention, Perception, & Psychophysics*, 72(7), 1765-1775.
- Horowitz, T. S., Klieger, S. B., Fencsik, D. E., Yang, K. K., Alvarez, G. A., & Wolfe, J. M. (2007). Tracking unique objects. *Perception & psychophysics*, 69(2), 172-184.

- Horvath, J. C., Forte, J. D., & Carter, O. (2015). Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: A systematic review. *Neuropsychologia*, 66, 213-236.
- Howe, P. D., Horowitz, T. S., Morocz, I. A., Wolfe, J., & Livingstone, M. S. (2009). Using fMRI to distinguish components of the multiple object tracking task. *Journal of Vision*, 9(4), 10.
- Humphreys, M. S., & Revelle, W. (1984). Personality, motivation, and performance: a theory of the relationship between individual differences and information processing. *Psychological review*, 91(2), 153.
- Iuculano, T., & Kadosh, R. C. (2013). The mental cost of cognitive enhancement. *The Journal of Neuroscience*, 33(10), 4482-4486.
- 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.
- Jaeggi, S. M., Buschkuhl, M., Jonides, J., & Shah, P. (2011). Short-and long-term benefits of cognitive training. *Proceedings of the National Academy of Sciences*, 108(25), 10081-10086.
- Jaeggi, S. M., Buschkuhl, M., Etienne, A., Ozdoba, C., Perrig, W. J., & Nirkko, A. C. (2007). On how high performers keep cool brains in situations of cognitive overload. *Cognitive, Affective, & Behavioral Neuroscience*, 7(2), 75-89.

- Javadi, A. H., & Walsh, V. (2012). Transcranial direct current stimulation (tDCS) of the left dorsolateral prefrontal cortex modulates declarative memory. *Brain stimulation*, 5(3), 231-241.
- Jiao, Q., Lu, G., Zhang, Z., Zhong, Y., Wang, Z., Guo, Y., & Liu, Y. (2011). Granger causal influence predicts BOLD activity levels in the default mode network. *Human brain mapping*, 32(1), 154-161.
- Jones, K. T., & Berryhill, M. E. (2012). Parietal contributions to visual working memory depend on task difficulty. *Frontiers in psychiatry*, 3.
- Jones, K. T., Gözenman, F., & Berryhill, M. E. (2015). The strategy and motivational influences on the beneficial effect of neurostimulation: a tDCS and fNIRS study. *Neuroimage*, 105, 238-247.
- Jonides, J., Lacey, S. C., & Nee, D. E. (2005). Processes of working memory in mind and brain. *Current Directions in Psychological Science*, 14(1), 2-5.
- Jovicich, J., Peters, R. J., Koch, C., Braun, J., Chang, L., & Ernst, T. (2001). Brain areas specific for attentional load in a motion-tracking task. *Journal of Cognitive Neuroscience*, 13(8), 1048-1058.
- Kadosh, R. C., Levy, N., O'Shea, J., Shea, N., & Savulescu, J. (2012). The neuroethics of non-invasive brain stimulation. *Current Biology*, 22(4), R108-R111.
- Kadosh, R. C., Soskic, S., Iuculano, T., Kanai, R., & Walsh, V. (2010). Modulating neuronal activity produces specific and long-lasting changes in numerical competence. *Current Biology*, 20(22), 2016-2020.

- Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic bulletin & review*, 9(4), 637-671.
- Kelly, A. C., & Garavan, H. (2005). Human functional neuroimaging of brain changes associated with practice. *Cerebral Cortex*, 15(8), 1089-1102.
- Kincses, T. Z., Antal, A., Nitsche, M. A., Bártfai, O., & Paulus, W. (2003). Facilitation of probabilistic classification learning by transcranial direct current stimulation of the prefrontal cortex in the human. *Neuropsychologia*, 42(1), 113-117.
- Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain*, 122(5), 981-991.
- Kopp, B., Rist, F., & Mattler, U. W. E. (1996). N200 in the flanker task as a neurobehavioral tool for investigating executive control. *Psychophysiology*, 33(3), 282-294.
- Krause, B., & Kadosh, R. C. (2014). Not all brains are created equal: the relevance of individual differences in responsiveness to transcranial electrical stimulation. *Frontiers in systems neuroscience*, 8.
- Lamble, D., Kauranen, T., Laakso, M., & Summala, H. (1999). Cognitive load and detection thresholds in car following situations: safety implications for using mobile (cellular) telephones while driving. *Accident Analysis & Prevention*, 31(6), 617-623.

