An Experimental Evaluation of the Influence of Transcranial Direct Current Stimulation to the Trigeminal Nerve on Attention and Arousal

by

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ABSTRACT

Sustained attention, the ability to concentrate on a stimulus or task over a prolonged period, is essential for goal pursuit and fulfillment. Sustained attention failures can have catastrophic consequences, underscoring the importance of understanding the mechanisms that underlie variability in sustained attention, and developing interventions targeting these mechanisms to reduce such failures. A growing body of research implicates the brainstem locus coeruleus (LC) as a core modulator of attention and arousal. Activation of LC afferents, such as the trigeminal nerve, may indirectly modulate the LC. The altered LC activity could theoretically be tracked via well-established psychological and physiological indicators of attention and arousal, such as performance, self-reports of attention state, and pupillary activity during attention tasks.

The present study tests the hypothesis that continuous transcranial direct current stimulation (tDCS) over the trigeminal nerve of the face improves attentional state, attentional performance, and pupillary reactivity via indirect modulation of the LC. Participants received 2 mA of anodal or cathodal stimulation or sham stimulation over the dorsolateral prefrontal cortex while completing the Psychomotor Vigilance Task. Participants occasionally reported on their attentional state. Pupillary activity was recorded continuously throughout the task. To compare patterns of attention task performance, frequency of task-unrelated thoughts, and pupillary activity across time by stimulation condition, linear mixed-effects models were implemented.

The results replicate the complex interplay between attentional state, attentional performance, and pupillary activity reported in the literature. Specifically, a ubiquitous pattern of performance deterioration was observed, which coincided with an increase in

task-unrelated thoughts and reduced pretrial and task-evoked pupil responses. However, tDCS over the face did not produce significant effects compared to the sham condition in attention task performance, proportion of task-unrelated thoughts, and pupillary activity that would indicate LC modulation. This study addresses the causal relations between LC activity, attentional state, attentional performance, and pupillary reactivity that are still poorly understood in human subjects. The findings reported here support the dominant theory of the role of the LC in attentional processes but fail to support hypotheses suggesting that tDCS of the trigeminal nerve influences activity of the LC and indicators of LC activity.

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CHAPTER 1

INTRODUCTION

Sustained attention, the ability to concentrate on a stimulus or task over a prolonged period, is essential for goal pursuit and fulfillment in everyday life. This ability enables one to maintain focus on goal-relevant information, filter out goal-irrelevant incoming information, and disengage focus when the costs of focusing outweigh the benefits of goal completion. Failure to sustain attention can have a range of consequences from trivial to catastrophic. For example, a student daydreaming during class may fail to note critical information and become embarrassed when called on by her teacher to answer a question. Meanwhile, a doctor becoming distracted during a medical exam may fail to notice a fatal medical indicator in a patient, causing the patient's demise. This is especially problematic in environments where humans must sustain their attention for long periods of time without much environmental support because maintaining attention is notoriously difficult for people (Mackworth, 1948). Partly for this reason, individual differences in abilities like sustaining attention have been regarded as a cornerstone for higher-order cognitive processes such as memory, fluid intelligence, and sensory discrimination—underscoring the prevalence and severity of downstream effects of attentional failures (Robison & Brewer, 2019; Burgoyne & Engle, 2020). Accordingly, investigating the causes of attentional failures is important for understanding individual differences in higher-order cognition that is in part dependent on the control of attention but can also inform ways to prevent, modulate, and mitigate attentional failures.

In contrast to a singular-construct conceptualization of attention, sustained attention has been theorized to consist of two distinct but related components: intensity

and consistency (Kahneman, 1973). Intensity refers to the amount of attentional effort one is dedicating to a stimulus or task, while consistency refers to the pattern of intervals where one is allotting attentional effort. Variability in these two components occurs within individuals across time and between individuals (Miller & Unsworth, 2021; Unsworth & Miller, 2021) and sheds light on how to conceptualize and approach attention research. It is therefore an important goal to better understand the mechanisms of variability in sustained attention in a precise manner if researchers are to develop interventions targeting these mechanisms to reduce sustained attention failures. The present study aims to address this goal.

In laboratory settings, researchers measure sustained attention by having participants monitor for a specific stimulus and respond to that stimulus in an appropriate manner over long periods of time. A classic example of a sustained attention task is the psychomotor vigilance task (PVT), which requires that the participant make a specific response upon detection of a change in a stimulus (Dinges et al., 1997; Dinges & Powell, 1985). A variant of the PVT (used in this study) requires that participants attend to a row of zeroes at the center of a computer screen that, after a random intertrial interval, will begin to count like a stopwatch. In the PVT, the participant's goal is to press the spacebar on the keyboard as quickly as possible to halt the count. Because this target event is unpredictable, participants must remain vigilant to detect the stimulus change and respond quickly. Aggregate performance throughout the PVT shows a robust slowing in response times from the beginning to the end of the task (Mackworth, 1964; McCormack, 1960). This classic group-level pattern of performance deterioration observed during sustained attention tasks is referred to as the vigilance decrement. In simple reaction time

tasks such as the PVT, the vigilance decrement manifests as a slowed response time to detect change across trials and increased variability in response times.

A Neural Account of Sustained Attention and the Vigilance Decrement

The literature is replete with theories describing the processes involved in sustained attention and the vigilance decrement (see Giambra, 1989; Helton & Warm, 2008; Manly et al., 1999; Robertson et al., 1997; Robison et al., 2021; Smallwood et al., 2004; Thomson et al., 2015; Warm et al., 2008). However, the neural mechanisms driving these processes remain ambiguous. The prefrontal cortex and midbrain dopamine systems have been implicated in attentional processes but are not fully understood. Recent research has identified another neuromodulatory system that may play a critical role in the optimization of engagement and disengagement from tasks based on evaluations of task utility, the brainstem Locus Coeruleus Norepinephrine system (LC-NE; Aston-Jones & Cohen, 2005; Poe et al., 2020).

The LC is a small nucleus of approximately 16,000 norepinephrine-producing neurons (per hemisphere) in the human brainstem. The LC has widespread projections and is the sole source of norepinephrine to the central nervous system. Through these diffuse projections, the LC has wide-ranging effects on cognition that appear to be modular in nature (Poe et al., 2020; Schwarz & Luo, 2015). According to the Adaptive Gain Theory (Aston-Jones & Cohen, 2005), modulation of various neural pathways by the LC is accomplished by a continuum of baseline tonic LC activity and stimulus-evoked phasic LC responses. These patterns of activity facilitate attentional engagement and disengagement by optimizing responsiveness to salient events. The relation between LC activity and attentional performance follows an inverted U shape–optimal

performance is achieved at intermediate LC activity (Figure 1). During low tonic activity, where phasic responses are small or absent, LC neurons are less responsive to salient events thereby creating lower than optimal phasic firing rates to enhance goal-relevant stimuli. Low tonic activity is therefore associated with inattentiveness, being non-alert, and disengagement from the environment, resulting in poor attentional performance (Foote et al., 1980; Aston-Jones & Bloom, 1981; Aston-Jones et al., 1991). On the opposite end of LC activity, during high tonic activity, the LC fires persistently and is indiscriminately responsive to incoming stimuli. In a high tonic mode, the LC is unable to enhance goal-relevant stimuli (phasic responses) amidst the increased noise also being enhanced. High tonic activity is associated with distractibility and exploratory behavior, anxiety/stress, hyperactivity, and over-arousal, resulting in poor attentional performance (Aston-Jones et al., 1999; Howells et al., 2012). In terms of attentional performance, much like Goldie Locks, the LC has a "just right" mode where neurons in the LC fire optimally to goal-relevant stimuli while suppressing goal-irrelevant stimuli. In this state, tonic activity is intermediate and phasic responses to salient stimuli are optimal (Aston-Jones et al., 1991; Aston-Jones & Cohen, 2005).

The Adaptive Gain Theory (Aston-Jones & Cohen, 2005) would predict that performance deterioration in attention tasks likely reflects an increasing dearth of salient events across trials leading to reductions in tonic and phasic LC firing rates necessary for optimizing effective signal-to-noise ratios in critical sensory processing sites. Theories linking LC activity to goal pursuit provide insight into the vigilance decrement but much of the research on the LC has been performed on animal models. The LC is a challenging structure to study due to its size and location in the brain. Its small size makes it difficult

to structurally and functionally image while its location makes it dangerous to modulate to assess for causal relations between LC activity and attention performance. As expected, researchers have developed clever approaches to track and potentially modulate LC activity by leveraging its diffuse projections.

