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# **Transcranial Electrical Stimulation to Sustain Aviator Performance: The Effects of Timing of Stimulation and Individual Differences**

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Future Army aviation operations will require aviators to be able to maintain attention while interacting with high levels of automation. This will necessitate that they not only engage in vigilant attention, but also be able to redirect attention to tasks that arise, such as unanticipated emergencies. Therefore, the tasks they will be responsible for completing will require not only monitoring the automated system, but also maintaining the progression of the flight and making quick decisions as high workload scenarios arise. The primary objective of this study was to evaluate whether tDCS can sustain aviator performance through its effects on sustaining vigilance (alertness and attention). This study employed a single-blind, randomized, sham-controlled, mixed design to evaluate the main effects of stimulation and timing of delivery on flight performance. There was one within-subjects factor, stimulation mode, with two levels: active stimulation and sham stimulation. There was one between-subjects factor, timing of stimulation delivery, with two levels: prior to the flight (preflight) and during the flight (during flight).

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14. Abstract (continued)

The results of this study suggest that tDCS stimulation improves aviator performance in a highly skilled set of pilots when that stimulation is delivered during flight. These effects, however, were moderated by multiple individual differences thus potentially limiting the applicability of tDCS in an operational environment.

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## Background

Currently, the Army is developing a new fleet of aircraft under the Future Vertical Lift (FVL) program (Freedberg, 2019). The focus to modernize is one of the efforts of the Department of Defense to ensure a competitive edge is maintained over near peer adversaries (Haelig, 2017). These new aircrafts will replace the existing fleet and feature new technology, including increased automation. Along with increased automation, the FVL aircraft will be able to fly longer duration missions than currently seen in Army aviation. Extended missions, coupled with increased automation, may pose risks to aviator performance. In particular, aviators will need to sustain attention for longer durations of time with possible infrequent changes in the system due to automation maintaining the majority of flight parameters. This places aviators at risk for becoming inattentive, and could lead to breakdowns in performance (e.g., Greenlee et al., 2018). An additional compounding factor aviators will face is their trust in the automation within the aircraft. The aviator's level of reliance and trust on the system will have significant impacts on their performance by affecting their levels of vigilance or disregard for system parameters, and/or changes in workload and fixation times, which could ultimately result in the disregarding of manual cues (Koeppen, 2012).

Although the optimal method of maintaining aviator alertness is through system design, long duration flights will further tax aviators' abilities to maintain attention and decrease their cognitive readiness. Biomedical intervention through transcranial electrical stimulation (tES) may be able to aid aviators in maintaining attention in such circumstances. One promising method of tES is transcranial direct current stimulation (tDCS). tDCS delivers a low-intensity current (1 to 2 milliamps [mA]) to the brain through electrodes placed on the scalp (Brunoni et al., 2012; Dedoncker et al., 2016). It is generally accepted that the electrical current modifies the neuronal excitability and activity in the area below the electrodes (Nitsche et al., 2008). Moreover, changes in neuronal activity have been associated with changes in behavior (e.g., Coffman et al., 2014; Kuo & Nitsche, 2012; Parasuraman & McKinley, 2014). These behavioral changes are reversible and typically last up to one hour (Nitsche et al., 2007), although some studies have found some effects lasting longer (e.g., McIntire et al., 2014; McIntire et al., 2017). Because these effects are reversible and generally short-lived, they offer an alternative to pharmacological intervention, which once applied, cannot be reversed until the medication has worn off. An example of this can be observed in one popular pharmaceutical intervention, Modafinil, which has a half-life of 13 hours (Darwish et al., 2009). Moreover, tDCS may also enable a more controlled and targeted method of altering behavior. However, should tDCS be applied repeatedly for longer durations, there is the possibility of longer durations of effects, which requires further study (e.g., Das et al., 2016; Santarnecchi et al., 2015).

The effectiveness of tDCS depends on a number of parameters regarding its application. These include the following: where tDCS is applied (via placement of electrodes); direction of current flow; duration of application; intensity of current; and timing of application (before versus during task). A number of reviews thoroughly describe these considerations (e.g., Dedoncker et al., 2016; Paulus, 2011; Woods et al., 2016). For the purpose of this study, we were most interested in the location of stimulation, direction of current, and timing of application. Location of stimulation refers to where on the scalp the electrodes are placed. Typical practice includes placement of the electrodes over the region of the brain responsible for the targeted behavioral outcome. In addition, tDCS features two electrodes: anodal and

cathodal. It is generally understood that the anodal electrode produces neuronal excitability, whereas the cathodal electrode decreases excitability (Nitsche & Paulus, 2001; Brunoni et al., 2012), although this has been debated in recent years (see Jacobson et al., 2012). Placement locations of each of these electrodes affects how the direction of the current flows, and thus how neuronal activity is altered (Bikson et al., 2010). Finally, tDCS affects neuronal activity by preferentially acting on neuronal networks that are already being activated (Bikson et al., 2013). That is, in order to increase the likelihood of tDCS having an effect on performance, the neuronal networks responsible for that task should be engaged at the time of stimulation. In many studies, researchers accomplished this by applying stimulation during the completion of a cognitive task (e.g., Katsoulaki et al., 2016). Understanding this aspect of tDCS is of particular importance for determining its utility for operational settings. If tDCS is only or most effective when applied *during* a task, it may not be feasible, based on current technology, for use in certain settings such as flying an aircraft. Indeed, the main motivation of the current study was to evaluate the effectiveness of stimulation delivered at two periods (pre-flight and during flight) to determine its feasibility for future use.

Future Army aviation operations will require aviators to be able to maintain attention while interacting with high levels of automation. This will necessitate that they not only engage in vigilant attention, but also be able to redirect attention to tasks that arise, such as unanticipated emergencies. Therefore, the tasks they will be responsible for completing will require not only monitoring the automated system, but also maintaining the progression of the flight and making quick decisions as high workload scenarios arise. The primary objective of this study was to evaluate whether tDCS can sustain aviator performance through its effects on sustaining vigilance (alertness and attention). In doing so, we also sought to characterize the conditions under which it is most effective. This included evaluation of the optimal time of delivery (stimulation prior to the flight or during the flight), and effects of individual differences (e.g., experience, trait motivation). Finally, we evaluated the duration of tDCS effects (e.g., impact on cognitive tasks post-flight, sleep) and the presence and severity of side effects that may impede its use in operational settings. The following hypotheses were tested:

H<sub>1</sub>: Application of tDCS *during* the flight will better maintain aviator performance in comparison to the application of tDCS *preflight*. Active stimulation, compared to sham stimulation, in both conditions, will maintain or improve aviator performance.

H<sub>2</sub>: Individual differences in experience, trait motivation, attention, and/or boredom proneness will moderate the effectiveness of tDCS within these conditions.

## **Methods**

The U.S. Army Medical Research and Development Command Office of Research Protections Institutional Review Board reviewed and approved the protocol for this study. Researchers conducted all procedures according to institutional ethical standards. Prior to participation, all participants provided written informed consent.

## Study Design

This study employed a single-blind, randomized, sham-controlled, mixed design to evaluate the main effects of stimulation and timing of delivery on flight performance. There was one within-subjects factor, stimulation mode, with two levels: active stimulation and sham stimulation. There was one between-subjects factor, timing of stimulation delivery, with two levels: prior to the flight (*preflight*) and during the flight (*during flight*).

## Participants

Twenty-six male Army aviators (active duty, National Guard, or reservist), recruited from the local Fort Rucker, AL area, consented to participate in the study. Of the twenty-six consented, we report data on twenty-two aviators. One participant was disqualified due to being outside of the age range, one for medical reasons, and two were postponed due to equipment failures ( $n = 4$ ; their data will be evaluated at a later time). Participants were randomly assigned to groups, with 10 participants in the *preflight* stimulation group, and 12 participants in the *during flight* stimulation group. Participants were required to be no older than 40 years of age ( $M = 36.69$ ;  $SD = 2.75$ ). Participants were required to have a minimum of 200 hours of flight time, and have flown within the previous six months, as measured by self-report. Participants' flight time within the previous 90 days ranged from 100 to 350 hours, with a mean of 214 hours ( $SD = 74.90$  hours). Additionally, none of the participants scored within the clinical range for Attention Deficit Hyperactivity Disorder (ADHD) as measured by the Adult ADHD Self-Report Scale (scores ranged from 0 to 3;  $M = 0.68$ ;  $SD = 1.03$ ). Scores of four or higher are highly consistent with ADHD in adults (Kessler et al., 2005). None of the participants scored within the clinical range for depression using the Beck Depression Inventory (scores ranged from 0 to 4;  $M = 0.18$ ;  $SD = 0.85$ , indicative of minimal depression [0 to 13]) (Beck et al., 1996).

All participants were required to adhere to the following guidelines prior to data collection: a minimum of six hours of sleep (recorded by an actigraphy watch; self-report was used for two participants due to technical failure) the night prior to participation. Participants also refrained from caffeine and medications that cause drowsiness (16 hours prior to participation), nicotine (2 hours prior to participation), and alcohol (24 hours prior to participation) throughout the duration of the study (assessed by self-report). All participants were screened by the study physician to ensure they had no underlying health concerns that may interfere or cause harm with the application of stimulation (summarized in Table 1 below), as well as whether caffeine habits may cause withdrawal symptoms that could impact the study. One participant was disqualified for medical reasons. Additionally, participants were screened by the study's research pilots (RP) to ensure their ability to meet performance standards for participation in the study (all screened participants were able to meet performance standards).

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Table 1. Study Inclusion Criteria

<b>Criteria</b>	<b>Inclusion</b>	<b>Exclusion</b>
Medications	No current medications affecting cognitive function or attention.	Currently taking medications that induce drowsiness, such as over-the-counter antihistamines. Note: self-medication will be assessed through self-report.
Medical History	No current medical conditions affecting cognitive function or attention.	History of psychological/psychiatric disorder.  History of a head injury involving loss of consciousness.
Other Medical Conditions	None.	Any metal implanted within the head (e.g., shrapnel, surgical clips) or any implanted devices (e.g., cardiac pacemaker, brain stimulator, hydrocephalic shunt).  Skin condition on the scalp, such as psoriasis or eczema, or wounds on the head.  Currently receiving hormonal therapy treatments.

## Materials

Several questionnaires and survey instruments were used to evaluate individual differences that may impact response to stimulation and performance outcomes. Cognitive tasks were used to assess the duration of the stimulation effects. Performance measures included primary and secondary tasks during flight.

### Questionnaires.

All of the questionnaires and survey instruments, along with their purpose, are presented in Table 2.