- Liddle, P. F., Kiehl, K. A., & Smith, A. M. (2001). Event-related fMRI study of response inhibition. *Human brain mapping, 12*(2), 100-109.
- Linden, D. E., Bittner, R. A., Muckli, L., Waltz, J. A., Kriegeskorte, N., Goebel, R., & Munk, M. H. (2003). Cortical capacity constraints for visual working memory: dissociation of fMRI load effects in a fronto-parietal network. *Neuroimage, 20*(3), 1518-1530.
- Loukopoulos, L. D., Berman, M. B. A., & Dismukes, R. K. (2012). *The Limits of Expertise: Rethinking Pilot Error and the Causes of Airline Accidents*. Ashgate Publishing, Ltd..
- Luber, B. (2014). Neuroenhancement by noninvasive brain stimulation is not a net zero-sum proposition. *Frontiers in systems neuroscience, 8*, 127.
- Luck, S. J., & Hillyard, S. A. (1994). Spatial filtering during visual search: evidence from human electrophysiology. *Journal of Experimental Psychology: Human Perception and Performance, 20*(5), 1000.
- Luck, S. J., & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature, 390*(6657), 279-281.
- Ma, W. J., Husain, M., & Bays, P. M. (2014). Changing concepts of working memory. *Nature Neuroscience, 17*(3), 347-356.
- Mackworth, N. H. (1948). The breakdown of vigilance during prolonged visual search. *Quarterly Journal of Experimental Psychology, 1*(1), 6-21.

- Malinowski, J. C., & Gillespie, W. T. (2001). Individual differences in performance on a large-scale, real-world wayfinding task. *Journal of Environmental Psychology*, 21(1), 73-82.
- Markham, J. A., & Greenough, W. T. (2004). Experience-driven brain plasticity: beyond the synapse. *Neuron glia biology*, 1(04), 351-363.
- Marois, R., & Ivanoff, J. (2005). Capacity limits of information processing in the brain. *Trends in cognitive sciences*, 9(6), 296-305.
- McKendrick, R., Shaw, T., de Visser, E., Saqer, H., Kidwell, B., & Parasuraman, R. (2013). Team performance in networked supervisory control of unmanned air vehicles effects of automation, working memory, and communication content. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 0018720813496269.
- 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.
- Meinzer, M., Antonenko, D., Lindenberg, R., Hetzer, S., Ulm, L., Avirame, K., ... & Flöel, A. (2012). Electrical brain stimulation improves cognitive performance by modulating functional connectivity and task-specific activation. *The Journal of Neuroscience*, 32(5), 1859-1866.
- Meinzer, M., Lindenberg, R., Antonenko, D., Flaisch, T., & Flöel, A. (2013). Anodal transcranial direct current stimulation temporarily reverses age-associated

- cognitive decline and functional brain activity changes. *The Journal of Neuroscience*, 33(30), 12470-12478.
- Moos, K., Vossel, S., Weidner, R., Sparing, R., & Fink, G. R. (2012). Modulation of top-down control of visual attention by cathodal tDCS over right IPS. *The Journal of Neuroscience*, 32(46), 16360-16368.
- Motowildo, S. J., Borman, W. C., & Schmit, M. J. (1997). A theory of individual differences in task and contextual performance. *Human performance*, 10(2), 71-83.
- Mueller, S. T., & Piper, B. J. (2014). The psychology experiment building language (pebl) and pebl test battery. *Journal of neuroscience methods*, 222, 250-259.
- Nelson, J. T., McKinley, R. A., Golob, E. J., Warm, J. S., & Parasuraman, R. (2014). Enhancing vigilance in operators with prefrontal cortex transcranial direct current stimulation (tDCS). *Neuroimage*, 85, 909-917.
- Neubauer, A. C., & Fink, A. (2009). Intelligence and neural efficiency. *Neuroscience & Biobehavioral Reviews*, 33(7), 1004-1023.
- Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of physiology*, 527(3), 633-639.
- Nobre, A. C., Sebestyen, G. N., Gitelman, D. R., Mesulam, M. M., Frackowiak, R. S., & Frith, C. D. (1997). Functional localization of the system for visuospatial attention using positron emission tomography. *Brain*, 120(3), 515-533.