Pupillometry: Leveraging LC Projections to Track LC Activity

Anatomically, the LC has projections that influence sympathetic and parasympathetic nervous systems, which allow LC activity to indirectly modulate pupil constriction and dilation (Figure 2; Joshi, 2021; Joshi & Gold, 2020; Liu et al., 2017; Spector, 1990). Pupillary constriction is mainly under the control of the parasympathetic Edinger–Westphal nucleus in the brainstem, which receives direct input from the LC. Due to hemi-decussation of pupillary fibers at the optic chiasm, both pupils will receive signals from ipsilateral and contralateral Edinger–Westphal nuclei and indirectly from either LC nucleus (Joshi, 2021; Joshi & Gold, 2020; Liu et al., 2017; Spector, 1990). Pupil dilation is modulated by the ipsilateral superior cervical sympathetic ganglion (SCG)—research suggests that the LC modulates pupil dilation indirectly through its connections to the SCG in an ipsilateral manner (Joshi & Gold, 2020; Liu et al., 2017).

A growing body of research has consistently shown that the pupil size of the eye partially indexes LC neuron firing rates. Pharmacological manipulations of LC firing have demonstrated how LC activity plays a causal role in pupil responses. For example, α2-adrenoreceptor agonists (such as clonidine) reduce tonic LC firing and result in decreased baseline and phasic pupil size while α2-adrenoreceptor antagonists (such as modafinil, yohimbine) increase tonic LC firing and result in increased baseline and phasic pupil size (Phillips, et al., 2000; Hou et al., 2005; Liu et al., 2017).

Electrophysiological recordings from the LC have shown that there is a strong relation between tonic LC firing and baseline pupil diameter (Aston-Jones & Cohen, 2005; Joshi et al., 2016).

In psychological research settings, pretrial pupillary activity (pupil activity in preparation for a behavioral task response) is thought to reflect tonic LC activity, following a U-shaped relationship between pretrial pupil size and attention performance (Figure 1; Jepma & Nieuwenhuis, 2011; Mittner et al., 2016; Murphy et al., 2011; Unsworth, et al., 2020; Unsworth & Robison, 2016, 2017). Specifically, according to the LC-NE Account of Individual Differences in Working Memory and Sustained Attention (Unsworth & Robison, 2017) smaller or larger pretrial pupil sizes reflect lower and higher levels of tonic LC activity, respectively (Figure 1). In terms of behavioral indicators, smaller or larger than baseline pretrial pupil measures predict poor attentional performance as well as self-reports of inattentiveness (Robison, 2018; Unsworth & Robison, 2016). Whereas, intermediate pretrial pupil size reflects phasic activity, self-reports of focused attention, and predicts optimal attentional performance.

Task-evoked pupil responses (TEPRs) also track fluctuations in attention predicted by the Adaptive Gain Theory (Aston-Jones & Cohen, 2005). Weak TEPRs to target stimuli preceded by larger than baseline pretrial pupils are associated with self-reports of distractibility and poor performance on attention tasks (Mittner, et.al., 2016; Unsworth & Robison, 2016, 2017). Conversely, weak TEPRs or strong TEPRs that are time-locked to internal events preceded by smaller than baseline pretrial pupil size are associated with self-reports of mind wandering and poor performance on attention tasks (Mittner, et.al., 2016; Pelagatti, Binda, & Vannucci, 2020; Unsworth & Robison, 2016,

2017). Strong TEPRs that are time-locked to target stimulus onset preceded by intermediate pretrial pupils are associated with focused attention and optimal task performance (Mittner, et.al., 2016; Unsworth & Robison, 2016, 2017).

There are additional pupillary and behavioral signals that can be extracted from pupil recordings during cognitive tasks that are important for understanding sustained attention. Pupillary reactivity can be used to distinguish intensity and consistency of attention which theoretically reflect patterns of LC activity (Unsworth & Miller, 2021). Intensity can be extracted from mean measures of pretrial pupil diameter as well as mean TEPRs across time. Consistency can be calculated as the relative variability in mean pretrial pupil diameter and TEPR diameter across an attention task. These measures of mean pupil size and pupil size variability are closely tied to slow responses and patterns of performance failures on attention tasks, and self-reports of attention state. These signals will be examined in the current study.

tDCS: Leveraging LC Projections to Modulate LC Activity

Pupillometry leverages LC projections to index fluctuations in tonic activity. The diffuse projections of the LC may also be leveraged to modulate tonic activity. Appreciation for the anatomical features of the LC, including its many efferent and afferent connections has led researchers to hypothesize that the LC and indicators of LC activity can be indirectly modulated via stimulation of these afferent projections. The LC is part of the Ascending Reticular Activating System (ARAS), a collection of brainstem nuclei that integrate peripheral sensory information from the cranial nerves and play an instrumental role in attentional processes (De Cicco et al., 2018; Parvizi & Damasio, 2001). The ARAS receives input from Cranial Nerve V, the trigeminal nerve—the

trigeminal nerve innervates the face by 3 major branches and is responsible for facial sensations. The LC receives signals from the trigeminal nerve by a multitude of pathways to/through the ARAS. Researchers have thus hypothesized that stimulation of the trigeminal nerve could activate the LC and modulate attention and arousal (De Cicco et al., 2018; Adair et al., 2020; van Boekholdtet al., 2021).

The trigeminal nerve has been stimulated in clinical settings using transcranial direct current stimulation (tDCS) for many years to treat nociceptive disorders (Adair et al., 2020). tDCS involves the placement of two electrodes over the scalp—the anode delivers positive electrical charge, and the cathode produces negative charge and receives current from the anode (Reinhart et al., 2017). tDCS has been thought to pass current from the anode to the cathode, however, there is debate as to how and if stimulation is achieved at the target sites (Horvath, Carter, & Forte, 2014; Horvath, Forte, & Carter, 2015; Price, & Hamilton, 2015; Riggallet al., 2015; Stagg, & Nitsche, 2011).

Some researchers have argued that the electrical current traverses the scalp, skull, meninges and cerebral-spinal fluid, and several layers of the cortex to reach a target brain area. By this account, much of the electrical charge is lost but sufficient electrical current from the anode reaches the target brain area to change the membrane potential of targeted neurons making neurons more or less likely to fire (Reinhart et al., 2017; van Boekholdt et al., 2021). Specifically, excitation of neurons via a reduction in GABA concentrations has been recorded under anodal electrodes; conversely, neuron inhibition via a reduction in glutamate concentration has been recorded under cathodal electrodes (Stagg, et. al, 2009). This stimulation, then, has short-term effects on neural plasticity which are argued to manifest as changes in behavior and cognition.

Researchers who have used anodal tDCS over the dorsolateral prefrontal cortex in humans have reported positive effects on attention processes and performance on attention tasks. For example, Pope and colleagues (2015) implemented an attentionally demanding auditory arithmetic task and a visual analog scale for assessing attention and mental fatigue while administering anodal, cathodal, and sham tDCS over the forehead. Participants in the anodal condition had higher attention performance (faster and more accurate responses) compared to the sham and cathode groups. Similarly, in a study conducted by Miler and colleagues (2018), participants who performed an Attention Network Task under anodal tDCS performed better compared to sham (smaller reaction time difference score in the executive control component of attention).

The cognitive changes reported in the above tDCS studies may be a result of induced neurochemical changes in target areas identified by Stagg and colleagues (2009). However, the forehead is densely innervated by the terminal branches of the trigeminal ganglion (Adair, et al., 2020). Some researchers argue that the transcranial mode of action seems unlikely given that electricity will take the path of least resistance. Instead, tDCS may work via a transcutaneous mechanism rather than a transcranial one (van Boekholdt et al., 2021). Research on similar transcutaneous electrical stimulation devices reports stimulation of peripheral nerves, but this mechanism is yet to be validated for tDCS (Adair et al., 2020; van Boekholdt et al., 2021). Transcutaneous stimulation has implications for interpretations of the significant effects of tDCS on cognition—particularly, stimulation over the forehead. Montages (MRI-derived finite element models) from a current-diffusion imaging study revealed that electrical current from tDCS passes over the scalp and targets the trigeminal nerve (Adair et al., 2020). Thus,

researchers have begun to hypothesize that observed cognitive and behavioral effects are due to downstream stimulation of the LC rather than stimulation of targeted subcortical structures.

Thought Probes: Leveraging Behavioral Manifestations of LC Activity

As discussed above, LC activity will manifest as observable changes in performance that are due to changes in attention state. Studies on task-unrelated thoughts have become popular as they have been associated with vigilance decrements on cognitive tasks (Giambra, 1989; McVay & Kane, 2012; Smallwood et al., 2004; Weinstein, 2018). Task-unrelated thoughts refer to thoughts that are not directly related to one's current goals. These thoughts may be directed internally, externally, or seemingly nowhere (i.e., daydreaming, external distractions, and mind-blanking, respectively). Further, these self-realized lapses of attention may serve as a phenomenological experience of inefficient tonic/phasic LC activity.