Table 2. Questionnaire and Survey Instrument Descriptions

<b>Instrument</b>	<b>Description</b>	<b>Purpose</b>
Medical History Questionnaire	The study physician used the medical history questionnaire to determine study eligibility and current health status. The questionnaire was developed in-house by the study physicians. The questionnaire includes 52 items asking yes/no questions regarding various health concerns (e.g., implanted devices) and current medications and substances (alcohol, caffeine, nicotine) used.	Health assessment / Qualification screening

Demographics Questionnaire	The demographic questionnaire, developed in-house, includes 12 items to collect basic demographic information such as ethnicity, education history, and vision ability. Information related to flight experience, such as aircrafts flown, recency of time on controls, and typical flights, was also collected. The main outcome variables are flight experience and age.	Moderator Variable / Individual Differences
Morningness-Eveningness Questionnaire (MEQ)	The MEQ (Horne & Östeberg, 1976) is a 19-item self-report questionnaire requiring participants to rate questions regarding preferred sleep and wake times. The questionnaire requires approximately 15 minutes. It produces a score that ranges from 16 to 86 to describe typology (lower scores indicate tendency towards eveningness, higher scores indicate tendency towards morningness). The outcome variable is total score.	Individual Differences / Confounding Factor
Adult ADHD Self Report Scale Symptom Checklist (ASRS)	The ASRS contains 18 items and requires 2 minutes for completion. It was developed in conjunction with the World Health Organization (WHO) and the Workgroup on Adult ADHD (Kessler et al., 2005) and is used as a screening tool with adult patients. The items are consistent with the Diagnostic and statistical manual of mental disorders, version IV criteria (American Psychiatric Association, 2000). The outcome variables include Total Scores from Part A and Part B.	Individual Differences / Confounding Factor
Sleep Timing Questionnaire (STQ)	The STQ is an 18-item self-report measure of sleep habits and requires 3 minutes for completion. Research shows it to be valid (such that it correlates with sleep diary information) and reliable across repeated administrations (Monk et al., 2003). Outcome variables include sleep quantity (minutes) and wake after sleep onset (minutes).	Sleep Habits / Confounding Factor
Beck Depression Inventory (BDI)	The BDI-II (Beck, Steer, & Brown, 1996) is a commonly used 21-item, multiple-choice self-report which captures affect, cognition, and physical symptoms of depression over the most recent two week period. It requires approximately 2 minutes for completion. Higher scores indicate greater endorsement of depression symptoms. The outcome variable is total symptom score.	Confounding Factor / Side Effect

ShIPLEY Institute of Living Scale (SILS)	The SILS assesses general intellectual functioning in adults and adolescents. The SILS yields three major summary scores: Vocabulary, Abstraction, and combined Total scores (converted to Weschler Adult Intelligence Scale-Revised [WAIS-R] intelligence score). The Vocabulary sub-scale consists of 40 multiple-choice verbal reasoning questions, and primarily taps crystallized intelligence. The Abstraction subscale includes 20 series completion items of inductive reasoning that tap fluid ability (Zachary, 1986). Convergent validity of both the Vocabulary and Abstraction measures with crystallized and fluid intelligence, respectively, has been assessed and confirmed in a general population (Matthews et al., 2011). Completion time is up to 20 minutes.	Confounding Factor / Individual Differences
Convergence Insufficiency Symptom Survey (CISS)	The CISS (Borsting et al., 1999) is a 15-item questionnaire that ask participants to rate the severity of symptoms consistent with convergence insufficiency, by rating 15 statements about how their eyes feel when reading or doing close work on a Likert-type scale from 0 (never occurs) to 4 (always). It requires approximately 2 minutes for completion. Summed responses give an overall composite score, with higher scores indicating greater endorsement of symptoms characteristic of convergence insufficiency. The outcome variable is the total score.	Confounding Factor / Individual Differences
Samn-Perelli Fatigue Scale	The Samn-Perelli Fatigue Scale (Samn & Perelli, 1982) is a single item scale requiring participants to rate their current level of fatigue from 1 (fully alert, wide-awake) to 7 (completely exhausted, unable to function effectively). It requires less than 1 minute for completion. The outcome variable is fatigue rating.	Confounding Factor
Behavioral Inhibition/Avoidance Scales (BIS/BAS)	The BIS/BAS scales are a valid and reliable set of scales that assess behavioral inhibition (BIS) and behavioral avoidance (BAS) (Carver & White, 1994). The scales include 24-items and require approximately 10 minutes for completion. The BAS provides three indices of behavioral approach: reward responsiveness (positive anticipation of rewarding events), drive (pursuit of rewards), and fun seeking (search for new rewarding situations). These scales provide a measurement of motivational behavioral systems. The outcome variables are behavioral inhibition (BI) score, BA drive score, BA fun seeking score, and BA responsiveness score.	Moderator / Individual Differences
Karolinska Sleepiness Scale (KSS)	The KSS is a well-validated single item questionnaire where participants rate how sleepy they feel at the moment (Kaida et al., 2006). This scale requires approximately 1 minute for completion. The KSS measures daytime sleepiness with higher scores indicating greater daytime sleepiness. The outcome variable is participants' sleepiness score.	Confounding Factor / Side Effect

Profile of Mood States – Short Form (POMS-SF)	The POMS-SF is a valid and reliable short version of the POMS, a measure of psychological distress and mood (McNair et al., 1981). The POMS-SF contains 35 items, in each, an adjective is provided and participants rate how much it describes them using a 5-point Likert scale format (Curran et al., 1995). It requires approximately 3 minutes for completion. The outcome variables are six mood subscales and total mood disturbance score.	Side Effects
Side Effects Questionnaire	The side effects questionnaire is an adaptation of Thair’s and colleagues’ (2017) questionnaire. Participants rate the severity of fourteen symptoms on a Likert-type scale ranging from 1 (absent) to 10 (severe). Participants also have the opportunity to provide notes related to the appearance of symptoms. The questionnaire requires approximately 2 minutes for completion. Scores greater than 4 indicate concerning side effects may be present. The outcome variables are symptom ratings.	Side Effects
Post Stimulation Questionnaire	The Post Stimulation Questionnaire was developed in-house based on recent research on the efficacy of blinding procedures in studies examining tDCS. Participants indicate whether they thought they received sham or active stimulation, following a similar procedure in a recent study by Wallace et al. (2016). This questionnaire also includes questions to evaluate whether the participant perceives the use of non-invasive stimulation as beneficial or harmful to performance, following the Technology Acceptance Model (TAM), which finds that individuals were likely to use the technology if it was found to be meaningfully useful or helpful (Jonas & Norman, 2009).	Manipulation Efficacy / Usability of Stimulation
NASA Task Load Index (NASA-TLX)	The NASA-TLX (Hart & Staveland, 1988) is a questionnaire that measures subjective workload. The participant rates the previous task, in this case flight, on the following categories, using a 100-point scale: mental demand, physical demand, temporal demand, performance, effort, and frustration. Participants also perform a weighting procedure during which they evaluate every pair of subscales (e.g., mental demand vs. temporal demand) and determine which subscale contributed more to the workload of the task. The NASA-TLX then provides a weighted total workload score and scores for the six subscales.	Manipulation Efficacy
Post Study Questionnaire	The Post Study Questionnaire was developed in-house based on trust in technology research by Miltgen et al. (2013) as well as literature related to the TAM (Davis, 1993). This instrument is intended to gauge participants’ familiarity of and comfort with the potential to use tDCS as a cognitive enhancement tool in operational environments.	Usability of Stimulation

40 Mini-Marker Personality Scale	The 40 Mini-Marker Personality Scale, developed by Saucier (1994), is a briefer version of a scale developed by Goldberg (1992) which uses 100 unipolar terms to describe personality traits based on the Big-Five Factor Structure (Tupes & Christal, 1992): agreeableness, conscientiousness, extraversion, neuroticism, and openness. The scale consists of 40 common human traits and participants are asked to rate how accurately these traits describe themselves using a 9-point Likert scale. This scale requires approximately 10 minutes for completion. The outcome variable is total score for each factor, where higher scores indicate a likelihood of that trait.	Moderator / Individual Differences
Boredom Proneness Scale	The Boredom Proneness Scale (Farmer & Sundberg, 1986) is composed of 28 statements that participants rate on a scale from 1 (highly disagree) to 7 (highly agree). Reliability and validity of this instrument have been extensively studied and consistently shown to be strong (Vodanovich & Watt, 2016). This scale requires approximately 5 minutes for completion. The outcome variable is total score, where higher scores indicate more proneness to boredom.	Moderator / Individual differences

## Physiological Recordings

### Actigraphy Watch.

The Actiwatch<sup>®</sup> is a small, lightweight, limb-worn device that uses an accelerometer to monitor the occurrence and degree of motion. The sensor integrates the degree and speed of motion and produces an electrical current that varies in proportional magnitude at a sampling rate of up to 32 hertz (Hz). Data were wirelessly downloaded to a reader connected to a personal computer, and the Actiwatch<sup>®</sup> software was used to process the data. For the purpose of this study, sleep efficiency, which indicates the amount of time that the wearer is assumed to be “in bed” or attempting to sleep, was used to determine compliance with sleep instructions.

### Vital Signs.

The Welch Allyn Connex Vital Signs Monitor 6000 series collected vital signs information for evaluating the health and safety of participants. Vital signs included temperature, blood pressure, respiration rate, pulse, and oxygen saturation.

## Cognitive Tasks

### Rapid Visual Information Processing Task (RVIP).

The RVIP is a well-validated measure of sustained attention (Bakan, 1959). Each trial presented participants with a sequence of digits from which participants must detect “target” sequences. The target sequence is an even-odd-even string of numbers. When participants detect this string, they press the spacebar as quickly as possible. The speed of number presentations

(one versus two seconds) changed to increase difficulty. The task takes approximately seven minutes to complete. The outcome variables for this task included  $d'$  to measure sensitivity, reaction time in milliseconds, and accuracy (See Appendix B for a depiction of the task).

### **Continuous Performance Task (CPT).**

The continuous performance task (Conners & Sitarenios, 2011) is a well-validated measure of sustained attention and response inhibition. In this task, participants are presented with a series of letters and are instructed to respond when they see any letter except for the letter X. Participants are presented with 360 trials with varied intervals of 1, 2, and 4 seconds. Total time to complete this task is 14 minutes. The outcome variables for this task are speed in milliseconds and accuracy (See Appendix C for a depiction of the task).

### **Visual Secondary Task.**

A tablet mounted within the cockpit presented the visual secondary task (See Appendix D for a depiction of the task). The task included two lit squares (one green [primary stimuli], one colorless [secondary stimuli]) presented on a tan background. At random time intervals, the green square turned colorless or the colorless square turned red. The participant monitored these changes, and if detected, responded by touching the appropriate square on the tablet within 10 seconds of the event occurring. The outcomes measured were reaction times and accuracy for primary and secondary stimuli. This task was modeled after the well-validated Multi-Attribute Task Battery-II (Santiago-Espada et al., 2011) and is included to ascertain latent performance decrements resulting from reductions in vigilance attention (Hockey, 1997).

## **Equipment**

### **Flight Simulator.**

Data were collected using the U.S. Army Aeromedical Research Laboratory's (USAARL) full-motion NUH-60 research flight simulator. The NUH-60 consists of a simulator compartment containing a cockpit, instructor/operator station, and observer station and a six-degree-of-freedom motion system. It is equipped with six Dell precision 450 personal computer visual image generator system that simulates the natural helicopter environment surroundings for day, dusk, or night, and with blowing sand or snow. A Dell Precision laptop receives information concerning changes in the aircraft/simulator state parameters at a 60 hertz (times per second) capture rate. The spatial resolution is 1/256 of a foot, and data files are reported to two decimal places.

### **Flight Scenarios.**

The flight scenarios used in this study were two long-duration scenarios (90 minutes each) that featured low event rate tasks. The flight path was a familiar path to aviators recruited from the area (Cairns Army Airbase, AL to Montgomery, AL, and vice versa) and featured good weather conditions (e.g., clear sky, minimal wind or turbulence). The intention of the scenario was to create a vigilant state. Radio calls occurred throughout the en-route portion of the flight with a 33% own-ship rate. The end of each flight featured an emergency event. Table 3 below summarizes the flights, including the presentation of secondary tasks and performance

variables measured. The tasks for the flights were the same, with the flight path changing such that during one flight, participants flew from Cairns to Montgomery, and during the other flight condition, flew from Montgomery to Cairns. The starting point for each flight was counterbalanced amongst participants. Each flight also included completion of aircraft start-up procedures, lasting approximate 20 minutes.