- Oksama, L., & Hyönä, J. (2004). Is multiple object tracking carried out automatically by an early vision mechanism independent of higher order cognition? An individual difference approach. *Visual cognition*, 11(5), 631-671.
- Oostenveld, R., & Praamstra, P. (2001). The five percent electrode system for high-resolution EEG and ERP measurements. *Clinical neurophysiology*, 112(4), 713-719.
- Paas, F. G., & Van Merriënboer, J. J. (1994). Instructional control of cognitive load in the training of complex cognitive tasks. *Educational psychology review*, 6(4), 351-371.
- Parasuraman, R., & Manzey, D. H. (2010). Complacency and bias in human use of automation: An attentional integration. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 52(3), 381-410.
- Parasuraman, R., & McKinley, R. A. (2014). Using noninvasive brain stimulation to accelerate learning and enhance human performance. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 0018720814538815.
- Parasuraman, R., Mouloua, M., & Molloy, R. (1996). Effects of adaptive task allocation on monitoring of automated systems. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 38(4), 665-679.
- Parasuraman, R., & Riley, V. (1997). Humans and automation: Use, misuse, disuse, abuse. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 39(2), 230-253.

- Parasuraman, R., Sheridan, T. B., & Wickens, C. D. (2000). A model for types and levels of human interaction with automation. *Systems, Man and Cybernetics, Part A: Systems and Humans, IEEE Transactions on*, 30(3), 286-297.
- Parasuraman, R., Warm, J. S., & See, J. E. (1998). Brain systems of vigilance.
- Perlow, L. A. (1999). The time famine: Toward a sociology of work time. *Administrative science quarterly*, 44(1), 57-81.
- Peters, M., Laeng, B., Latham, K., Jackson, M., Zaiyouna, R., & Richardson, C. (1995). A redrawn Vandenberg and Kuse mental rotations test-different versions and factors that affect performance. *Brain and cognition*, 28(1), 39-58.
- Plewnia, C., Zwissler, B., Längst, I., Maurer, B., Giel, K., & Krüger, R. (2013). Effects of transcranial direct current stimulation (tDCS) on executive functions: Influence of COMT Val/Met polymorphism. *Cortex*, 49(7), 1801-1807.
- Prakash, V., Koczmara, C., Savage, P., Trip, K., Stewart, J., McCurdie, T., & Trbovich, P. (2014). Mitigating errors caused by interruptions during medication verification and administration: interventions in a simulated ambulatory chemotherapy setting. *BMJ quality & safety*, bmjqs-2013.
- Pylyshyn, Z. W., & Storm, R. W. (1988). Tracking multiple independent targets: Evidence for a parallel tracking mechanism. *Spatial vision*, 3(3), 179-197.
- Radman, T., Datta, A., Ramos, R. L., Brumberg, J. C., & Bikson, M. (2009, September). One-dimensional representation of a neuron in a uniform electric field. In *Engineering in Medicine and Biology Society, 2009. EMBC 2009. Annual International Conference of the IEEE* (pp. 6481-6484). IEEE.

- Rahman, A., Reato, D., Arlotti, M., Gasca, F., Datta, A., Parra, L. C., & Bikson, M. (2013). Cellular effects of acute direct current stimulation: somatic and synaptic terminal effects. *The Journal of physiology*, 591(10), 2563-2578.
- Ratwani, R. M., & Trafton, J. G. (2008). Spatial memory guides task resumption. *Visual Cognition*, 16(8), 1001-1010.
- Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *science*, 306(5695), 443-447.
- Roe, J. M., Nesheim, M., Mathiesen, N. C., Moberget, T., Alnæs, D., & Sneve, M. H. (2016). The effects of tDCS upon sustained visual attention are dependent on cognitive load. *Neuropsychologia*, 80, 1-8.
- Rypma, B., & D'Esposito, M. (1999). The roles of prefrontal brain regions in components of working memory: effects of memory load and individual differences. *Proceedings of the National Academy of Sciences*, 96(11), 6558-6563.
- Salas, E., Wilson, K. A., Burke, C. S., & Wightman, D. C. (2006). Does crew resource management training work? An update, an extension, and some critical needs. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 48(2), 392-412.
- Saqer, H., & Parasuraman, R. (2014). Individual performance markers and working memory predict supervisory control proficiency and effective use of adaptive automation. *International Journal of Human Factors and Ergonomics* 55, 3(1), 15-31.