In humans, attentional states can be tracked throughout attention tasks by implementing self-report measures such as thought probes, which are subjective reports of a participant's current attentional state. Using thought probes that are interspersed throughout vigilance tasks allows researchers to examine individual differences in self-reported attentional state (specifically the tendency toward task-unrelated thinking), patterns of sustained attention, and they do not require extra effort from the participant when making reports (Robison et al., 2019; Weinstein, 2018; Wiemers & Redick, 2019). Since vigilance decrements are predicted by the frequency of task-unrelated thoughts, researchers can use thought probes to track the vigilance decrement and validate whether performance on sustained attention tasks corresponds with one's current attentional state

and tendency to mind wander. According to Mindlessness theories or Resource-Control Theory (and consistent with predictions made by the Adaptive Gain Theory), individuals who demonstrate steeper vigilance decrements should also be those who have higher instances of mind wandering across trials (Helton & Warm, 2008; Thomson et al., 2015; Aston-Jones & Cohen, 2005).

The Current Study

In the current study, we will examine the influence of trigeminal nerve stimulation on attentional state, attentional performance, and pupillary reactivity. Participants will receive either true tDCS or sham tDCS stimulation while completing a psychomotor vigilance task. Participants will have their pupils continuously recorded and will provide self-reports of attentional state during and after completion of the task. This study tests the hypothesis that consistent anodal tDCS current will result in improved attentional state, attentional performance, and pupillary reactivity that is distinct from the sham group. Further, we expect that the distinct patterns for each group will coincide with the complex interplay of LC activity illustrated in Table 1.

CHAPTER 2

METHOD

Ethics and Researcher Training

This study was approved by the Institutional Review Board of Arizona State University. To ensure ethical principles were upheld, researchers obtained written informed consent, provided descriptions at each step of the procedure, and ensured consent was continuous throughout the experiment. Participants were debriefed upon completion of the experiment. Participants were informed that their participation was fully voluntary and were informed that withdrawal at any point of the study would not result in penalty or loss of benefits. Participants were encouraged to communicate any symptoms or discomfort that did not coincide with the anticipated side effects described to them (i.e., itching, tingling, and redness at the electrode sites). All researchers were trained on the administration of tDCS and potential adverse effects in line with Woods et al. (2016). Guidance for administration and discontinuation of a tDCS session was detailed within a standard operating procedure. Researchers were present throughout the entirety of each experiment and monitored participants for any adverse effects or signs of discomfort.

Participants and Sampling

Arizona State University undergraduates were recruited to participate in the current study. An a-priori power analysis with an alpha 0.05 (two-tailed) and power of 0.80 indicated a minimum sample size of 194 participants (64 per experimental condition) to recover a medium effect size (d = 0.5) (Faul et al., 2007). A total of 225 students participated in this study and were evenly and randomly assigned to one of three experimental conditions (75 per condition). Participants were recruited via SONA Systems

as part of their course requirement/to earn course credit. Eligible participants were required to be at least 18 years of age, be enrolled in PSY 101 or PSY 290, have normal or corrected-to-normal vision, and have no history of epileptic seizures.

tDCS: Materials and Procedure

tDCS stimulation was administered using the Soterix Medical 1x1 tDCS Model 1300A Low-Intensity Stimulator (Soterix Medical Inc., 2011). For user safety, the tDCS delivery system automatically shuts off if the electrical current exceeds 2.0 mA—what has been deemed safe for humans and has been associated with cognitive effects when placed over the forehead (Boggio et al., 2006; Iyer et al., 2005). For reproducible and precise tDCS operation, the Soterix stimulator reads out actual current, contact quality, and has a timer for stimulation duration.

A between-subjects experimental design was implemented with one factor (tDCS type) tested at three levels (true anodal tDCS, true cathodal tDCS, and sham). Participants were assigned to true anodal tDCS, true cathodal tDCS, or sham tDCS conditions on an alternating basis relative to their time of participation in the study. Prior to administering stimulation, the F4 dorsolateral prefrontal cortex and P10 Mastoid were identified using the International 10/20 System of Electrode Placement and superficial anatomical markers.[1] Condition assignment determined whether the anode was placed over F4 or over P10 and vice versa for cathode placement. [2]

[1] These regions were targeted based on research that has stimulated the trigeminal nerve for clinical treatment of trigeminal neuralgia (Adair et al., 2020), research that has used other variations of electrical stimulation to modulate attentional performance of the PVT (Piquet et al., 2011), and current density imaging montages developed by Adair, et al. (2020) suggesting that current flow from F4 to P10 targets the trigeminal nerve.

[2] The reason for including the cathode condition was based on completeness. No hypotheses were made regarding the effect of cathodal stimulation as there was no guidance in the literature regarding the effect of direction of current flowing over the trigeminal nerve.

Saline-soaked electrodes (Soterix Medical 5cm x 7cm EASYpads) were placed over the scalp and were secured in place with tubular elastic retainer netting and a head strap. Stimulation was administered for the entirety of the PVT (approximately 22 minutes). In the true tDCS conditions, the tDCS machine ramps up to 2.0 mA for 30 seconds, then provides a continuous 2.0 mA electrical current to the subject's scalp. In the sham condition, the anode was placed over F4 and the cathode was placed over P10. The sham tDCS condition ramps up to 2.0 mA for 30 seconds then ramps down to 0.0 mA for the next 30 seconds, at which point the machine is discretely shut off by the experimenter.[3] The tDCS apparatus was kept out of the sight of participants, who were unaware of their group assignment.

Pupillometry: Materials, Measures, and Procedure

Participants used a chinrest and wore a fiducial marker to accurately track changes in pupil diameter.[4] Participants were instructed to keep their heads still for the duration of the experiment. Pupillary reactivity was recorded continuously at 60 Hz using a GazePoint G3 HD eye tracker (Figure 3; Gazepoint Research Inc., 2019) to track fluctuations in LC activity and attentional state. The eye tracker was calibrated and validated for each participant before initiating the PVT. The room was kept dark except for the screen lighting, which was kept constant within and across participants.

[3] Horvath et al. (2014) and Woods et al. (2016) suggest that participants are able to identify whether they are in a true stimulation or sham condition, to control for this, participants were informed that sensations associated with stimulation vary widely from absent to mild. Additionally, participants were told how in the pilot study, participants often reported initial sensation that subsided. The cathodal stimulation then served as a masked control condition.

[4] This helps control for individual differences in pupil size and changes in pupil size recording due to head movements or changes in distance from the eye tracker.

Data from the right eye was used for data analysis.[5] Missing data due to blinks, off screen fixations or eye movements, head movements, or eye tracker malfunctions were excluded from data analysis. Pretrial baseline responses were computed as mean pupil size and pupil size variability for each condition during the 2 seconds of the fixation screen prior to the initiation of each trial. Mean TEPRs were extracted from a 0 ms to 2000 ms timeframe post-stimulus change (when the zeroes on the screen began counting). The mean amplitude was identified at 600 ms to 750 ms post-stimulus change. Mean pupil size at the mean amplitude timeframe was calculated and compared across quintiles of the PVT for each tDCS condition. Pupillary activity (mean and variability) will be evaluated in relation to intensity and consistency of attention.

Psychomotor Vigilance Task: Materials, Measures, and Procedure

A variation of the PVT was used to track changes in sustained attention (Dinges & Powell, 1985). The task was designed and executed using Pygaze (Dalmaijer et al., 2014). The task was presented on an 18.5" HD Dell monitor.

Participants completed five practice trials followed by a total of 120 experimental trials (Figure 3). At the start of each trial, participants are shown a fixation screen for two seconds. This was followed by a set of blue zeroes, '0.000', on the screen with the digit in the ones place indicating seconds elapsed and the digits following the decimal indicating milliseconds elapsed. The zeroes began counting like a stopwatch at a random interval

[5] In healthy individuals, pupils tend to be equal in size and respond in tandem regardless of discrepant input. This is because of the hemi-decussation of pupillary fibers at the optic chiasm—both pupils will receive signals from ipsilateral and contralateral Edinger–Westphal nuclei which control pupil constriction (Spector, 1990). Additionally, the LC will send input to the ipsilateral superior cervical ganglion, which results in pupillary dilation (Yang et al., 2017). However, it appears that the LC has bilateral inputs from the trigeminal nerve (Simpson et al., 1997). Thus, the choice of left or right eye is arbitrary and should not make a difference in recordings.

between two and ten seconds, requiring that participants be vigilant or potentially miss their cue to respond. Participants were instructed to press the spacebar as quickly as possible to halt the digits that had begun counting but were discouraged from responding preemptively. Upon pressing the spacebar, the digits froze on the screen, and the response time remained on the screen in red font for one second. A blank screen appeared for 500 milliseconds. The subsequent screen was either a new trial or a thought probe.

Average response time (mean) and response time variability (coefficient of variation) were measured in milliseconds as a function of block (i.e., 5 blocks of trials such that each block represents a quintile of total valid trials) to indicate patterns in attention performance. Missing data were excluded from the analysis and participants with more than 10 instances of "bad" response times (defined as response times less than 200 milliseconds or greater than 3000 milliseconds) were excluded.