*Table 3. Summary of Flight Scenarios and Data Collected*

Primary Flight Task	Approximate Time Elapsed (in minutes)	Secondary Flight Tasks	Frequency Rate	Variables Measured
Stationary Hover Power Check	2	Not applicable (NA)	NA	NA
Takeoff	10	NA	NA	NA
Straight and Level Acceleration	12	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. 2 events per minute	Secondary Tasks
Torque Split Emergency	40	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. Two events per minute	Time to Identify EP Secondary Tasks
Pre-Turn Straight and Level En-Route	70	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. 2 events per minute	Heading, Altitude, Airspeed, Secondary Tasks
Emergency Event IIMC	73	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. 2 events per minute	Secondary Tasks
Procedure Turn	79	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. 2 events per minute	Secondary Tasks
Post-Turn Straight and Level En-Route	81	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. Two events per minute	Heading, Altitude, Airspeed, Secondary Tasks
ILS Approach & Landing	82	1. Radio Calls 2. Response to visual target	1. 33% ownship 2. 2 events per minute	Glideslope, Localizer
Total Flight Time				90 minutes

### **Transcranial Direct Current Stimulator.**

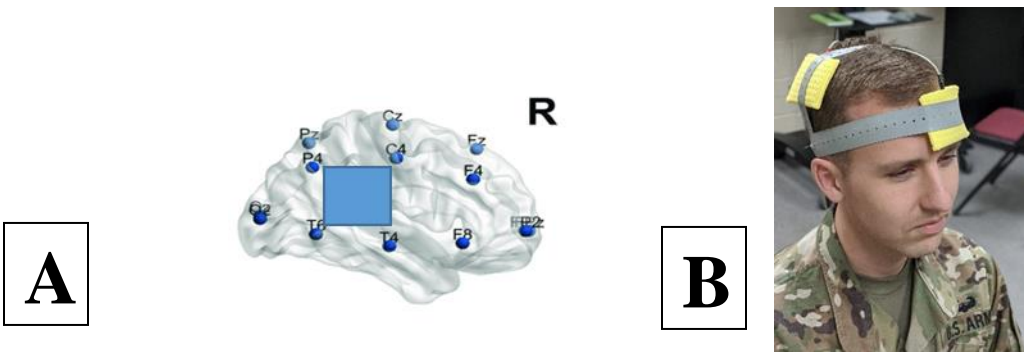
Newronika’s HDCKit transcranial direct current stimulation device delivered stimulation in the study. The HDCKit consists of the following components: HDCStim, HDCProg and HDCEI. The HDCStim device delivered the (tDCS) currents to modulate neural activity in the parietal cortex. The HDCProg and HDCEI are both accessories to the HDCStim device. The HDCProg programs the HDCStim device, while the HDCEI are the accompanying electrodes used with the device. The HDCStim device is not approved by the Federal Drug

Administration for use in the United States for any indication, therefore, all uses of this device under a research protocol in the United States are considered investigational uses and are subject to the U.S. regulations under 21 CFR 812. The HDCStim device is labeled with the following statement: “CAUTION-Investigational Device.”

### ***Stimulation Procedures.***

Application of stimulation occurred over the right posterior parietal cortex (PPC). Targeting of this region used the 10-20 electroencephalogram (EEG) system as a reference location for placement of the anode (Thair et al., 2017). Placement of the anode, a 5-centimeter (cm) x 5 cm square sponge-electrode, occurred with the top left corner at P4, and the bottom left corner at T6, aligned with the P4-T6 line (Figure 1). This placement ensured coverage of the TPJ, and IPL that make up the target regions of the PPC (Rojas et al., 2018).

The cathode (reference electrode) was centered and placed over the contralateral supraorbital region corresponding to 10-20 EEG system location FP1. To locate the P4 site, the research team used the already-applied EEG sensors to indicate its location, and marked with a washable marker (Figure 1A).



*Figure 1.* Placement of electrodes for stimulation.

Prior to electrode placement, a member of the research team inspected participants’ skin for pre-existing damage to the skin. A saline-soaked sponge bag held the electrode. The side of the electrode that contacted the skin was coated with a conductive gel. Rubber headbands and/or 3M™ Coban™ wrap (Figure 1B) held the sponge-electrodes in place.

Stimulation intensity for all conditions was 2 mA, chosen based on previous studies that have compared 1 mA to 2 mA and found the higher intensity produced reliable changes to performance (e.g., Moos et al., 2012). Total time of active stimulation was the same for each group (20 minutes), as well as the total duration of the sham stimulation (2 minutes), although these times were split for the *during flight* group. Table 4 summarizes stimulation conditions for each group.

Table 4. Stimulation Timing per Group

Group	Preflight Timing	Flight Timing		Duration		Power
	Stimulation 1	Stimulation 1	Stimulation 2	Active	Sham	
Preflight	Preflight Checklist	NA	NA	20 min	120 s	2 mA
Flight	NA	30 min into Flight	60 min into Flight	10 min	60 s each	2 mA

The order of stimulation conditions (active or sham) were randomized. When stimulation was turned on, the current gradually increased from 0.00 to 2.00 mA over a period of 30 seconds, as well as decreased over a period of 30 seconds at the end of stimulation.

### Procedure

Data collection for this study occurred during the COVID-19 pandemic, from November 2020 to May 2021. As such, the research team took additional precautions and emplaced procedures to ensure the health and well-being of participants and the research team. All participants were screened prior to entering into the laboratory for any COVID-19 symptoms. Participants were required to wear cloth masks throughout the duration of the study procedures. When inside of the simulator, members of the research team, including the research pilot, wore KN-95 masks. There were no noted issues with communication with wearing masks, as supported by Cave et al.’s evaluation of mask wearing within the aircraft (Cave et al., 2021).

Participants came to the laboratory for four separate visits. During the first visit, consent procedures, eligibility screening, and baseline measures were completed. During the second and third visits, the participants received stimulation and completed experimental flights. Finally, during the fourth visit, participants returned their Actiwatch® and completed questionnaires. These are further described below.

#### Visit One.

During this visit, participants completed informed consent procedures and received the guidelines for participation (sleep requirements; caffeine, nicotine, alcohol restrictions). Upon completion of consent procedures, participants completed the medical history questionnaire and vital signs taken. Next, the study physician reviewed the medical history questionnaire with participants and discussed caffeine habits. Once determined eligible by the study physician, participants received an Actiwatch® to wear for the duration of the study. Following this, participants met the research pilot who briefed the flight tasks required and the research nature of some of the tasks (e.g., you may be asked to complete tasks that you normally would not do in actual flight). Then the research pilot escorted the participant into the simulator for completion of up to three familiarization flights. The RP rated the participants’ ability to complete the tasks. If determined able to complete the tasks required for the study, participants then moved on to completing questionnaires. See table 5 for included questionnaires and administration method.

Table 5. Administered Questionnaires

Administration Method	Questionnaire	
Electronic	Demographic Questionnaire	Adult ADHD Self Report Scale
	Sleep Timing Questionnaire	Convergence Insufficiency Symptom Survey
	Samn-Perlli Fatigue Scale	Short Stress State Questionnaire
	Karolinska Sleepiness Scale	Profile of Moods State – Short Form
	40 Mini-Marker Personality Scale	Boredom Proneness Scale
	Behavioral Inhibition / Avoidance Scales	
Non-electronic	Shipley Institute of Living Scale	Beck Depression Inventory

Upon completion of the questionnaires, participants were offered a 5-minute stimulation familiarization session to have the opportunity to experience stimulation prior to the full the stimulation sessions. Three participants took part in the familiarization session. During the familiarization session, stimulation was applied to the left dorsolateral prefrontal cortex (anodal) with the reference electrode (cathodal) placed on the right bicep.

### Visits Two and Three.

Participants returned for Visit Two at least 16 hours following Visit One. Visits Two and Three were separated by at least 48 hours (e.g., Monday, Visit One; Tuesday, Visit Two; Thursday, Visit Three). Procedures remained the same for Visits Two and Three, unless otherwise indicated.

Upon arrival, a member of the research team verified participants' compliance with study instructions (e.g., medication, stimulation, alcohol consumption, and sleep instructions). Confirmation relied on self-report, except for sleep, which relied on the Actiwatch<sup>®</sup>. Participants completed the Side Effects Questionnaire, KSS, Samn-Perelli Fatigue Scale, and POMS-SF to document any symptoms or elevated scores prior to stimulation. Vital signs were also recorded. Next, participants trained on the visual secondary task until comfortable (visit two only). Procedures were also completed for the collection of electroencephalograph data prior to the flight and stimulation; however, that data is not reported here.

Next, the stimulation electrodes were put in place, and the RP briefed participants on the day's flight and escorted participants to the simulator. Inside the simulator, all participants completed the pre-flight checklist procedures, although only the *preflight group* received stimulation at this time. As the flight commenced the visual secondary task and radio calls began. The *during flight group* received stimulation for 10 minutes at each the 30 minute and 60 minute point in flight (the flight did not pause). A member of the research team was in the simulator operator station monitoring stimulation impedance levels throughout the flight, and was able to intervene if necessary. Only one participant required stopping of the stimulation during flight due to discomfort. This was during a sham stimulation condition, and so the flight continued and the data was kept for analyses.

After the flight, participants left the simulator, a member of the research team removed the stimulation electrodes, and the participant completed questionnaires. Questionnaires included the NASA-TLX, Side Effect Questionnaire, KSS, Samn-Perelli Fatigue Scale, POMS-SF, and BDI. Post-stimulation EEG data were also recorded (not reported here) during the RVIP and CPT (counterbalanced). Next, the Post-Stimulation Questionnaire was administered and participants remained at the laboratory for one hour of observation. Prior to release, researchers took the participants vitals and the participants consulted a physician to ensure no adverse effects occurred.

#### **Visit Four.**

Visit Four occurred at minimum 48 hours after participation. When participants returned for Visit Four, they turned in the Actiwatch<sup>®</sup>, completed the KSS, STQ, and Post Study Questionnaire. Finally, the participant was released and their participation in the study completed.

#### **Statistical Analysis and Quality Control**

All hand-entered data were double-checked for accuracy using a 10% random sample validation check. Prior to analyses, all electronically recorded data were inspected for any impossible values or output errors. Distributions of all performance (flight, secondary tasks, cognitive tasks) and questionnaires were evaluated for normality and inspected for outliers exceeding three standard deviations from the mean (no outliers were identified).

To address the first hypothesis, *t*-tests were performed to evaluate whether performance on the primary and secondary flight tasks were impacted by the application of tDCS. Specifically, paired samples *t*-tests compared performance *within* groups between the *sham* and *active* stimulation conditions to determine whether there was an effect of stimulation on performance. Independent sample *t*-tests compared performance *between* groups in the *active* stimulation conditions to determine whether the timing of delivery affected performance outcomes. Prior to these analyses, independent sample *t*-tests were conducted to evaluate whether the groups differed on any potential confounds (Sleep Timing Questionnaire, Karolinska Sleepiness Scale, Morningness-Eveningness Questionnaire, and Convergence Insufficiency Symptom Survey).

To address the second hypothesis, repeated measures moderation models were used. The moderation models were used to evaluate whether the effect of active stimulation on flight performance was moderated by individual differences and timing of stimulation delivery. Specifically, we were interested in whether differences between individuals on attention (inattentiveness, hyperactivity), trait motivation, proneness to boredom, or flight experience facilitated or inhibited the effects of stimulation on the performance outcomes, and whether that was further impacted by timing of delivery (*preflight*, *during flight*). The repeated measures moderation models were completed using Mediation and Moderation for Repeated Measures (MEMORE) (Montoya, 2019) in Statistical Package for the Social Sciences (SPSS) version 25. Before evaluating the moderation models, the moderator variables were first compared using independent samples *t*-tests to evaluate any differences between groups on each of the moderators (no differences were noted). Separate models were completed for each outcome

variable, and each moderator. Group was also included as the between-subjects factor moderator in the models.

Finally, to evaluate the duration of effects on both cognitive tasks (RVIP, CPT), performance was evaluated using paired samples and independent *t*-tests. Performance was examined within each group by comparing sham to active conditions with paired samples *t*-tests. Performance during the active stimulation conditions were also compared between groups using independent samples *t*-tests. Side effects were examined using a mixed-model repeated-measures analysis of variance (ANOVA) to compare baseline and post-flight responses (BDI, SPFS, POMS), as well as baseline, post-flight, and follow-up responses (KSS). The within-subjects factor was condition (3 levels: baseline, post-flight one, post-flight two [BDI, SPFS, POMS]; 4 levels: baseline, post-flight one, post-flight two, follow-up [KSS]) and the between-subjects factor group (*pre-flight, during flight*).

## **Results**

### **Evaluation of Potential Confounding Variables**

Independent samples *t*-tests were performed to evaluate any significant differences in responses between groups. There were no statistically significant differences between groups. Table 6 summarizes the descriptive statistics for each measure.

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Table 6. Potential Confounding Variables Summary Statistics

Measure	Outcome	Pre-flight Group		During Flight Group	
		Mean	SD	Mean	SD
*Sleep Timing Questionnaire	Sleep Quantity Weekdays (hours)	8.00	1.01	8.21	0.72
	Sleep Quantity Weekends (hours)	8.17	0.56	8.50	0.85
	Wake after Sleep Onset (minutes)	17.20	6.18	16.70	11.50
+Karolinska Sleepiness Scale	Sleepiness Score Flight 1	2.20	1.03	2.42	0.67
	Sleepiness Score Flight 2	2.60	1.17	2.50	1.00
Shipley Institute of Living Scale	Vocabulary Score	30.80	4.66	34.12	2.69
	Abstraction Score	32.60	4.22	35.23	4.21
	WAIS-R	105.30	6.78	110.77	5.54
40-Mini Marker Personality Scale	Neuroticism	6.13	1.10	6.17	1.04
	Agreeableness	6.91	0.98	6.80	1.03
	Extraversion	6.00	1.29	6.64	1.09
	Openness	6.20	0.99	6.50	1.13
	Conscientiousness	7.43	0.83	6.80	1.03
Morningness-Eveningness Questionnaire	Total Score	60.80	9.78	60.60	7.98
Convergence Insufficiency Symptom Survey	Total Score	10.80	5.20	10.10	5.09

Note. \*Missing one participant's (*pre-flight* group) data due to recording errors.