- Satterfield, K., Ramirez, R., Shaw, T., & Parasuraman, R. (2012, September). Measuring workload during a dynamic supervisory control task using cerebral blood flow velocity and the NASA-TLX. In *Proceedings of the Human Factors and Ergonomics Society Annual Meeting* (Vol. 56, No. 1, pp. 163-167). Sage Publications.
- 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.
- Schmiedek, F., Lövdén, M., & Lindenberger, U. (2010). Hundred days of cognitive training enhance broad cognitive abilities in adulthood: Findings from the COGITO study. *Frontiers in aging neuroscience*, 2, 27.
- Scholl, B. J., Pylyshyn, Z. W., & Feldman, J. (2001). What is a visual object? Evidence from target merging in multiple object tracking. *Cognition*, 80(1), 159-177.
- Sears, C. R., & Pylyshyn, Z. W. (2000). Multiple object tracking and attentional processing. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie experimentale*, 54(1), 1.
- Shaw, T., Finomore, V., Warm, J., & Matthews, G. (2012). Effects of regular or irregular event schedules on cerebral hemovelocity during a sustained attention task. *Journal of clinical and experimental neuropsychology*, 34(1), 57-66.

- Shaw, T. H., Matthews, G., Warm, J. S., Finomore, V. S., Silverman, L., & Costa, P. T. (2010). Individual differences in vigilance: Personality, ability and states of stress. *Journal of Research in Personality*, 44(3), 297-308.
- Shaw, T. H., Warm, J. S., Finomore, V., Tripp, L., Matthews, G., Weiler, E., & Parasuraman, R. (2009). Effects of sensory modality on cerebral blood flow velocity during vigilance. *Neuroscience letters*, 461(3), 207-211.
- Shen, Y. J., & Jiang, Y. V. (2006). Interrupted visual searches reveal volatile search memory. *Journal of Experimental Psychology: Human Perception and Performance*, 32(5), 1208.
- Shepard, R. N., & Metzler, J. (1971). Mental rotation of three-dimensional objects.
- Singh, K. D., & Fawcett, I. P. (2008). Transient and linearly graded deactivation of the human default-mode network by a visual detection task. *Neuroimage*, 41(1), 100-112.
- Sparing, R., Thimm, M., Hesse, M. D., Küst, J., Karbe, H., & Fink, G. R. (2009). Bidirectional alterations of interhemispheric parietal balance by non-invasive cortical stimulation. *Brain*, 132(11), 3011-3020.
- Spettell, C. M., & Liebert, R. M. (1986). Training for safety in automated person-machine systems. *American Psychologist*, 41(5), 545.
- Spira, J., & Feintuch, J. (2005). *The Cost of Not Paying Attention: How Interruptions Impact Knowledge Worker Productivity*. New York, NY: Basex, Inc.
- Spreng, R. N., Sepulcre, J., Turner, G. R., Stevens, W. D., & Schacter, D. L. (2013). Intrinsic architecture underlying the relations among the default, dorsal attention,

- and frontoparietal control networks of the human brain. *Journal of cognitive neuroscience*, 25(1), 74-86.
- Stone, D. B., & Tesche, C. D. (2009). Transcranial direct current stimulation modulates shifts in global/local attention. *Neuroreport*, 20(12), 1115-1119.
- Strenziok, M., Parasuraman, R., Clarke, E., Cisler, D. S., Thompson, J. C., & Greenwood, P. M. (2014). Neurocognitive enhancement in older adults: comparison of three cognitive training tasks to test a hypothesis of training transfer in brain connectivity. *Neuroimage*, 85, 1027-1039.
- Svensson, E., Angelborg-Thanderez, M., Sjöberg, L., & Olsson, S. (1997). Information complexity-mental workload and performance in combat aircraft. *Ergonomics*, 40(3), 362-380.
- Tanoue, R. T., Jones, K. T., Peterson, D. J., & Berryhill, M. E. (2013). Differential frontal involvement in shifts of internal and perceptual attention. *Brain stimulation*, 6(4), 675-682.
- Todd, J. J., & Marois, R. (2004). Capacity limit of visual short-term memory in human posterior parietal cortex. *Nature*, 428(6984), 751-754.
- Todd, J. J., & Marois, R. (2005). Posterior parietal cortex activity predicts individual differences in visual short-term memory capacity. *Cognitive, Affective, & Behavioral Neuroscience*, 5(2), 144-155.
- Trafton, J. G., Altmann, E. M., Brock, D. P., & Mintz, F. E. (2003). Preparing to resume an interrupted task: Effects of prospective goal encoding and retrospective