Thought Probes: Measures and Procedure

Throughout the PVT, participants were prompted with thought probes that examine on-task thinking, task-related interference, internal distraction, external distraction, and mind blanking. Respectively, participants reported one of the following: 1) I was totally focused on the current task. 2) I was thinking about my performance on the task. 3) I was distracted by sights/sounds happening around me. 4) I was thinking about things unrelated to the task. 5) My mind was blank. 24 total thought probes were evenly interspersed throughout the PVT–a thought probe was presented after every fifth trial.

For each participant, the proportion of task-unrelated thinking was calculated. Task unrelated thoughts were calculated as the sum of responses three through five across the task. Then an average of task unrelated thoughts was calculated across PVT blocks.

Attention and Arousal Survey: Measures and Procedure

After completing the PVT, participants completed a brief survey that probed the participants' levels of attentiveness, engagement, intensity of attention, consistency of attention, motivation, and whether they thought the tDCS apparatus helped them perform better on the task. Participants provided a subjective rating of their performance in comparison to how well they assumed others performed. Participants were allowed to provide any additional comments that were relevant to their performance of the task.

Upon completion of the study, the tDCS session was aborted and the apparatus was allowed to ramp down, then the apparatus was shut down. The electrodes were removed carefully from the participant's scalp. Participants were debriefed by the researcher and granted course credit for participating in the study.

CHAPTER 3

RESULTS

Data were processed and visualized in R using tidyverse, data.table, and psych packages (R Core Team, 2020; Wickham, et. al., 2019; Dowle & Srinivasan, 2019; Revelle, 2015). Data were analyzed using the lmerTest package (Kuznetsova, et al., 2017).

Linear mixed-effects models were implemented to compare changes in mean pretrial pupil size and relative variability, mean task-evoked pupil response, mean and relative variability in response time on the PVT, and proportion thought probe responses across tDCS conditions at the subject level. All linear mixed-effects models are specified in Tables 2-4. The decision to use a linear mixed-effects model was based on validation via an inter-class correlation (ICC) value above the predetermined threshold of 10%. Random effects that were included in each model were determined by conducting a 50:50 mixture chi-square test to compare a random intercepts model to the random-effects model. The normality of residuals was checked by creating a Q-Q plot. It was determined that residuals were normally distributed.

Pupillometry

The first analysis focused on the general prediction that pupillary dynamics will indicate both increased consistency and intensity of attention for the anodal stimulation condition. Specifically, the first two models tested the hypothesis that anodal stimulation to the trigeminal nerve will result in a greater proportion of intermediate pretrial pupil size (mean) and less pretrial pupil variability (coefficient of variation) compared to the true cathodal stimulation and sham conditions. The third model tested the hypothesis that

anodal stimulation to the trigeminal nerve will result in a greater proportion of large TEPRs.

Mean Pretrial Pupil Size

The first model revealed that an effect of block on mean pretrial pupil size (mm) was significant (b = -0.02, t(215.34) = -3.86, p < 0.05, 95% CI [-0.03, -0.01]). Across blocks, participant pretrial pupil size decreased by 0.02 mm. The effect of anodal stimulation on pretrial pupil size was not significant (b = 0.02, t(215.34) = 0.25, p = 0.79, 95% CI [-0.15, 0.20]) nor was the effect of cathodal stimulation (b = 0.009, t(215.34) = 0.06, p = 0.92, 95% CI [-0.17, 0.18]). In the anodal tDCS condition, pretrial pupil size increased by 0.2 mm across trial blocks. Pretrial pupil size in the cathodal condition increased by 0.009 mm. Neither of these increases were statistically significant. There was no significant interaction between block and tDCS stimulation on pretrial pupil size (anodal tDCS and block: b = 0.01, t(215.34) = 1.63, p = 0.10 , 95% CI [-0.003, 0.03]; cathodal tDCS and block: b = -0.004 , t(215.34) = -0.47, p = 0.63, 95% CI [-0.02, 0.01]). The relation between mean pretrial pupil size and trial blocks across tDCS condition can be visualized in Figure 4.

Relative Pretrial Pupil Variability

The second model again revealed a significant effect of block on relative pretrial pupil size variability (coefficient of variation; b = 0.004, t(266) = 5.42, p <0.05, 95% CI [0.003, 0.006]). Across blocks, participant pretrial pupil diameter became more variable. However, tDCS stimulation did not influence pupil size variability (anodal tDCS: b = 0.008 t(266) = 1.15, p = 0.24, 95% CI [-0.006, 0.02]; cathodal tDCS: b = 0.006, t(266) = 0.85 , p = 0.39, 95% CI [-0.008, 0.002]). Finally, there was no significant interaction between block

and tDCS stimulation (anodal tDCS and block: b = -0.001, t(266) = -0.84, p = 0.39, 95% CI [-0.003, 0.001]; cathodal tDCS and block: b = -0.002, t(266) = -1.93, p = 0.05, 95% CI [-0.004, 0.00002]). The relation between relative pretrial pupil size variability and trial blocks across tDCS condition can be visualized in Figure 4.

Mean Task-Evoked Pupil Response

The third model revealed a significant effect of block on TEPR mean amplitude (b = -0.01, t(396.90) = -4.14, $p < 0.05$, 95% CI [-0.01, -0.006]). Mean amplitude of TEPRs decreased in magnitude across trial blocks. tDCS stimulation did not produce a significant effect on TEPRs (anodal tDCS: b = 0.03, t(400.70) = 1.87, p = 0.06, 95% CI [-0.001, 0.06], cathodal tDCS: b = -0.01, t(400.60) = -1.13, p = 0.25, 95% CI [-0.05, 0.01]). tDCS did not produce unique declines nor increases in TEPRs across the PVT. Finally, there was no interaction detected between block and tDCS condition (anodal tDCS and block: b = -0.006, t(396.90) = -1.49, p = 0.13, 95% CI [-0.01, 0.001]; cathodal tDCS and block: b = -0.0003, t(396.90) = -0.07, p = 0.93, 95% CI [-0.008, 0.007]). The relation between TEPRs and trial blocks across tDCS condition can be visualized in Figure 5.

Psychomotor Vigilance Task

The second analysis (fourth and fifth models) tested the hypothesis that anodal stimulation to the trigeminal nerve will result in improved performance and less variability on the PVT across trial blocks compared to sham stimulation. At the aggregate level, participants responded to stimulus onset at an average of 388.03 ms (SD = 50.94 ms), which closely replicates the literature (Unsworth, Miller, & Robison, 2020; Robison, 2018).

Mean Response Time

The fifth linear mixed effects model revealed that a significant effect of block on mean response time (ms) for the PVT was significant (b = 11.15, t(237.36) = 8.18, p < 0.05, 95% CI [8.48, 13.81]). Across blocks, participant response time slowed by 11.15 ms. There was a significant effect of anodal stimulation on mean response time such that response times were 14.03 ms slower for those who received anodal stimulation (b = 14.03, t(237.36) = 2.03, p < 0.05, 95% CI [0.51, 27.54]). There was not a significant effect of cathodal stimulation on mean response time (b = -3.38, t(237.36) = -0.49, p = 0.36, 95% CI [-16.85, 10.07]. There was no interaction effect between block and either stimulation condition (anodal tDCS and block: b = -2.63, t(237.36) = -2.63, p = 0.17, 95% CI [-6.41, 1.14]; cathodal tDCS and block: b = -1.75, t(237.36) = -0.90, p = 0.36, 95% CI [-5.52, 2.01]). The relation between mean response time and trial blocks across tDCS condition can be visualized in Figure 6.

Relative Response Time Variability

The fifth linear mixed effects model revealed a significant effect of trial block on response time variability (coefficient of variation; b = -0.01, t(431.58) = 3.71, p < 0.05, 95% CI [-0.006, 0.01]). This means that overall participant response times became more variable across the PVT. Additionally, there was a significant effect of anodal stimulation on response time variability (anodal tDCS: b = 0.02, t(431.58) = 2.08, p < 0.05, 95% CI [-0.001, 0.05]). However, no effect was identified for cathodal stimulation (b = 0.001, t(431.58) = 1.23, p = 0.21, 95% CI [-0.01, 0.04]). Finally, there was no significant interaction between block and tDCS stimulation (anodal tDCS and block: b = -0.008, t(431.58) = -1.69, p = 0.09, 95% CI [-0.01, 0.001]; cathodal tDCS and block: b = -0.002,

t(431.58) = -0.59, *p* = 0.55, 95% CI [-0.01, 0.006]). The relation between response time variability and trial blocks across tDCS condition can be visualized in Figure 6.

Thought Probe Responses

The third and final analysis (the sixth model) tested the hypothesis that anodal stimulation to the trigeminal nerve will result in fewer task-unrelated thoughts compared to the sham condition. Task-unrelated thoughts are calculated as the proportion of external distraction, mind wandering, and mind blanking reported throughout the task.