+*Pre-flight* group scores only.

### Performance Outcomes

Responses to the NASA TLX were examined prior to looking at performance outcomes to ensure there were no significant differences between the two flights. No significant differences were found between flights,  $t(21) = -1.78, p = 0.09$ . Participants rated overall workload for flights starting at Cairns ( $M = 44.80, SD = 14.00$ ) similarly to those starting at Montgomery ( $M = 49.00, SD = 15.80$ ).

### Flight Performance.

Flight performance data were compared each within groups and between groups. There were no statistically significant differences within or between groups for either the pre-turn or post-turn metrics. For the approach metrics, both glideslope and localizer values were statistically different between groups,  $t(9.33) = 2.49, p = 0.033, d = 1.62$ ;  $t(15.46) = 2.92, p = 0.010, d = 1.50$ , respectively. In both cases, who received stimulation *during flight* had values closer to zero, indicating improved performance. Moreover, there was also a statistically significant difference between the sham and active conditions within the *during flight group* for glideslope values,  $t(10) = -2.57, p = 0.028, d = 1.50$ . When participants received active stimulation *during flight*, compared to sham stimulation, they demonstrated significantly improved performance, as glideslope values were closer to zero. Descriptive statistics are provided in Table 7 below.

Table 7. Primary Flight Outcome Variables Summary Statistics

Portion of Flight	Outcome	Pre-Flight				During Flight			
		Sham		Active		Sham*		Active	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pre-Turn	RMSD Altitude	40.50	11.20	36.10	7.93	32.00	5.32	34.10	7.82
	RMSD Airspeed	1.10	0.35	1.21	0.31	1.33	0.63	1.26	0.69
	RMSD Heading	1.20	0.44	1.15	0.56	1.15	0.45	1.06	0.64
	Torque Split ID	193.00	103.00	199.00	89.70	215.00	63.00	207.00	105.00
Post-Turn	RMSD Altitude	41.90	10.20	39.40	7.99	42.30	13.60	37.70	8.94
	RMSD Airspeed	1.04	0.33	1.26	0.56	1.50	0.94	1.42	1.08
	RMSD Heading	1.14	0.75	0.99	0.51	1.57	1.22	1.73	1.49
Approach	+Glideslope	0.13	0.10	0.15 <sup>b</sup>	0.13	0.17 <sup>a</sup>	0.15	0.05 <sup>a,b</sup>	0.02
	+Localizer	0.13	0.14	0.17 <sup>c</sup>	0.09	0.09	0.08	0.07 <sup>c</sup>	0.06

Note. \*Missing participant four in *during flight group* sham stimulation data due to recording error (no flight data were recorded). <sup>+</sup>Missing one participant's data due to recording error in sham condition in *preflight group*. Means with the same superscript differ statistically at  $p < 0.05$ .

### Secondary Performance.

Secondary performance data were compared within and between groups. No statistically significant differences were found within or between groups for the reaction times to the visual secondary task nor for the radio calls task (Table 8).

Table 8. Secondary Flight outcome Variables Summary Statistics

Task	Outcome	Pre-Flight				During Flight			
		Sham		Active		Sham		Active	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Visual Task	Primary Response RT	1,773.00	265.00	1,711.00	220.00	1,731.00	190.00	1,724.00	194.00
	Secondary Response RT	1,715.00	397.00	1,634.00	244.00	1,603.00	172.00	1,623.00	231.00
Radio Calls	No. Misunderstood Calls	0.20	0.42	1.20	1.81	0.17	0.39	0.58	0.90
	No. Inappropriate Actions	0.30	0.66	0.30	0.48	0.42	0.70	0.33	0.56

Note. Means with the same superscript (e.g., <sup>a</sup>) are statistically different by  $p < 0.05$ .

### Moderator Variable Outcomes

Prior to including the moderator variables into any models, independent samples *t*-tests were done to ensure there were no statistically significant differences between groups on the measures. None were noted. Table 9 below summarizes the descriptive statistics of the variables that were included in the moderation models as potential moderators.

Table 9. Moderator Variables Summary Statistics

Measure	Outcome	Pre-Flight		During Flight	
		Mean	SD	Mean	SD
*Demographics Questionnaire	Flight Hours within Last Year	207.00	69.30	221.00	81.70
Adult ADHD Self Report Scale	Inattentive	9.10	3.76	10.30	2.96
	Hyperactive	7.80	2.74	10.10	2.61
Behavioral Inhibition / Avoidance Scale	Behavioral Inhibition Score	17.60	4.09	18.40	3.45
	BA Drive Score	13.00	2.06	13.00	1.65
	BA Fun Seeking Score	12.20	2.10	12.70	1.30
	BA Responsiveness Score	18.00	1.16	17.80	1.03
Boredom Proneness Scale	Total Score	4.10	2.28	5.75	2.53

Note. \*Two participants' data missing due to recording errors (one from each group).

## Repeated-Measures Moderation Models

All moderation analyses were completed using Model 3 (multiplicative moderation) in MEMORE. For each model, the focal predictor was stimulation (within-subjects, 2 levels: sham, active), the first moderator entered was the individual difference variable, and the second moderator entered was group (between-subjects, 2 levels: *pre-flight*, *during flight*). Separate models were completed for each outcome variable, and each individual difference variable. Only models that were significant are included below. Outcome variables were the difference of the performance metric from active stimulation to sham stimulation. Thus, a positive value indicated an improvement in the active condition over that in the sham condition; whereas a negative value indicated degraded performance (performance was worse in the active compared to sham conditions).

Conditional effects were examined using the pick-a-point approach due to the inclusion of a dichotomous moderator (group) in the models (Montoya, 2019). Using the pick-a-point approach, scores for each of the individual difference moderators were classified as “low,” “moderate,” or “high” based on percentile scores: 16<sup>th</sup> percentile (low), 50<sup>th</sup> percentile (moderate), and 84<sup>th</sup> percentile (high). These were then examined at the group level (*pre-flight*, *during flight*) to better understand the effects of stimulation. The simple slopes were also plotted to visualize the conditional effects.

### Pre-Turn Outcome Measures: Altitude.

Both models that included the ADHD subscales of inattentiveness and hyperactivity were significant, as was the model that included experience. For the inattentive model, the overall model was significant,  $F(3, 17) = 4.97, p = 0.012, R^2 = 0.47$ . Participants who received stimulation *pre-flight* showed *decreased* altitude deviations (improved performance) from sham to active stimulation conditions when inattentiveness scores were moderate ( $\beta = 4.91, p = 0.018$ ) to high ( $\beta = 7.25, p = 0.019$ ). Participants in the same group with low inattentiveness scores showed no statistically significant effects on altitude deviations ( $\beta = 2.57, p = 0.274$ ). Participants who received stimulation *during flight* with high inattentiveness scores showed the opposite effect. For these participants, altitude deviations *increased* (worse performance) from sham to active stimulation ( $\beta = -6.18, p = 0.019$ ). Participants in the same group with low and moderate inattentiveness scores showed no statistically significant effects on altitude deviations ( $\beta = 4.63, p = 0.144$ ;  $\beta = -0.77, p = 0.671$ , respectively). The simple slopes of the conditional effects are plotted in Figure 2.

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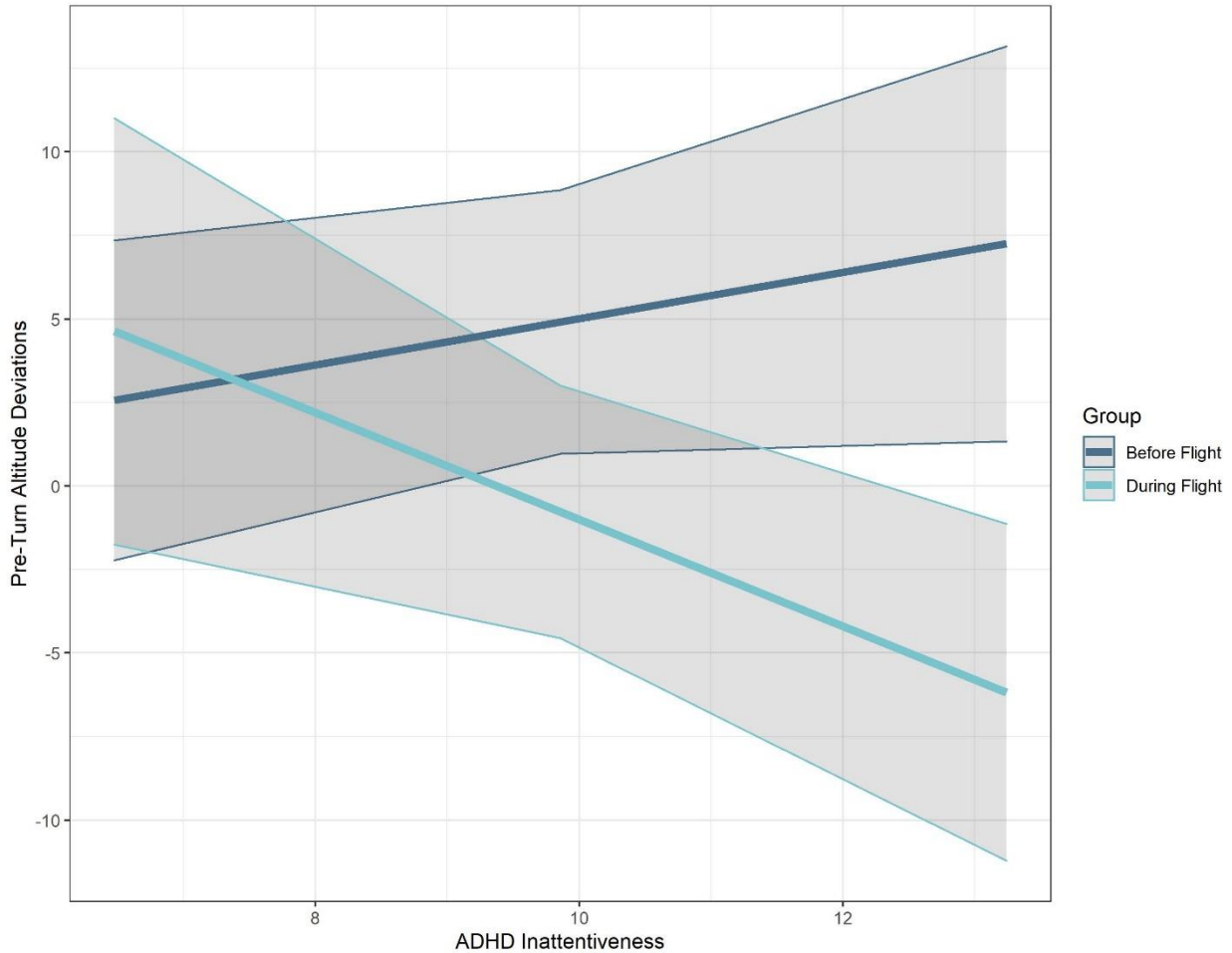


Figure 2. Simple slopes of ADHD inattentiveness and pre-turn altitude deviations.

For the hyperactivity model, the overall model was significant,  $F(3, 17) = 3.62, p = 0.035, R^2 = 0.39$ . Participants with moderate and high hyperactivity scores who received stimulation *pre-flight* showed *decreased* altitude deviations (improved performance) from sham to active stimulation conditions ( $\beta = 5.88, p = 0.014$ ;  $\beta = 9.61, p = 0.017$ , respectively). Participants in the same group with low hyperactivity scores showed no statistically significant effects on altitude deviations ( $\beta = 2.57, p = 0.274$ ). There were no effects noted within the *during flight* group. The simple slopes of the conditional effects are plotted in Figure 3.