- rehearsal. *Int. J. Hum. Comput. Stud.* 58:5, 583-603. doi: 10.1016/S1071-5819(03)00023-5
- Trafton, J. G., Altmann, E. M., & Ratwani, R. M. (2011). A memory for goals model of sequence errors. *Cogn. Syst. Res.* 12:2, 134-143. doi: 10.1016/j.cogsys.2010.07.010
- Trafton, J. G., & Monk, C. A. (2007). Task interruptions. *Rev. Hum. Factors Ergon.* 3:1, 111-126. doi: 10.1518/155723408X299852
- Tripp, L. D., & Warm, J. S. (2006). Transcranial Doppler sonography. *Neuroergonomics: The Brain at Work*. Ed. R. Parasuraman and M. Rizzo, 82-94.
- Tseng, P., Hsu, T. Y., Chang, C. F., Tzeng, O. J., Hung, D. L., Muggleton, N. G., & Juan, C. H. (2012). Unleashing potential: transcranial direct current stimulation over the right posterior parietal cortex improves change detection in low-performing individuals. *The Journal of Neuroscience*, 32(31), 10554-10561.
- Uddin, L. Q., Clare Kelly, A. M., Biswal, B. B., Xavier Castellanos, F., & Milham, M. P. (2009). Functional connectivity of default mode network components: correlation, anticorrelation, and causality. *Human brain mapping*, 30(2), 625-637.
- Vandenberg, S. G., & Kuse, A. R. (1978). Mental rotations, a group test of three-dimensional spatial visualization. *Perceptual and motor skills*, 47(2), 599-604.
- Voss, M. W., Prakash, R. S., Erickson, K. I., Boot, W. R., Basak, C., Neider, M. B., & Kramer, A. F. (2012). Effects of training strategies implemented in a complex videogame on functional connectivity of attentional networks. *Neuroimage*, 59(1), 138-148.

- Vossel, S., Weidner, R., Driver, J., Friston, K. J., & Fink, G. R. (2012). Deconstructing the architecture of dorsal and ventral attention systems with dynamic causal modeling. *The Journal of neuroscience*, 32(31), 10637-10648.
- Wagner, A. D., Maril, A., Bjork, R. A., & Schacter, D. L. (2001). Prefrontal contributions to executive control: fMRI evidence for functional distinctions within lateral prefrontal cortex. *Neuroimage*, 14(6), 1337-1347.
- Warm, J. S., Matthews, G., & Parasuraman, R. (2009). Cerebral hemodynamics and vigilance performance. *Military Psychology*, 21(S1), S75.
- Warm, J. S., & Parasuraman, R. (2007). Cerebral hemovelocity and vigilance. *Neuroergonomics: the Brain at Work*, MIT Press, Cambridge, MA.
- Weiss, M., & Lavidor, M. (2012). When less is more: evidence for a facilitative cathodal tDCS effect in attentional abilities. *Journal of cognitive neuroscience*, 24(9), 1826-1833.
- Westbrook, J. I., Woods, A., Rob, M. I., Dunsmuir, W. T., & Day, R. O. (2010). Association of interruptions with an increased risk and severity of medication administration errors. *Archives of Internal medicine*, 170(8), 683-690.
- Wiener, E. L. (1977). Controlled flight into terrain accidents: System-induced errors. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 19(2), 171-181.
- Xu, Y., & Chun, M. M. (2006). Dissociable neural mechanisms supporting visual short-term memory for objects. *Nature*, 440(7080), 91-95.

- Yantis, S. (1992). Multielement visual tracking: Attention and perceptual organization. *Cognitive psychology*, 24(3), 295-340.
- Yantis, S. (1998). *The attentive brain* (pp. 221-56). R. Parasuraman (Ed.). Cambridge, MA: Mit Press.
- Zhou, Z., Wang, X., Klahr, N. J., Liu, W., Arias, D., Liu, H., & Liu, Y. (2011). A conditional Granger causality model approach for group analysis in functional magnetic resonance imaging. *Magnetic resonance imaging*, 29(3), 418-433.

Biography

Eric J. Blumberg received his Bachelor of Arts from North Carolina State University in 2010. He continued his education at George Mason University, receiving his Master of Arts in Psychology in 2012. Finally, he received his Doctorate in Philosophy in Psychology from George Mason University in 2016.