The sixth model revealed a significant effect of block on proportion of task-unrelated thoughts, such that task-unrelated thoughts increased by 7% across blocks (*b* = 0.07, *t*(328.67) = 8.00, *p* < 0.05, 95% CI [0.05, 0.09]). There was no significant effect of tDCS condition on proportion of task-unrelated thoughts (anodal tDCS: *b* = 0.04, *t*(328.67) = 1.07, *p* = 0.28, 95% CI [-0.04, 0.13]; cathodal tDCS: *b* = 0.06, t(328.67) = 1.32, *p* = 0.18, 95% CI [-0.02, 0.14]). There was no significant interaction between block and tDCS stimulation (anodal tDCS and block: *b* = -0.01, *t*(328.67) = -0.76, *p* = 0.44, 95% CI [-0.03, 0.01]; cathodal tDCS and block: *b* = -0.02, *t*(328.67) = -1.69, *p* = 0.09, 95% CI [-0.04, 0.003]). The relation between task-unrelated thoughts and trial block can be visualized in Figure 7.

CHAPTER 4

DISCUSSION

The current study examined the influence of trigeminal nerve stimulation on physiological and behavioral indices of LC activity: pretrial pupil diameter, task-evoked pupil responses, attention performance, and proportion of task-unrelated thoughts. Participants were assigned to a continuous anodal tDCS stimulation group, cathodal tDCS stimulation group, or sham tDCS group. Participants had their pupils recorded continuously while completing the Psychomotor Vigilance Task. Participants provided self-reports of attentional state throughout and after completion of the task in the form of thought probe responses and survey responses. This study tested the hypotheses that continuous anodal tDCS will result in the improvement of attentional state, attentional performance, and pupillary reactivity compared to cathodal and sham stimulation.

The Locus Coeruleus, Attention, and Arousal

Importantly, this study replicated many group-level patterns of performance, attention state, and pupil activity previously reported in the literature (Robison, 2018; Unsworth & Robison 2016, 2017; Unsworth, Miller, & Robison, 2020). The Psychomotor Vigilance Task requires sustained attention as the target event that one must detect and respond to is unpredictable and requires a fast response. Across the duration of the task, participants responded more slowly, reflecting the vigilance decrement. Participant responses also became more variable. Based on theories of the LC, increases in mean response time and variability are to be expected, reflecting an increase in lapses of attention across the duration of the task. Consistent with the complex interplay between LC activity and behavior laid out in Table 1, the patterns of intensity (vigilance

decrement) and consistency (increased response time variability) coincide with increased reports of task-unrelated thoughts, particularly mind-wandering. Similarly, pretrial pupil responses mirrored these behavioral patterns as pupil diameter decreased in size and increased in variability in preparation for the target event across trial blocks. Finally, TEPRs were generally strong but followed the anticipated decline in amplitude with time on task. These findings support predictions made by theories of the role of the LC in attention and arousal as individuals began to disengage from the monotonous, low utility task (Aston-Jones & Cohen, 2005).

Stimulation of the Trigeminal Nerve

The results reported here failed to support the hypothesis that tDCS to the trigeminal nerve influences LC activity. Participants commonly reported tingling and itching sensations throughout the task or initial sensations that would subside upon initiating the task. This indicates that the trigeminal nerve was being stimulated but that the behavioral and physiological effects, however, the anodal stimulation did not uniquely impact these effects. Although anodal tDCS had a significant effect on mean response time, it is important to note that LC activity theoretically manifests as changes in behavior, state, *and* pupil activity, which was not found here. Additionally, the effect of anodal tDCS on response time was in the opposite direction of the anticipated effect. One could argue that stimulation over the dorsolateral prefrontal cortex replicated prior research findings (particularly the caveats posed by Woods, et al., 2016 regarding continuous stimulation). Furthermore, perhaps stimulation had a transcranial rather than transcutaneous effect. But one must be mindful about such speculations as cathodal

stimulation did not replicate the literature–there was no opposite effect on attention performance.

Reasons why tDCS effects were not detected here may be elucidated by Horvath, Carter, and Forte (2014) who highlight the role of intra- and inter-individual differences in tDCS effects. It may have been the case that some individuals began the task at a different mode of LC tonic activity—dysregulation and individual differences have been implicated in attention, anxiety, and sleep disorders, which likely affect task performance. Thus, for individuals with low tonic activity, tDCS may have pushed tonic activity into an intermediate state while pushing those initiating the task at an intermediate mode into a hypertonic state. Similarly, changes in tonic firing within the task would have been constantly pushed into a higher level of LC firing. Conversely, continuous stimulation may have an opposite effect due to the habituation of over-stimulated neurons. Woods and colleagues (2016) provide guidance regarding the administration of tDCS. In addition to the continuous stimulation approach used here, Woods and colleagues suggest a shorter session of stimulation prior to task initiation as an alternative method of achieving tDCS effects. Stimulation lasting longer than 13 minutes may result in an inversion of tDCS effects, which may explain the results reported here.

To address the potential confounds of individual differences, future studies may investigate the reliability of tDCS to the trigeminal nerve within participants across repeated sessions. Perhaps tDCS has different effects at the individual level, in which case, a titration of stimulation parameters would be beneficial (Woods, et. at., 2016). This

would allow for appropriate adjustment in the mA current delivered and/or the timing of mA current delivery, improving the precision of tDCS administration.

Conclusion

The findings here replicate research implicating the LC in cognitive processing via patterns of attention task performance, self-reports of attentive state, and pupillometric measures. The findings do not support the use of tDCS over the trigeminal nerve for indirect stimulation of the LC (indicated by pupil reactivity, self-reports of attention state, and attention task performance). tDCS is a highly debated method of neuromodulation in the literature. These findings raise more questions about the efficacy of tDCS for modulating human performance in attention tasks, at least by way of a transcutaneous route. While there remains much work to be done on new techniques and methods for neurostimulation, it may simply be the case that it is not possible to stimulate the LC indirectly by using tDCS to the trigeminal nerve.

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APPENDIX A

TABLES

Table 1

The Complex Interplay of Indicators of Locus Coeruleus Activity

LC Activity	Physiological Indicators			Behavioral Indicators		
	Network Connectivity	Pretrial Pupil Activity	Task-Evoked Pupil Response	Self-Reported State	Task Performance	Interpretations of Behavior
Tonic/Baseline: Low Phasic response: Low to absent	Intermediate	Reduced to Intermediate Increased variability	Strong response time-locked to internal events Reduced response to target stimulus	• Inattentive • Non-alert • Under-aroused	Decreased Performance: • Low responsivity to salient events Increased variability	Disengagement from the environment: • Mind wandering
Tonic/Baseline: Intermediate Phasic response: High	Strong Increased responsivity of neural circuits to salient stimuli	Intermediate Low variability	Strong response time-locked to target stimulus	• On-Task • Focused	Optimal Performance: • Strong, accurate responses to target stimuli • Weak to no response to distractor stimuli Low variability	Task engagement: • Task-relevant behavioral responses • Maintained, ongoing behavior • Attentional Filter: - Exploitation of high utility / goal-relevant targets - Suppression of low utility / goal-irrelevant distractors
Tonic/Baseline: High Phasic response: Low to absent	Intermediate Increased responsivity across global targets & circuits	Increased Increased variability	Reduced response to target stimulus	• Distractible • Anxious • Over-aroused	Decreased Performance: • Task disengagement • Elevated false alarms • Indiscriminate responsivity to stimuli Increased variability	Disengagement from low / decreased utility targets • Task switching • Behavioral flexibility • Exploration of alternative, potentially higher utility targets

Note: LC Activity is indexed by observable physiological and behavioral changes. Physiologically, LC activity manifests as systematic changes in network connectivity, pretrial pupil activity, and task-evoked pupil responses. Behaviorally, evidence suggests that LC activity manifests as systematic changes in self-reported attention and arousal state, task performance, and behavior. (Adapted from Mittner et al. (2016), Aston-Jones & Cohen (2005), Robison (2018), and Unsworth & Robison (2016, 2017))

Table 2
Pupillometry Linear Mixed Effects Models

	Equation
Model 1	$\text{MeanPretrialPupil}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$
Model 2	$\text{PretrialPupilCoV}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$
Model 3	$\text{TEPRMeanAmplitude}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$

Table 3

Psychomotor Vigilance Task Performance Linear Mixed Effects Models

	Equation
Model 4	$\text{MeanResponseTime}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$
Model 5	$\text{ResponseTimeCoV}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$