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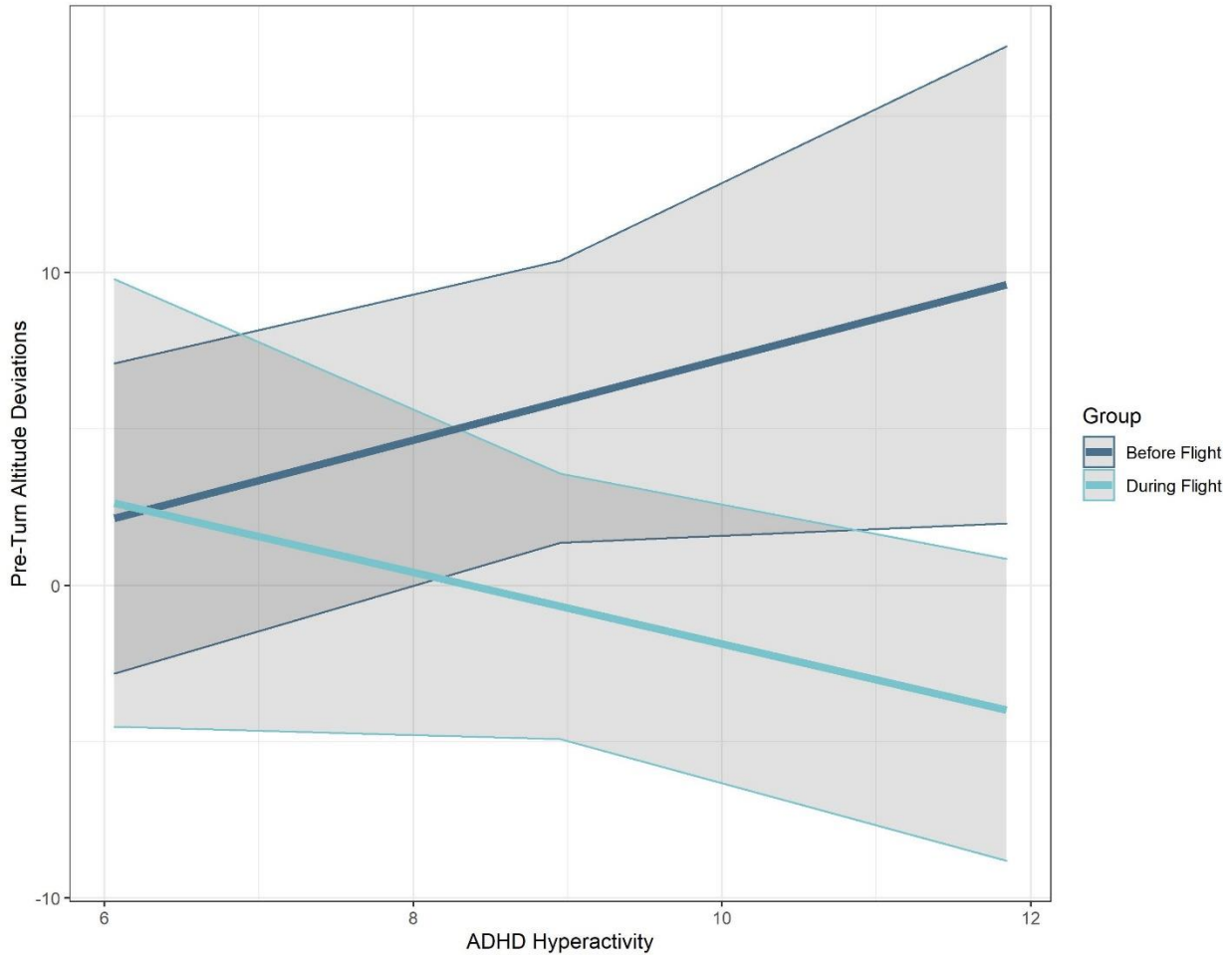


Figure 3. Simple slopes of ADHD hyperactivity and pre-turn altitude deviations.

For the flight experience model, the overall model was significant,  $F(3, 17) = 7.30, p = 0.002, R^2 = 0.56$ . Participants with low and moderate flight hours in the *pre-flight* group showed *decreased* altitude deviations (improved performance) from sham to active stimulation conditions ( $\beta = 10.79, p < 0.001; \beta = 4.08, p = 0.025$ , respectively). Participants in the same group with high flight hours in the last year showed no statistically significant effects ( $\beta = -2.62, p = 0.321$ ). There were no effects noted within the *during flight* group. The simple slopes of the conditional effects are plotted in Figure 4.

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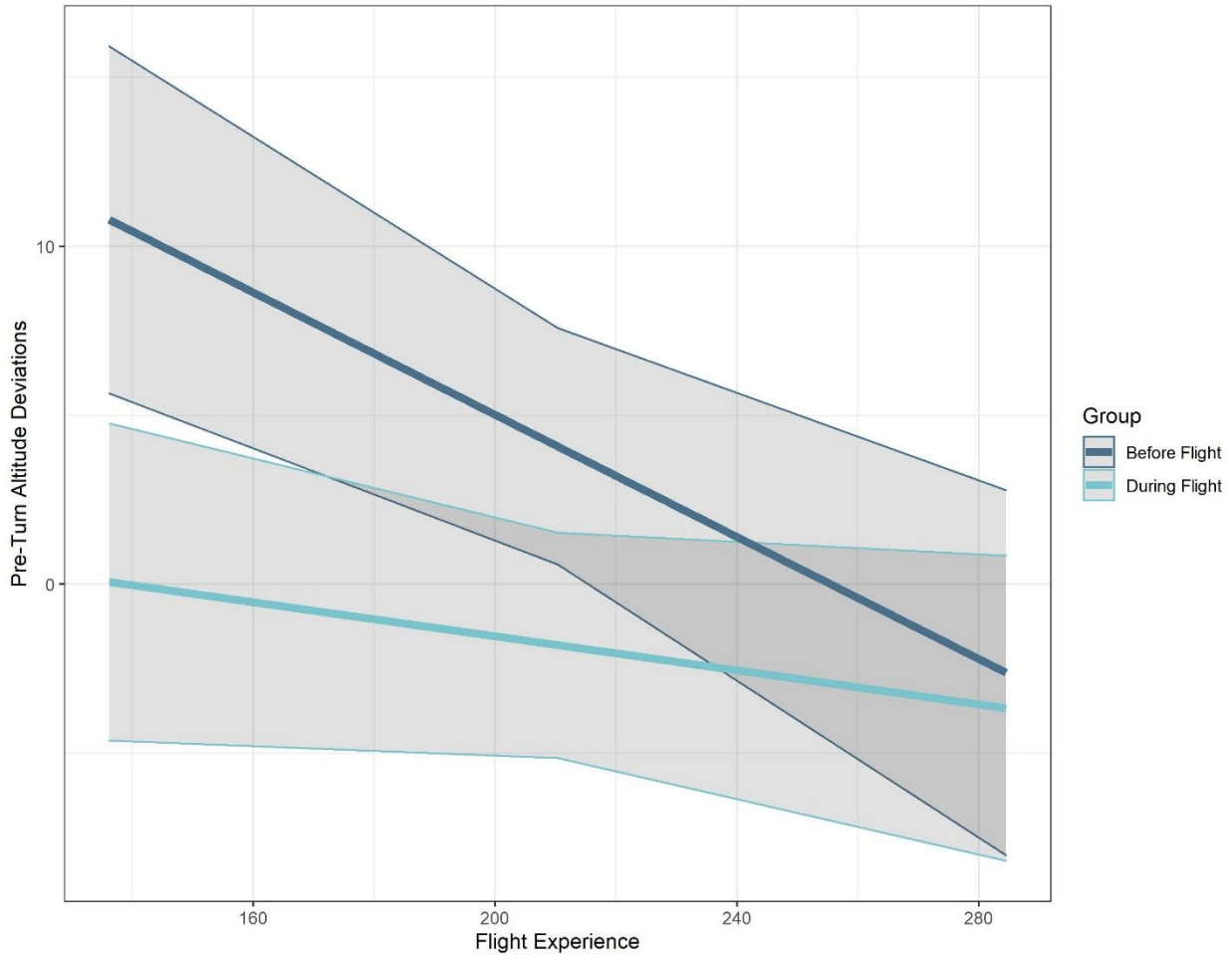


Figure 4. Simple slopes of flight experience last year and pre-turn altitude deviations.

**Pre-Turn Outcome Measures: Airspeed.**

None of the models with airspeed as the outcome variable resulted in significant moderation effects.

**Pre-Turn Outcome Measures: Heading.**

Only the model with BIS/BAS Reward included as a moderator was significant. Here, the overall model was significant,  $F(3, 17) = 3.79, p = 0.030, R^2 = 0.40$ . Participants with low reward scores in the *during flight* group showed *decreased* heading deviations (improved performance) from sham to active stimulation conditions ( $\beta = 0.70, p = 0.022$ ). However, those in the same group with high reward scores showed *increased* heading deviations (worse performance) from sham to active stimulation conditions ( $\beta = -0.70, p = 0.032$ ). Participants in the same group with moderate rewards scores showed no statistically significant effects on heading deviations ( $\beta = -0.04, p = 0.985$ ). There were no effects noted within the *pre-flight* group. The simple slopes of the conditional effects are plotted in Figure 5.

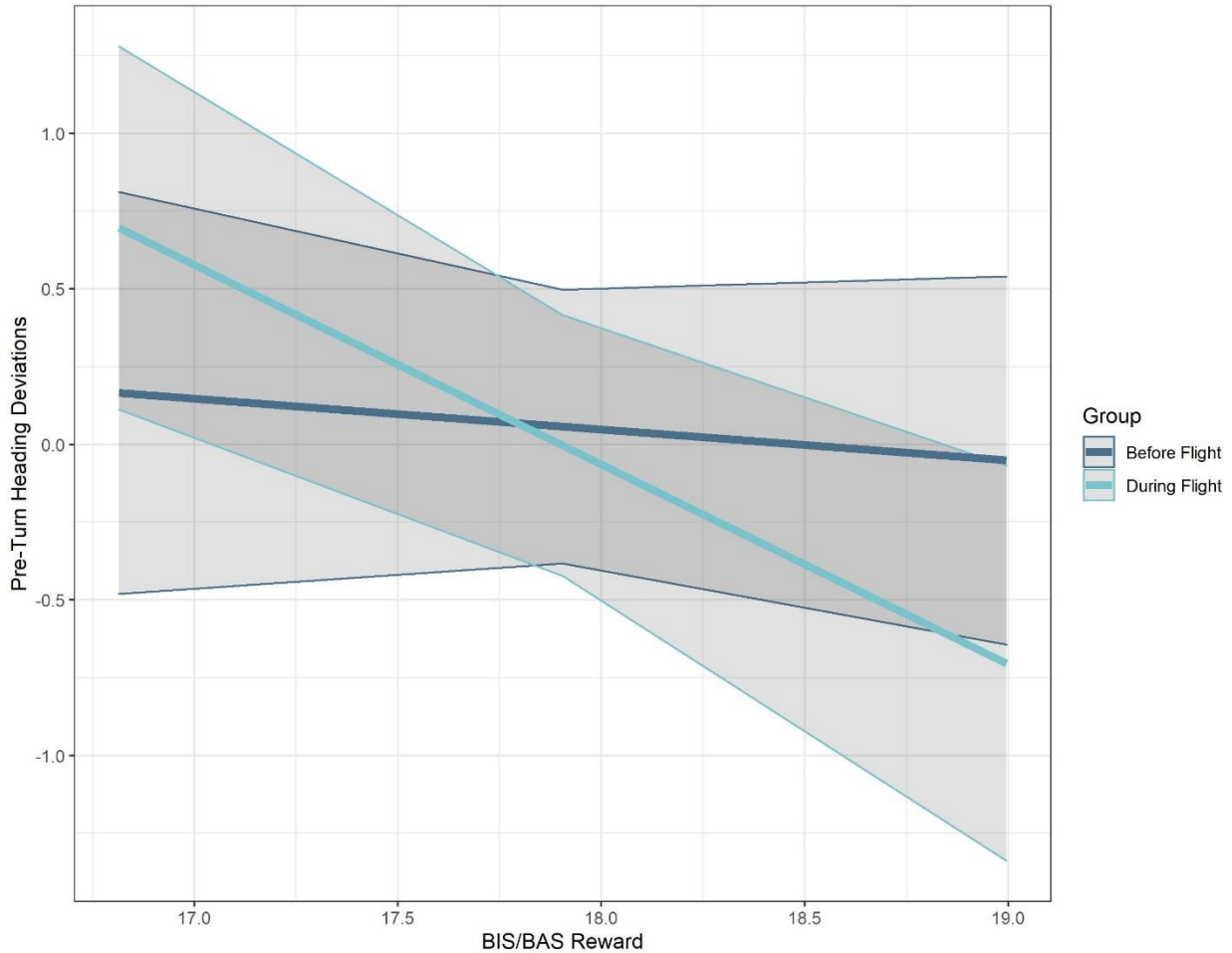


Figure 5. Simple slopes of BIS/BAS reward and pre-turn heading deviations.