Table 4

Proportion of Task-Unrelated Thoughts Linear Mixed Effects Models

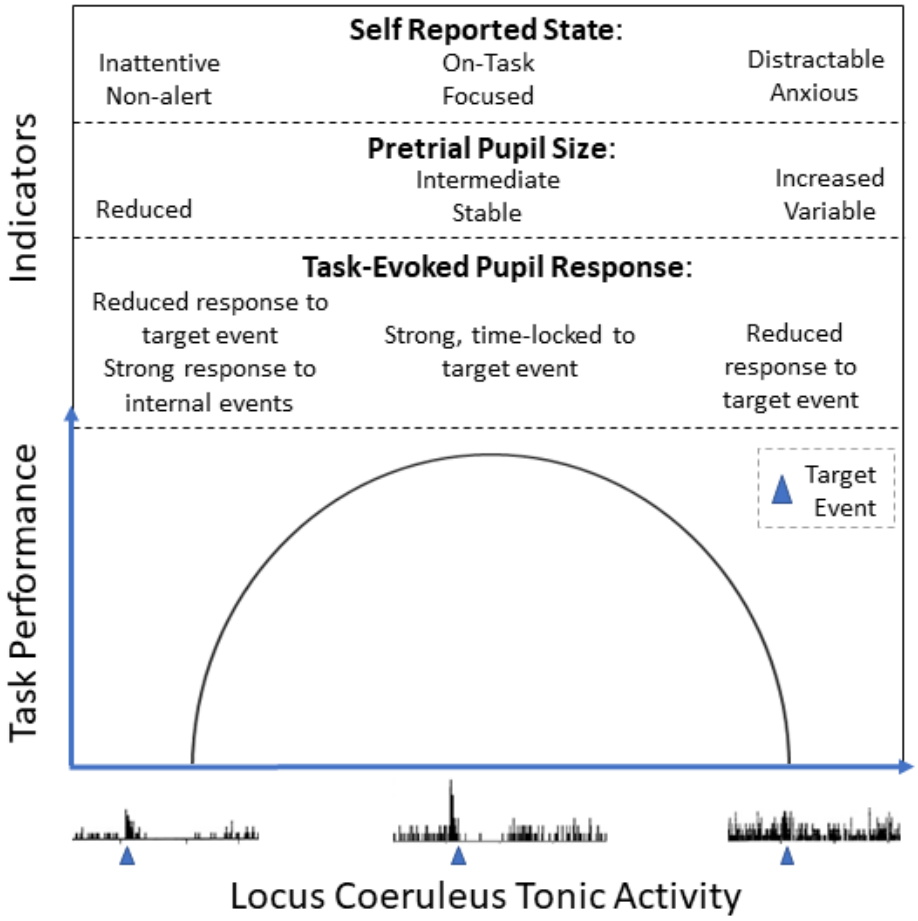
	Equation
Model 6	$\text{TaskUnrelatedThoughtsProportion}_{ij} = \beta_{0j} + \beta_{1j}\text{Block}_{ij} + \beta_{2j}\text{tDCSCondition}_j + \beta_{3j}(\text{Block}_{ij} \times \text{tDCSCondition}_j) + r_{ij}$ $\beta_{0j} = \gamma_{00} + u_{0j}$ $\beta_{1j} = \gamma_{10} + u_{1j}$ $\beta_{2j} = \gamma_{20}$ $\beta_{3j} = \gamma_{30}$ $\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \text{MVN}\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{bmatrix}\right)$

APPENDIX B

FIGURES

Figure 1

Inverted-U relation between Locus Coeruleus Activity and Task Performance



Note: Locus coeruleus tonic firing rates fall within a continuum of low tonic firing to high tonic firing. At the low-tonic end (low to absent phasic firing), individuals are withdrawn, inattentive, and non-alert resulting in poor performance. When tonic activity is intermediate and phasic firing in response to goal-relevant stimuli is elevated, individuals maintain on-task behaviors and focus of attention resulting in optimal performance. At the high-tonic end (low to absent phasic firing), individuals display flexible behavior such as task switching and exploratory behavior but will perform poorly on a task due to distractibility and indiscriminate responsivity to incoming stimuli. Locus coeruleus activity can be tracked via pretrial pupil activity and task-evoked pupil responses. (Adapted from Aston-Jones & Cohen (2005), Unsworth & Robison (2016), and Valentino & Van Bockstaele (2008))

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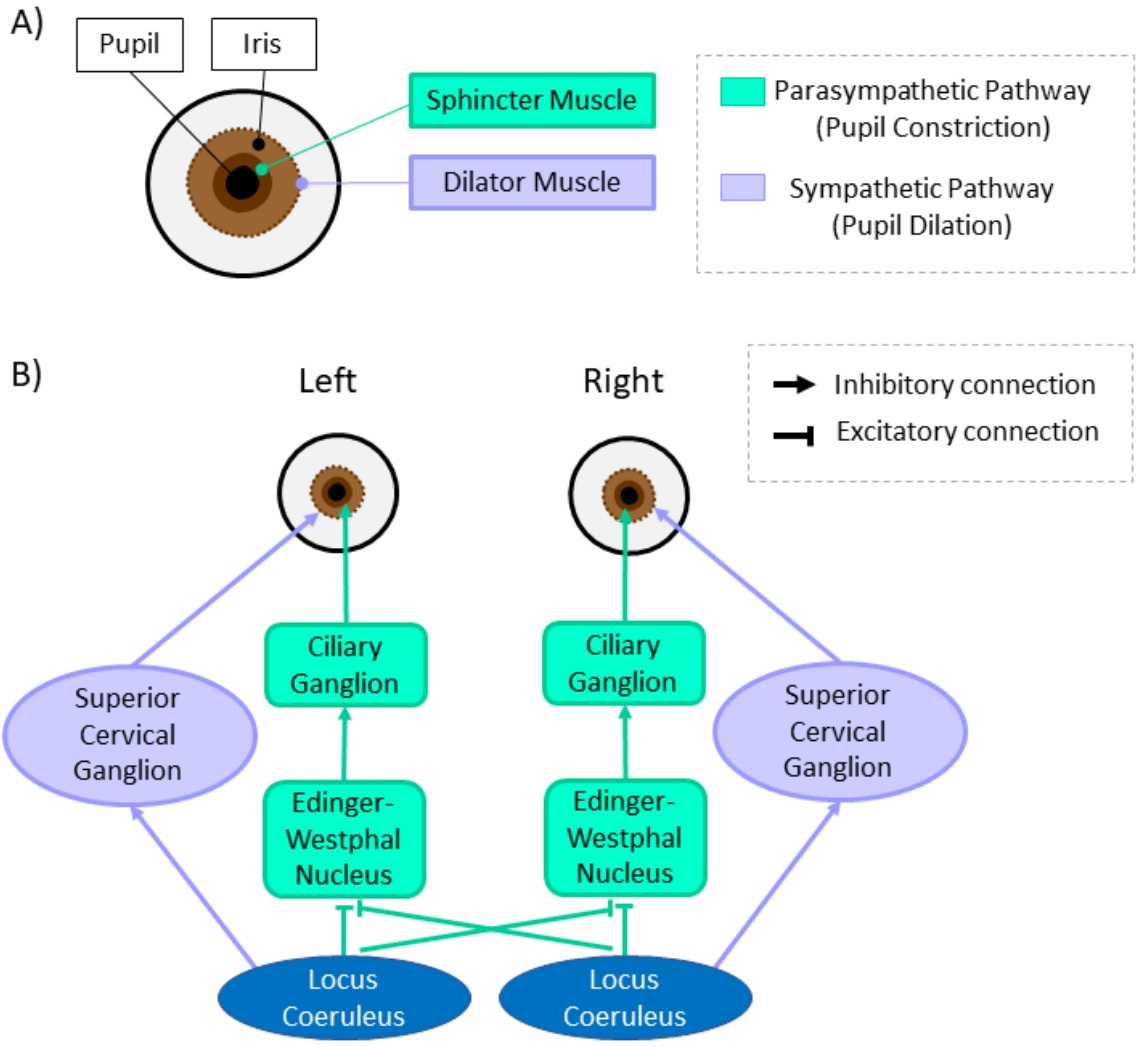
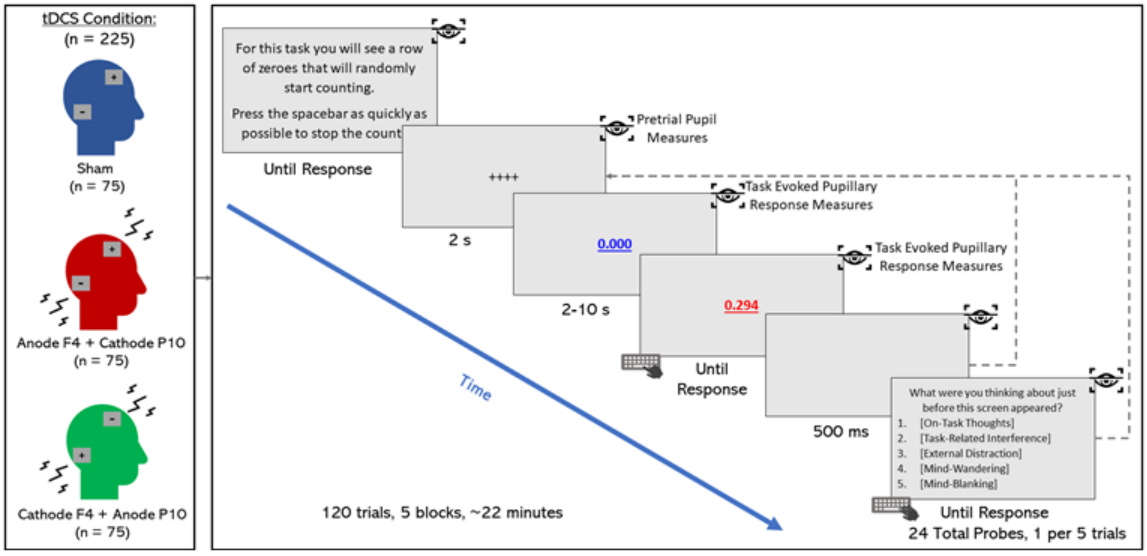
Figure 2
The Influence of the Locus Coeruleus on Pupil Activity



Note: A) The parasympathetic pathway controls pupil constriction by way of the sphincter muscle of the eye. The sympathetic pathway controls pupil dilation by way of the dilator muscle of the eye. B) The locus coeruleus influences ipsilateral and contralateral pupil constriction via its excitatory connections to the superior cervical ganglion. The locus coeruleus influences ipsilateral pupil dilation via its inhibitory projections to the brainstem Edinger-Westphal Nucleus. (Adapted from Nobukawa, et al. (2021), Liu, et al. (2017), and Joshi & Gold, (2012))

Figure 3

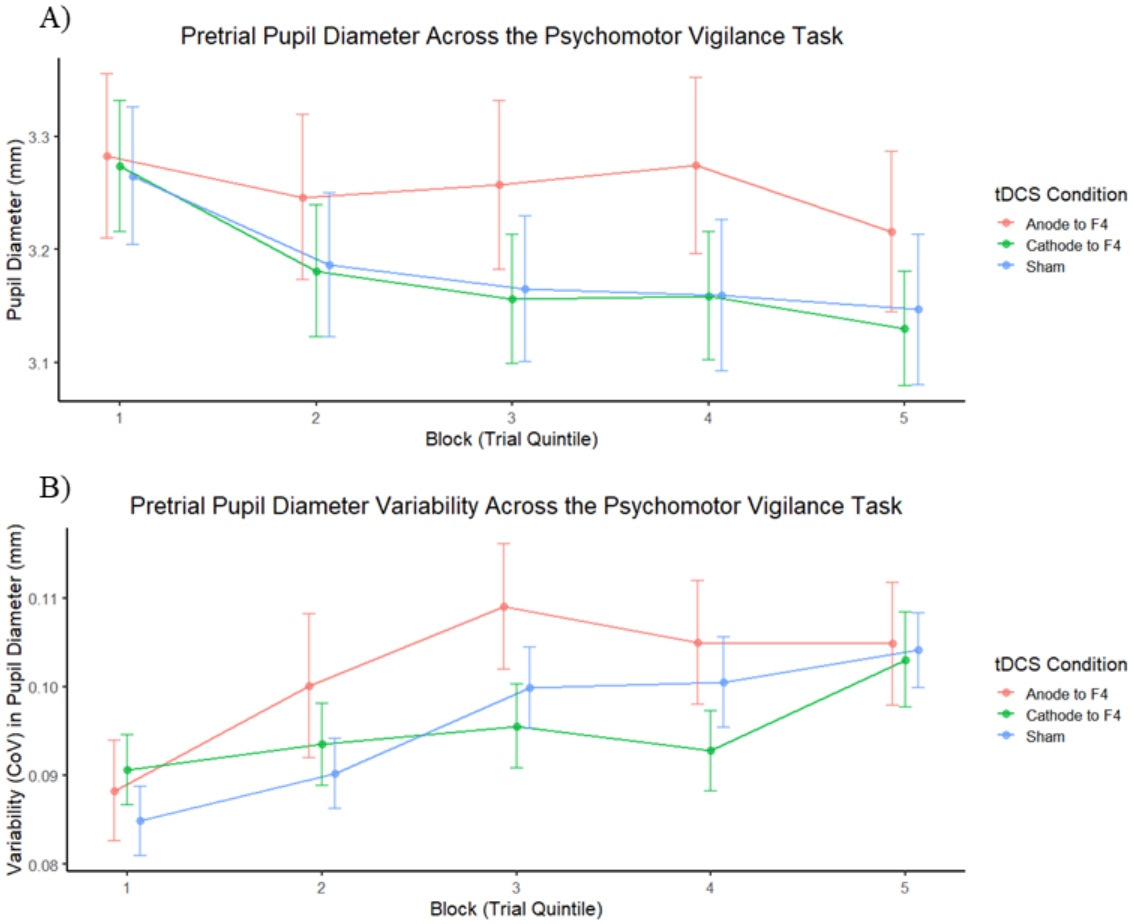
Experimental Paradigm



Note: Participants (n = 225) were randomly assigned to one of three tDCS conditions: sham, true anodal to F4, and true cathodal to F4. Participants completed 120 trials of the Psychomotor Vigilance Task. Pretrial pupil measures were extracted during the two-second intertrial interval preceding trial onset. Task-evoked pupil responses were extracted from the time frame between 200 ms prior to stimulus change to two-seconds post-stimulus change. After every fifth trial of the task, participants were prompted to report their attentional state. Pupillary activity was recorded continuously throughout the task.

Figure 4

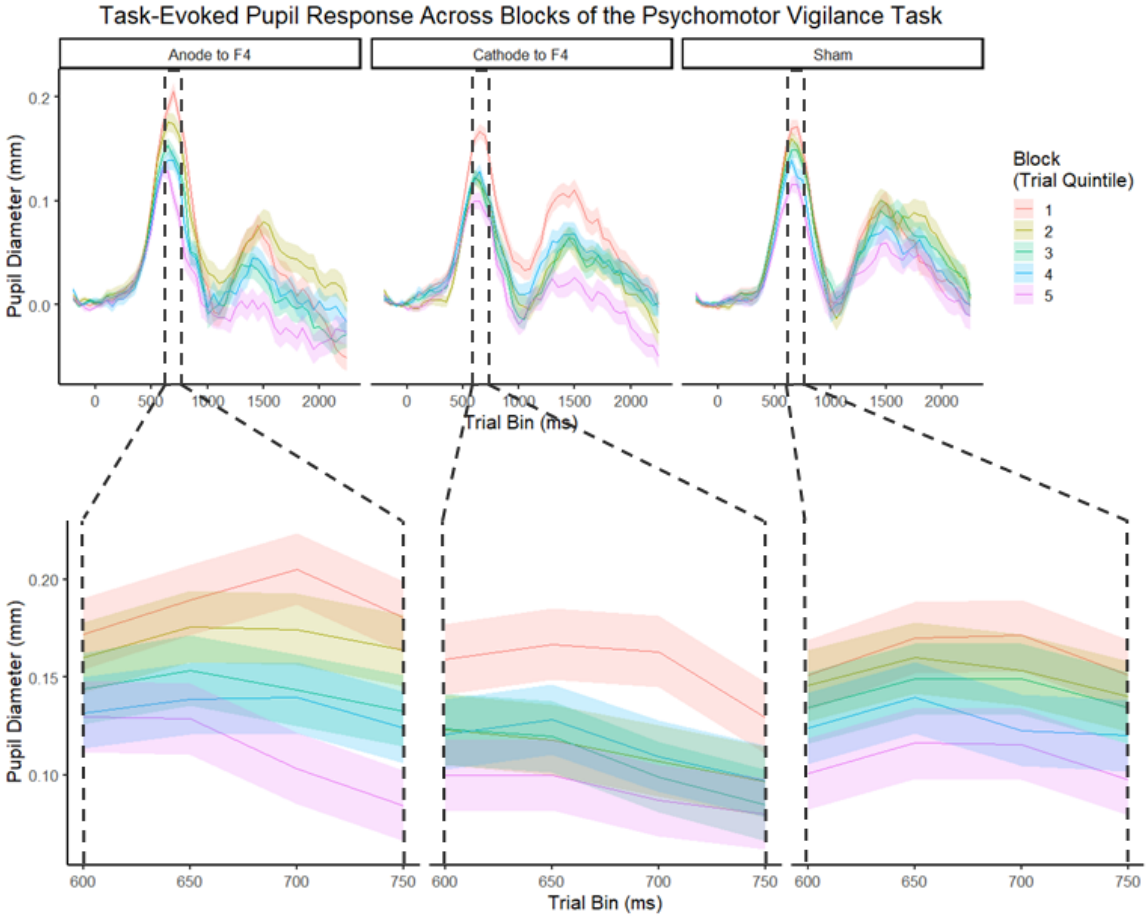
Pretrial Pupil Size Across the Psychomotor Vigilance Task by tDCS Condition



Note: A) tDCS condition-independent decrements in mean pretrial pupil diameter across trial blocks of the Psychomotor Vigilance Task reflect a decline in the intensity of attention in preparation for target stimuli. Error bars represent the standard error of the mean. B) tDCS condition-independent increases in relative pretrial pupil diameter variability (coefficient of variation) across trial blocks of the Psychomotor Vigilance Task reflect the declining consistency of attention in preparation for the target stimulus. Error bars represent the standard error of the coefficient of variation.