**Pre-Turn Outcome Measures: Torque Split Emergency.**

None of the models with reaction time to torque split as the outcome variable resulted in significant moderation effects.

**Post-Turn Outcome Measures: Altitude.**

None of the models with altitude deviations as the outcome variable resulted in significant moderation effects.

**Post-Turn Outcome Measures: Airspeed.**

Both models that included the BIS/BAS subscales of drive and fun were significant. For the BIS/BAS drive model, the overall model was significant,  $F(3, 17) = 4.53, p = 0.017, R^2 = 0.44$ . Participants with low drive scores in the *during flight* group showed *decreased* airspeed deviations (improved performance) from sham to active stimulation conditions ( $\beta = 0.64, p = 0.022$ ). Participants in the same group with moderate and high drive scores showed no statistically significant effects on airspeed deviations ( $\beta = 0.10, p = 0.481; \beta = -0.44, p = 0.069$ ,

respectively). There were no effects noted within the *pre-flight* group. The simple slopes of the conditional effects are plotted in Figure 6.

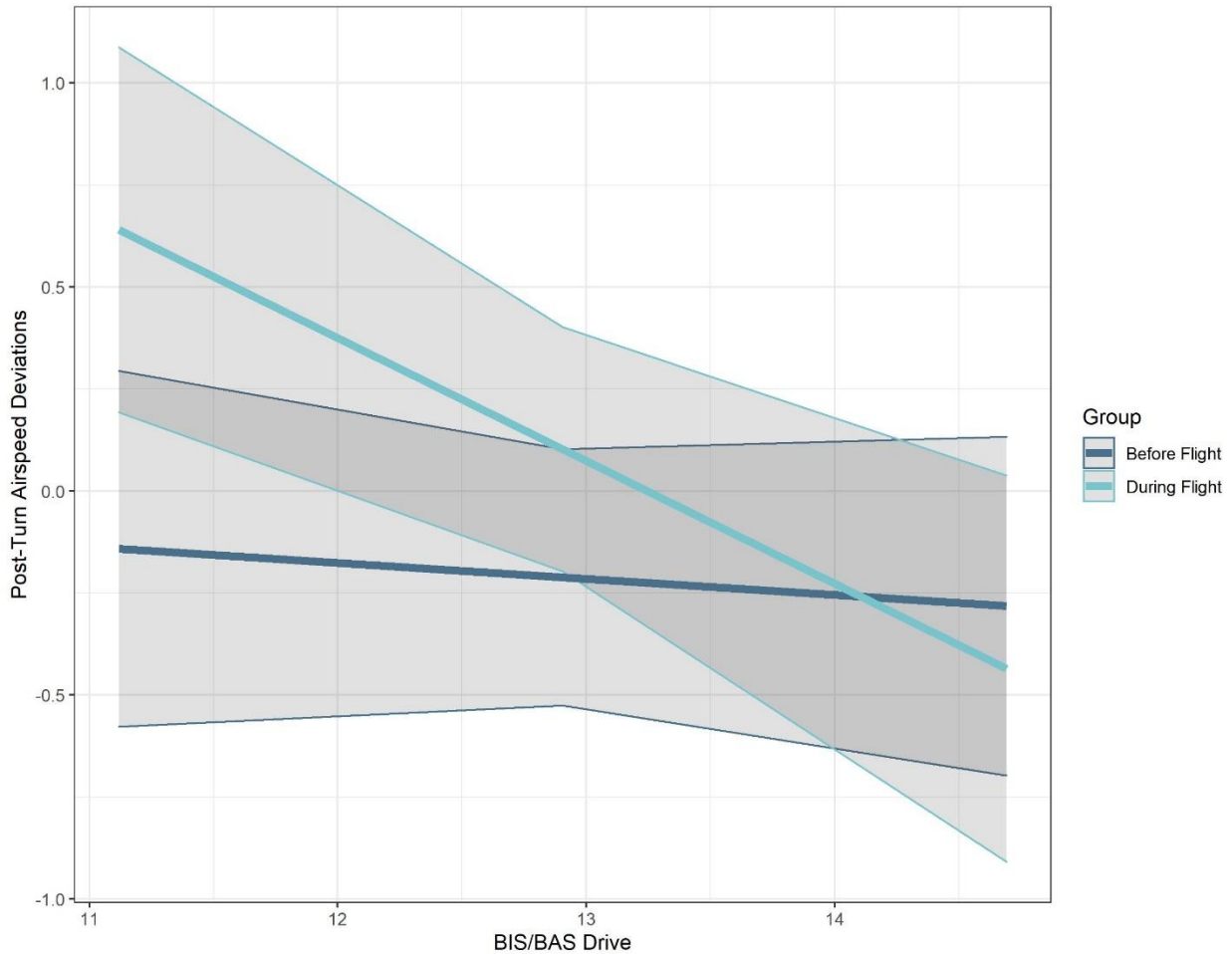


Figure 6. Simple slopes of BIS/BAS drive and post-turn airspeed deviations.

For the BIS/BAS fun model, the overall model was significant,  $F(3, 17) = 3.44, p = 0.040, R^2 = 0.38$ . Participants with low fun scores who received stimulation *during flight* showed *decreased* airspeed deviations (improved performance) from sham to active stimulation conditions ( $\beta = 0.77, p = 0.013$ ). Participants in the same group with moderate and high fun scores showed no statistically significant effects on airspeed deviations ( $\beta = 0.21, p = 0.188$ ;  $\beta = -0.35, p = 0.146$ , respectively). There were no effects noted within the *pre-flight* group. The simple slopes of the conditional effects are plotted in Figure 7.

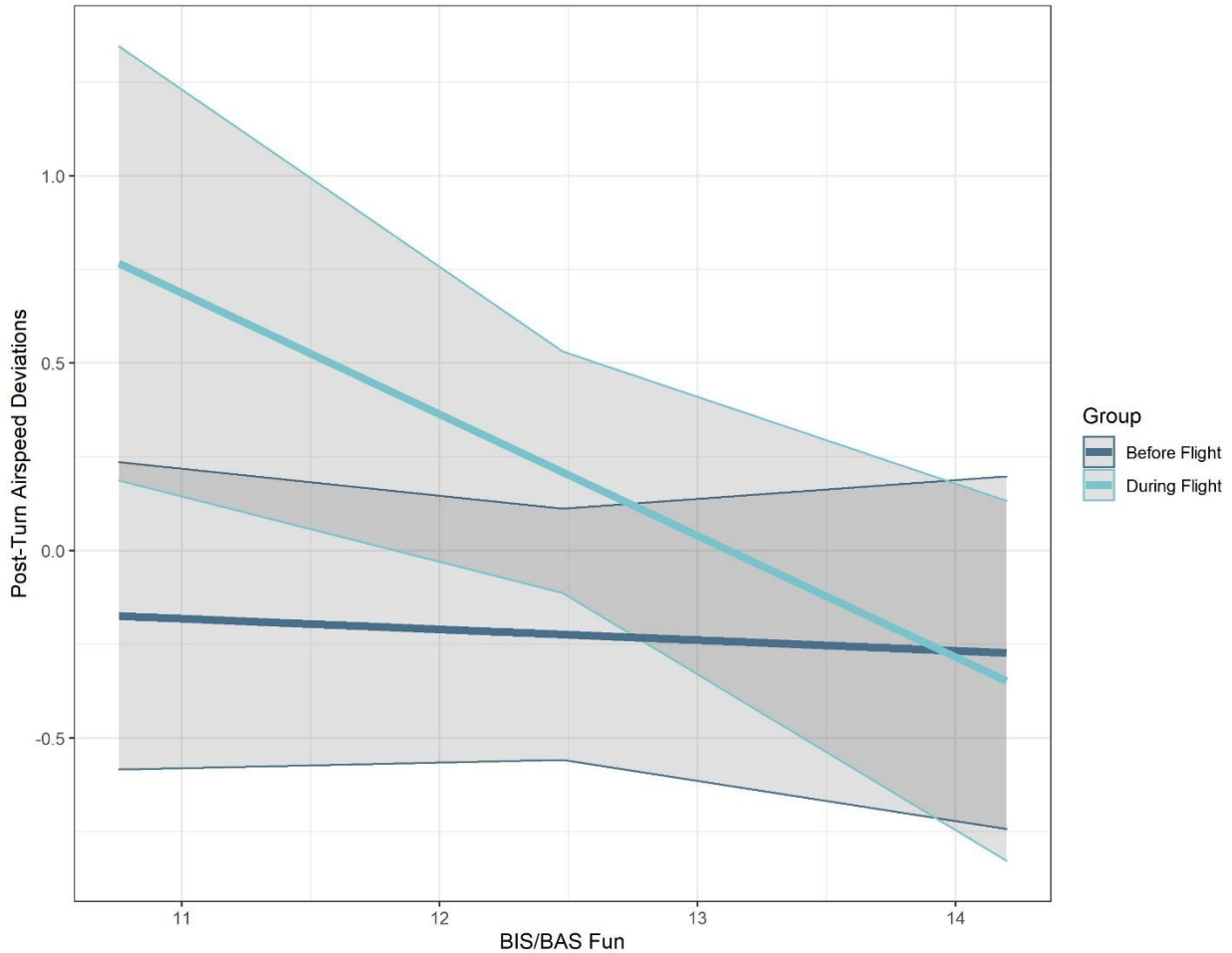


Figure 7. Simple slopes of BIS/BAS fun and post-turn airspeed deviations.

**Approach: Glideslope.**

For the glideslope outcome, only the model with BIS/BAS reward was significant. The overall model was significant,  $F(3, 16) = 3.86, p = 0.030, R^2 = 0.42$ . Participants with low and moderate reward scores who received stimulation *during flight* showed *decreased* glideslope values (improved performance) from sham to active stimulation conditions ( $\beta = 0.12, p = 0.047$ ;  $\beta = 0.12, p = 0.012$ , respectively). Participants in the same group who with high reward scores showed no statistically significant effects on glideslope values ( $\beta = 0.12, p = 0.074$ ). There were no effects noted within the *pre-flight* group. The simple slopes of the conditional effects are plotted in Figure 8.