Figure 5

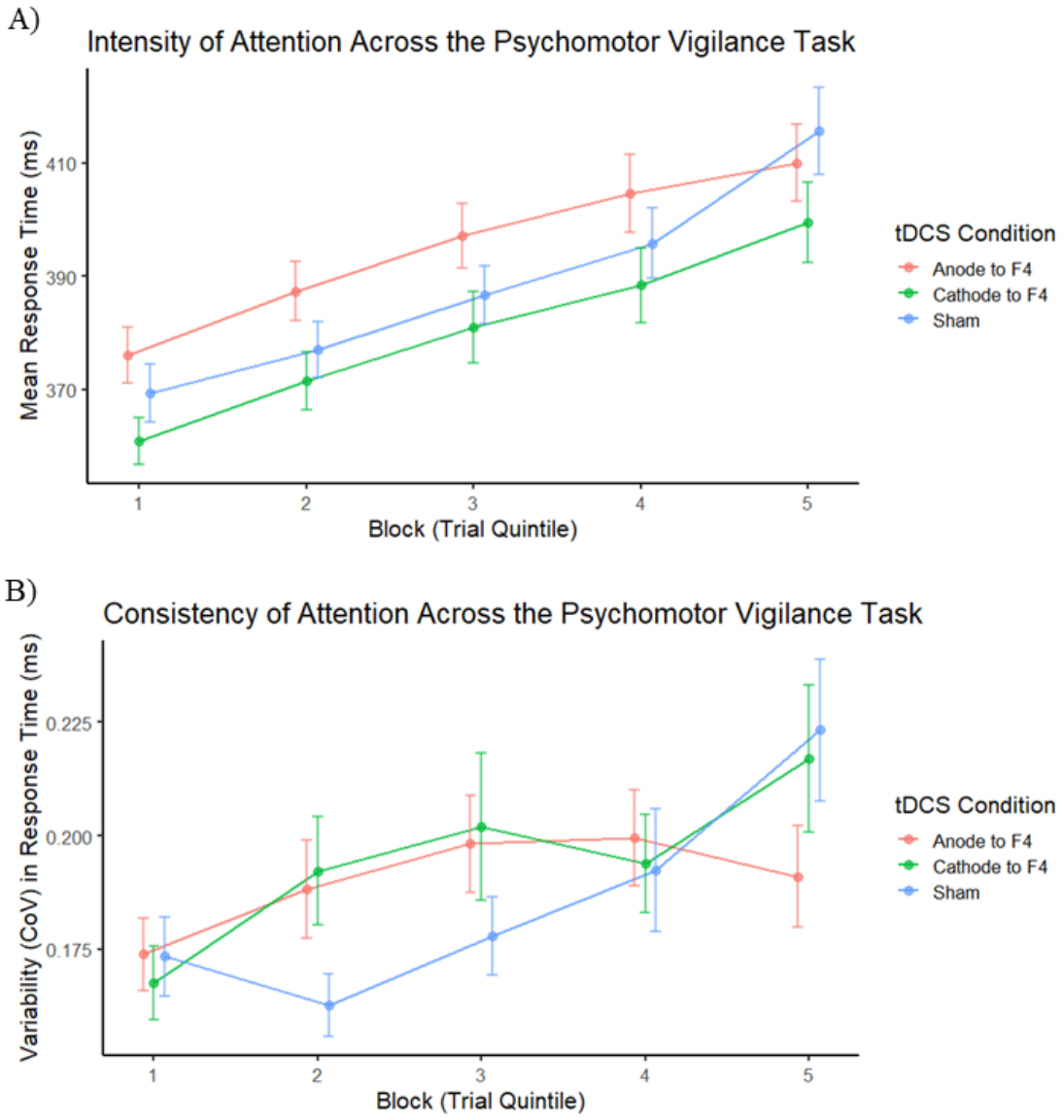
Phasic Pupil Size Across Trial Bins by tDCS Condition



Note: tDCS condition-independent declines in the mean amplitude of task-evoked pupil responses across an average trial of the Psychomotor Vigilance Task reflects a decline in the intensity of attention throughout the task.

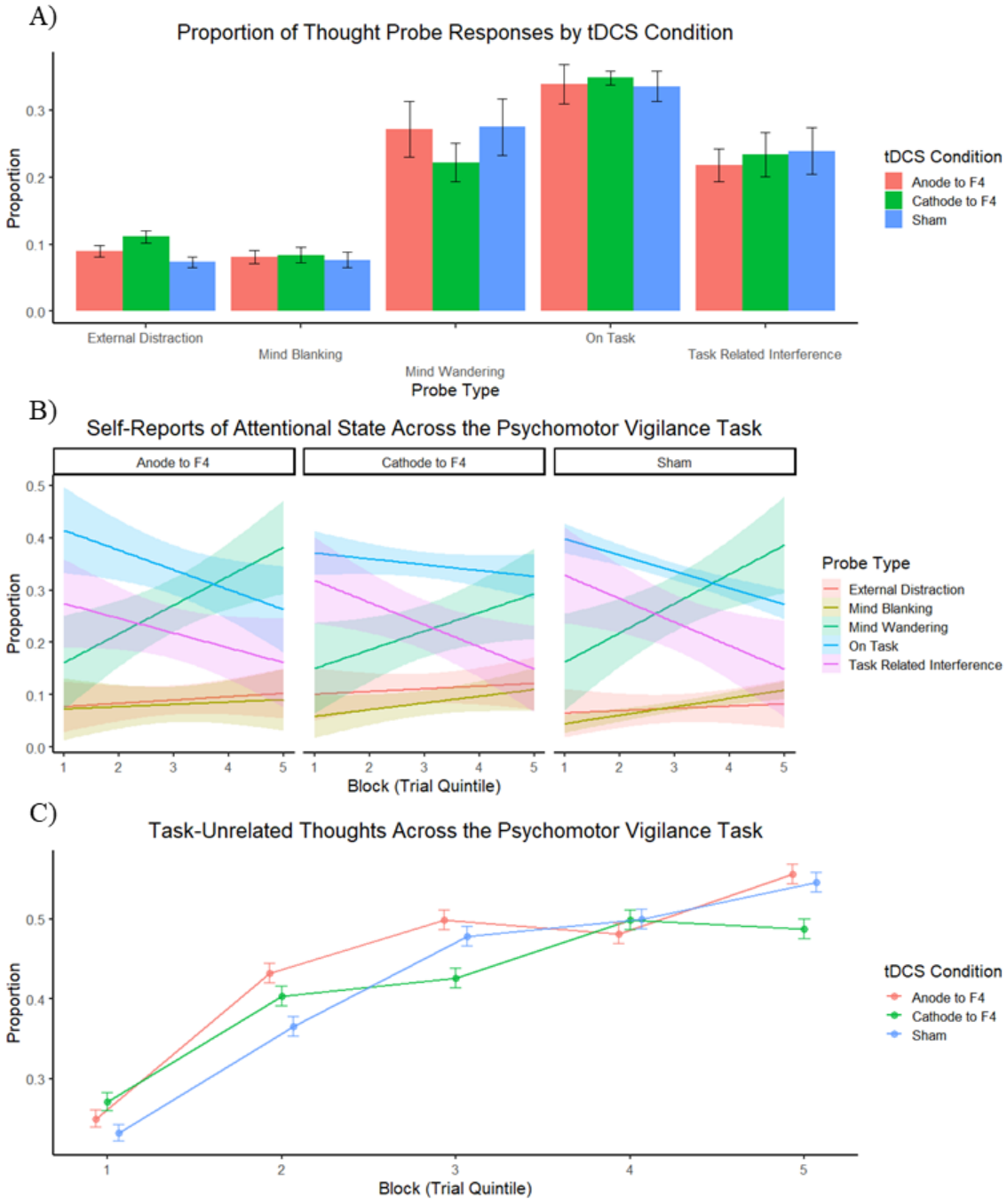
Figure 6

Performance Across the Psychomotor Vigilance Task by tDCS Condition



Note: A) Decrements in mean response time across trial blocks of the Psychomotor Vigilance Task by tDCS condition reflect a decline in the intensity of attention throughout the task. Error bars represent the standard error of the mean. B) Increases in relative response time variability (coefficient of variation) across trial blocks of the Psychomotor Vigilance Task reflect declines in the consistency of attention throughout the task. Error bars represent the standard error of the coefficient of variation.

Figure 7
Proportion of Thought Probe Responses Across tDCS Conditions



Note: A) Proportion of thought probe responses during the Psychomotor Vigilance Task by tDCS condition. Error bars represent the standard error of the mean. B) Proportion of thought probe responses across trial blocks of the Psychomotor Vigilance Task. Error ribbon represents the standard error of the mean. C) Proportion of task-unrelated thoughts across trial blocks of the Psychomotor Vigilance Task. Error bars represent the standard error of the mean.