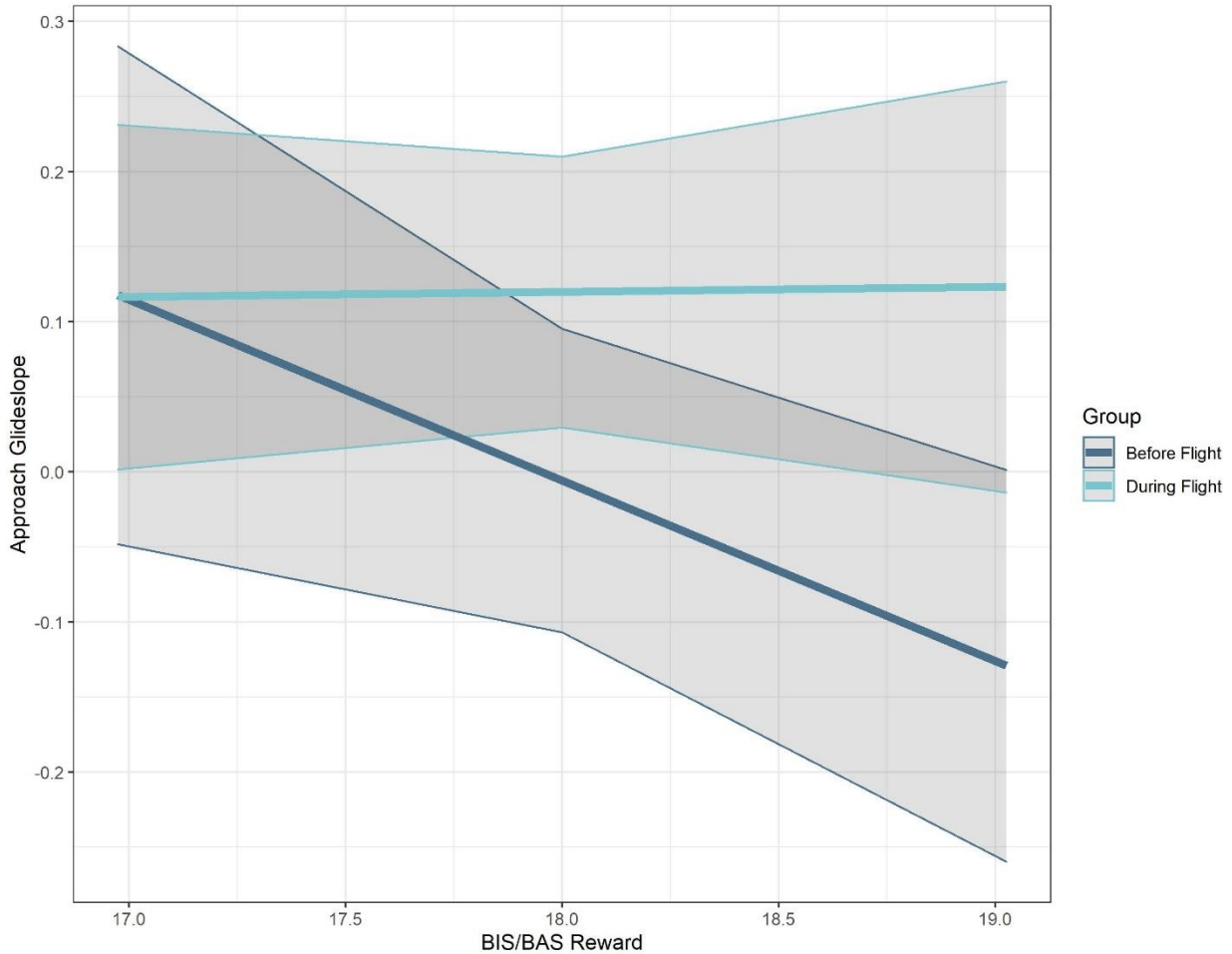


Figure 8. Simple slopes of BIS/BAS reward and approach glideslope.

**Approach: Localizer.**

None of the models with localizer as the outcome variable resulted in significant moderation effects.

**Approach: Heading.**

None of the models with heading deviations as the outcome variable resulted in significant moderation effects.

**Effects on Cognitive Tasks and Duration of Effects**

To evaluate the duration of effects, as well as whether the effects of tDCS are greater for cognitive tasks rather than functional tasks, performance on the Rapid Visual Information Processing Task and the Continuous Performance Task were examined. These tasks were completed approximately 30 minutes post-flight. Thus, for the *pre-flight* group they were completed approximately 120 minutes post-stimulation and 60 minutes after the second stimulation delivery for the *during flight* group. Given these differences in time, each group was examined separately. No significant differences between sham compared to active stimulation

were found for either task. Descriptive statistics are reported in Table 10 below.

Table 10. Duration of Effects Summary Statistics

Measure	Outcome	Pre-flight				During Flight			
		Sham		Active		Sham		Active	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
*Rapid Visual Information Processing	d' fast	2.93	1.35	2.94	0.91	2.94	1.24	2.58	0.89
	Accuracy fast	31.00	5.50	31.20	5.83	30.00	8.59	27.80	6.24
	RT fast	441.00	47.10	439.00	46.10	458.00	40.30	489.00	60.10
	d' slow	3.00	1.45	2.97	1.40	3.57	0.77	3.65	0.64
	Accuracy slow	15.60	3.61	15.00	3.54	16.80	1.82	17.00	1.66
	RT slow	537.00	109.00	647.00	217.00	572.00	120.00	585.00	131.00
Continuous Performance Task	Accuracy	341.00	11.30	341.00	10.90	343.00	9.00	340.00	15.80
	RTs	370.00	51.30	367.00	52.90	385.00	36.50	397.00	52.70

Note. \*Two participants' fast data missing due to recording error in the *during flight* group.

### Analysis of Side Effects

#### Beck Depression Inventory.

Repeated measures ANOVAs comparing conditions found significant differences between conditions after applying the Greenhouse-Geisser correct (Mauchly's test of sphericity  $p < 0.001$ ). Participants rated BDI symptoms highest in the baseline condition (see overall means in Table 11),  $F(1.27, 25.31) = 4.55, p = 0.035, \eta_p^2 = 0.19$ . However, the *pre-flight* group had a wider range in scores during all conditions (e.g., baseline scores ranged from 0 to 7 in the *pre-flight* group compared to from 0 to 2 the *during flight* group).

Table 11. BDI Total Scores

Condition	Pre-flight		During Flight		Overall	
	Mean	SD	Mean	SD	Mean	SD
Baseline	1.00	2.21	0.33	0.78	0.64	1.59
Sham	0.03	0.95	0.00	0.00	0.14	0.64
Active	0.40	1.26	0.17	0.58	0.27	0.94

#### Karolinska Sleepiness Scale.

For analyses, due to missing data, there were nine participants in the *pre-flight* group and 10 in the *during flight* group. The differences in ratings across conditions was not significant,  $F(3, 51) = 2.76, p = 0.052$ . Descriptive statistics are reported in Table 12.

### Samn-Perelli Fatigue Scale.

There was a significant difference between conditions, with participants reporting lower fatigue scores at baseline compared to both sham and active conditions (see Table 12),  $F(2, 38) = 3.38, p = 0.045, \eta_p^2 = 0.15$ .

### Profile of Mood States.

There were several significant differences noted in the subscales and the Total Mood Disturbance score. All descriptive statistics are reported in Table 12 below. Participants reported lower Esteem-Related Affect symptoms in the active stimulation conditions,  $F(2, 36) = 6.15, p = 0.005, \eta_p^2 = 0.26$ . There was a significant interaction between groups and conditions for Vigor symptoms. Participants in the *during flight group* reported higher values both in the sham and active conditions ( $M = 10.70, SD = 4.35; M = 10.80, SD = 2.57$ , respectively) compared to the *preflight group* ( $M = 8.70, SD = 3.65; M = 8.80, SD = 2.44$ , respectively). There was a significant difference in Confusion across conditions. Using the Greenhouse-Geisser correction, participants reported higher Confusion symptoms at Baseline than post-sham or post-active conditions,  $F(1.31, 23.58) = 5.24, p = 0.024, \eta_p^2 = 0.23$ . Additionally, there was significant interaction between group assignment and condition,  $F(1.31, 23.58) = 4.46, p = 0.036, \eta_p^2 = 0.20$ . Participants in the *during flight group* reported higher values at baseline ( $M = 1.30, SD = 1.70$ ) compared to the *preflight group* ( $M = 0.30, SD = 0.68$ ). Finally, there was a significant interaction between groups and conditions for Total Mood Disturbance. Participants in the *preflight group* reported higher symptoms ( $M = -28.80, SD = 7.47$ ) compared to the *during flight group* ( $M = -23.30, SD = 8.58$ ) at baseline.

Table 12. Descriptive Statistics of Side Effect Measures

Measure	Outcome	Baseline		Sham		Active		Follow-Up	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Karolinska Sleepiness Scale	Sleepiness Score	2.68	1.06	2.68	1.34	2.63	1.07	2.05	0.91
Samn-Perelli Fatigue Scale	Fatigue Score	1.57	0.81	2.14	0.96	2.00	1.05	-	-
	Tension	1.40	2.06	0.25	0.44	0.65	0.88	-	-
	Anger	0.20	0.70	0.20	0.41	0.20	0.52	-	-
	Fatigue	1.05	1.64	0.90	1.52	1.00	1.59	-	-
	Depression	0.20	0.52	0.05	0.22	0.20	0.70	-	-
Profile of Mood States	Esteem-Related Affect	18.65	2.83	18.50	3.09	17.30	3.16	-	-
	Vigor	11.05	3.22	9.70	4.04	9.80	2.65	-	-
	Confusion	0.80	1.36	0.25	0.55	0.25	0.55	-	-
	Total Mood Disturbance	-26.05	8.32	-26.55	7.85	-24.80	7.77	-	-

### Side Effect Symptoms.

The frequency of reported side effect symptoms are summarized in Table 13 below. No participants reported a symptom severity rating above a five, which would have required an evaluation by the study physician. In addition to the ratings, the most common comments from participants was the experience of “itching,” a “metallic taste,” and “distracting.” Additionally, some participants commented on not noticing when the stimulation was applied.

Table 13. Responses to Post-Stimulation Symptoms Questionnaire

Item	Sham			Active		
	Frequency of Positive Response	Mean Severity Rating (SD)	+Mean Time of Onset (SD)	Frequency of Positive Response	Mean Severity Rating (SD)	+Mean Time of Onset (SD)
Nervousness or Anxiety	1	1.00 (NA)	2.00 (NA)	3	2.00 (0.00)	60.00 (52.00)
Acute Mood Change	1	2.00 (NA)	30.00 (NA)	1	3.00 (NA)	30.00 (NA)
Headache	4	1.75 (0.50)	23.80 (17.00)	10	1.40 (0.97)	61.50 (52.70)
Nausea	0	-	-	0	-	-
Neck Pain	0	-	-	2	2.50 (0.71)	127.00 (90.00)
Increased Heart Rate *	1	3 (NA)	30.00 (NA)	1	3 (NA)	30.00 (NA)
Back Pain *	2	3 (0.00)	700 (0.00)	4	2 (0.82)	260.00 (164.00)
Blurred Vision	0	-	-	0	-	-
Scalp Irritation	0	-	-	2	2.00 (1.41)	37.50 (10.60)
Tingling	1	3.00 (NA)	60.00 (NA)	6	1.83 (1.17)	47.00 (43.20)
Itching	3	1.67 (1.16)	21.00 (15.60)	5	2.00 (0.71)	56.00 (41.60)
Burning Sensation	1	2 (NA)	20.00 (NA)	2	3.50 (0.71)	20.00 (14.10)
Hot Flush*	0	-	-	0	-	-
Dizziness*	0	-	-	0	-	-
Fatigue	0	-	-	1	3.00 (NA)	30.00 (NA)
Difficulty Concentrating	0	-	-	1	2.00 (NA)	30.00 (NA)

Note. \*Pseudo-items. +Mean Time of Onset are reported in minutes. Time of onset was defined as the number of minutes since the symptom began.

## Blinding Efficacy and Usability of Stimulation

Blinding efficacy and whether participants thought stimulation influenced their performance was assessed using an in-house-developed questionnaire. Results are presented in Tables 14 and 15.

Table 14. Blinding Efficacy and Post-Stimulation Questionnaire Results

Responses	Sham		Active		Total	
	N	%	N	%	N	%
<b>Item #1: The brain stimulation affected my performance.</b>						
Strongly Disagree	2	9.52	2	9.09	4	9.30
Disagree	0	0.00	2	9.09	2	4.65
Undecided	16	76.19	14	63.64	30	69.77
Agree	3	14.29	4	18.18	7	16.28
Strongly Agree	NA	NA	NA	NA	NA	NA
<b>Item #2: After receiving brain stimulation my performance was better.</b>						
Strongly Disagree	NA	NA	NA	NA	NA	NA
Disagree	2.00	9.52	4.00	18.18	6.00	13.95
Undecided	NA	NA	NA	NA	NA	NA
Agree	3.00	14.29	6.00	27.27	9.00	20.93
Strongly Agree	NA	NA	NA	NA	NA	NA
NA (stimulation did not have any effect on performance)	16.00	76.19	12.00	54.55	28.00	65.12
<b>Item #3: After receiving brain stimulation my performance was worse.</b>						
Strongly Disagree	1.00	4.76	0.00	0.00	1.00	2.33
Disagree	5.00	23.81	8.00	36.36	13.00	30.23
Undecided	NA	NA	NA	NA	NA	NA
Agree	1.00	4.76	1.00	4.55	2.00	4.65
Strongly Agree	0.00	0.00	1.00	4.55	1.00	2.33
NA (stimulation did not have any effect on performance)	14.00	66.67	12.00	54.55	26.00	60.47
<b>Item #4: Do you think that you received active stimulation during your participation today?</b>						
Yes	11.00	52.38	7.00	31.82	17.00	39.53
No	10.00	47.62	15.00	68.18	26.00	60.47

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Table 15. Usability of Stimulation and Post-Study Questionnaire Results

Responses	<i>N</i>	Total	<i>%</i>
<b>Item #1: I could easily learn how to use tDCS.</b>			
Strongly Disagree	NA		NA
Disagree	NA		NA
Undecided	6		27
Agree	14		64
Strongly Agree	2		9.1
<b>Item #2: It is a good idea for soldiers to use tDCS as a cognitive enhancement tool in operational environments.</b>			
Strongly Disagree	NA		NA
Disagree	3		14
Undecided	14		64
Agree	5		23
Strongly Agree	NA		NA
<b>Item #3: Most of my fellow soldiers will welcome the fact that I use tDCS as a cognitive enhancement tool.</b>			
Strongly Disagree	1		4.5
Disagree	4		18
Undecided	12		55
Agree	5		23
Strongly Agree	NA		NA
<b>Item #4: The military will encourage the use of tDCS as a cognitive enhancement tool.</b>			
Strongly Disagree	NA		NA
Disagree	4		18
Undecided	12		55
Agree	6		27
Strongly Agree	NA		NA
<b>Item #5: I feel comfortable with using tDCS in an operational environment.</b>			
Strongly Disagree	1		4.5
Disagree	4		18
Undecided	9		41
Agree	7		32
Strongly Agree	1		4.5
<b>Item #6: I intend to use tDCS as a cognitive enhancement tool in operational settings if/when the military makes it available to soldiers.</b>			
Strongly Disagree	1		4.5
Disagree	2		9.1
Undecided	9		41
Agree	10		46
Strongly Agree	NA		NA

## Discussion

The present study sought to determine whether: 1) active tDCS would maintain or improve aviator performance over sham, 2) the timing of stimulation (*preflight* or *during flight*) simulated flight significantly affected performance outcomes, and 3) the extent to which individual differences moderated those outcomes. Additionally, this study sought to document any side effects of stimulation. Specifically, it was hypothesized that: 1) active stimulation would maintain or improve aviator performance over sham, 2) the application of tDCS *during flight* would result in better aviator performance compared to stimulation delivered *preflight*, and 3) individual differences would moderate the efficacy of stimulation. When comparing approach performance in sham and active conditions between groups, results suggested performance was improved in the active condition versus the sham condition for the *during flight* group. Specifically, when comparing approach performance for the active stimulation conditions between groups, it was found that those who received stimulation *during flight* demonstrated a more precise approach compared to those who received stimulation *preflight*. The third hypothesis, that individual differences would moderate the effectiveness of tDCS was also found to be supported within the data. Specifically, the two ADHD subscales (inattentiveness, hyperactivity), recency of flight experience, and the behavioral activation subscales (reward responsiveness, drive, and fun seeking) all moderated the effect of tDCS on different aspects of performance.

### Timing of Stimulation and Individual Differences

Overall, the results of the study suggest that when stimulation is delivered in relation to when tasks occur influences task outcomes. This is in line with previous tDCS research that suggests online stimulation (i.e., stimulation *during* a task) is the most effective at creating behavioral changes (e.g., Bikson et al., 2013; Katsoulaki et al., 2016). Although the only comparisons between sham and active conditions that resulted in significant differences in performance were on the glideslope outcome during the approach phase, several moderation models were significant, suggesting that the effectiveness of tDCS is moderated by various individual differences.

Specifically, evaluation of performance data were split into *pre-turn*, *post-turn*, and *approach* phases of flight. This was done to evaluate the effectiveness of tDCS at different time points during flight while aligning with the delivery of tDCS during flight. Upon examining the results of the *pre-turn* moderation models, it was noted that the *preflight* stimulation group demonstrated performance improvements with different individual differences added to the separate models. It was found that altitude maintenance (i.e., fewer deviations from sham to active) was improved when inattentiveness, hyperactivity, experience, and BIS/BAS reward were entered into their separate models as potential moderators. Moreover, the moderation model that included inattentiveness indicated that the effects of stimulation had the opposite effect depending on group assignment. Those in the *preflight* stimulation group with moderate to high inattentive scores demonstrated improved altitude performance, whereas those in the *during flight* stimulation group with high inattentiveness scores showed worse altitude performance. This particular finding suggests that the timing, and possibly the duration, of the stimulation likely has an effect on how stimulation affects performance of those who score higher on inattention. Recent work by Sikström et al (2016) found a similar pattern, where

participants who measured high on inattention benefited from tDCS application during an attentional task. The authors suspected this effect was due to individuals who are more inattentive having a higher threshold for activation related to attention. The application of tDCS is thought to lower that threshold due its effect on neuronal activation thresholds. Particularly, given that this finding occurred during the *pre-turn* portion of the flight, and was not replicated in the *post-turn* data, it may be that those who demonstrate more inattentiveness require stimulation prior to fully engaging in the task, and/or longer duration of stimulation since the *during flight* stimulation bouts were only ten minutes.

The moderating effect of recency of flight experience is also noteworthy. Participants who reported low to moderate flight hours within the previous 90 days demonstrated fewer altitude deviations from sham to active if they received stimulation *preflight*. This may be considered a novel effect. As far as the authors were able to find, this has not been previously demonstrated nor investigated. One recent study by Toth et al. (2021) examined whether application of tDCS had differential effects amongst individuals with different video game skill levels. This group of researchers found that application of tDCS preferentially improved performance in novices when receiving stimulation prior to video game training. The authors believed this was due the application of tDCS facilitating skill acquisition through its effects on neuroplasticity. Although this improvement was only found in one performance parameter, it suggests that there may be benefit to those who have not flown recently to receive stimulation prior to a flight. The application of stimulation prior to the flight may aid in activating the neuronal pathways required of the flight tasks, which we speculate may have become weakened with less recent practice.

Finally, there is a recurring effect of the behavioral activation system with the application of tDCS *during flight*. Although all three subscales (reward responsiveness, drive, fun seeking) were significant for different models, they each measure portions of the BAS, suggesting the BAS itself was a factor here rather than just one of the subcomponents. Indeed, recent work suggests that the BAS can be viewed as a unidimensional scale, rather than three subscales (Maack & Ebesutani, 2017). The BAS is believed to be the neurophysiological mechanism for controlling motivation (Carver & White, 1994). Indeed, recent research has supported the role of the BAS in interacting with executive functions and cognitive control by playing a role in prioritizing behavioral goals (e.g., Pessoa, 2008; Pessoa, 2009). Research suggests that activation of this system aids a person in completing behavioral goals (e.g., Lowe & Ziemke, 2011). Thus, the BAS subscales reflect lower BAS activation for individuals who score lower. Therefore, the application of tDCS *during flight* may have had the effect of increasing activation for those who approached the flight tasks with lower activation within this neurophysiological system. Indeed, this notion is supported within the data. Heading deviations during the *pre-turn* portion of flight were moderated by BAS reward scores in those who received stimulation *during flight*. Specifically, individuals with low reward scores showed decreases in heading deviations whereas those with high reward scores increased heading deviations. In this case, the addition of stimulation *during flight* may have aided in activating the BAS in those who had low activation in this area, whereas those who already had high activation may have experienced an inhibitory effect of the stimulation. Moreover, we found within the *post-turn* models that BAS drive and fun seeking scores similarly moderated performance. Specifically, individuals in the *during flight* stimulation group who had low drive and fun seeking scores showed lower airspeed deviations from sham to active stimulation. This

again suggests that, although different subscales, those who have lower activation in the BAS benefited more from the delivery of stimulation *during flight*. This was demonstrated again for the glideslope measure during the *approach* phase of flight. Participants with lower to moderate BAS reward scores showed decreased glideslope values.

Taken together, application of tDCS *during flight* aids aviators in maintaining, or perhaps improving, performance at later points in the flight, when individuals present with lower BAS activation. Moreover, this is particularly important for the effect of stimulation during the approach phase of flight. Given that participants were exposed to an unexpected emergency event prior to the approach, requiring them to re-plan the approach to some extent, the application of tDCS *during flight* aided in their maintenance of a more precise approach. This is key for considering how tDCS could be used prescriptively during long-duration missions where attention could wane and the necessity for maintaining performance is high. Finally, there are also some considerations to be made for the duration of stimulation delivery and its effect on other individual differences, namely inattentiveness, hyperactivity, and recency of experience. These individual differences were only significant in the moderation models for the *pre-turn* outcome data. Further research is needed to evaluate whether whether tDCS applied for longer durations and/or repeatedly have an increased duration of effects.

### **Side Effects and Duration of Effects**

No significant side effects were reported within either group. Participants did report lower fatigue scores, as measured by the Samn-Perelli Fatigue Scale at baseline compared to both sham and active stimulation sessions. This was likely due to the length of testing. Regarding the Profile of Mood States, there were some differences noted between stimulation conditions (active and sham), as well as groups. Participants reported lower esteem-related affect symptoms when active stimulation was received. Additionally, participants in the *during flight* stimulation group reported higher Vigor symptoms compared to the *pre-flight* group, regardless of stimulation condition. Lastly, participants in the *preflight* group reported higher Total Mood Disturbance scores than the *during flight* group, regardless of condition. None of these differences in mood changes signify a concerning side effect resulting from stimulation, however. Finally, none of the reported symptoms from stimulation reached a severity level that would have required physician intervention. All of the symptoms participants reported experiencing were expected and typical of tDCS (e.g., headache, scalp irritation, tingling, itching, burning sensation, fatigue, difficulty concentrating).

Regarding the duration of effects of stimulation. No changes in performance were noted for either group in completing the RVIP and CPT post-stimulation. For both groups, these tasks were completed at least 1 hour following the last application of stimulation. Thus, it is possible that any potential effects of stimulation wore off, or were not present for these tasks in the first place.

The study blinding also appeared to be effective, with participants nearly equally split in thinking they received active stimulation during the sham condition (52% yes compared to 48% no), whereas only 32% thought they received active stimulation during the active condition. This lines up with participants' comments that they often did not notice whether or not they were receiving stimulation.

## **Limitations**

Several limitations were associated with this study. The examination of the duration of effects was limited such that the chosen tasks may not have been optimal for detecting any effects if they existed. It is also possible any effects experienced were not large enough to have been detected with this sample size. Although some evidence can be garnered from the differences in timing of application for duration of effects, to gain a clearer understanding of how long the effects of stimulation last in this population would require a more controlled study.

Additionally, many of the analyses conducted were exploratory in nature. Individual moderation models were used to examine the effects of the various hypothesized individual differences. The variables included were selected based on conceptual assumptions and findings from the literature. To fully evaluate the moderating effects of these factors, future work should combine the most meaningful moderators into a single model to get a more parsimonious understanding of how the different moderators interact together with the focal predictor (stimulation) to effect the various outcomes.

There are significant practical limitations in interpretation of the findings as well. First, the experience levels of the participants pose another limitation to the generalizability and interpretation of the findings. Specifically, the participants were primarily highly experienced instructor pilots. Participants with a wider range of skill levels would provide better insight as to the practicality and applicability of tDCS use in Army aviation. For example, less experienced pilots may yield greater benefit from stimulation in regards to performance. It is also unclear how novice pilots may benefit from stimulation during learning and skill acquisition. However, having found even minimal performance improvements in this highly experienced group is promising, and suggests that tDCS could be beneficial to the larger aviation population. Second, while effects are observed, there is not an agreed upon degree of improvement to use as a criterion or threshold for performance benefit. Finally, the effects of operational stressors were not evaluated in this study and must be evaluated prior to recommendations for stimulation in the operational environment.

## **Conclusion**

The results of this study suggest that tDCS stimulation improves aviator performance in a highly skilled set of pilots when that stimulation is delivered during flight. These effects, however, were moderated by multiple individual differences thus potentially limiting the applicability of tDCS in an operational environment.

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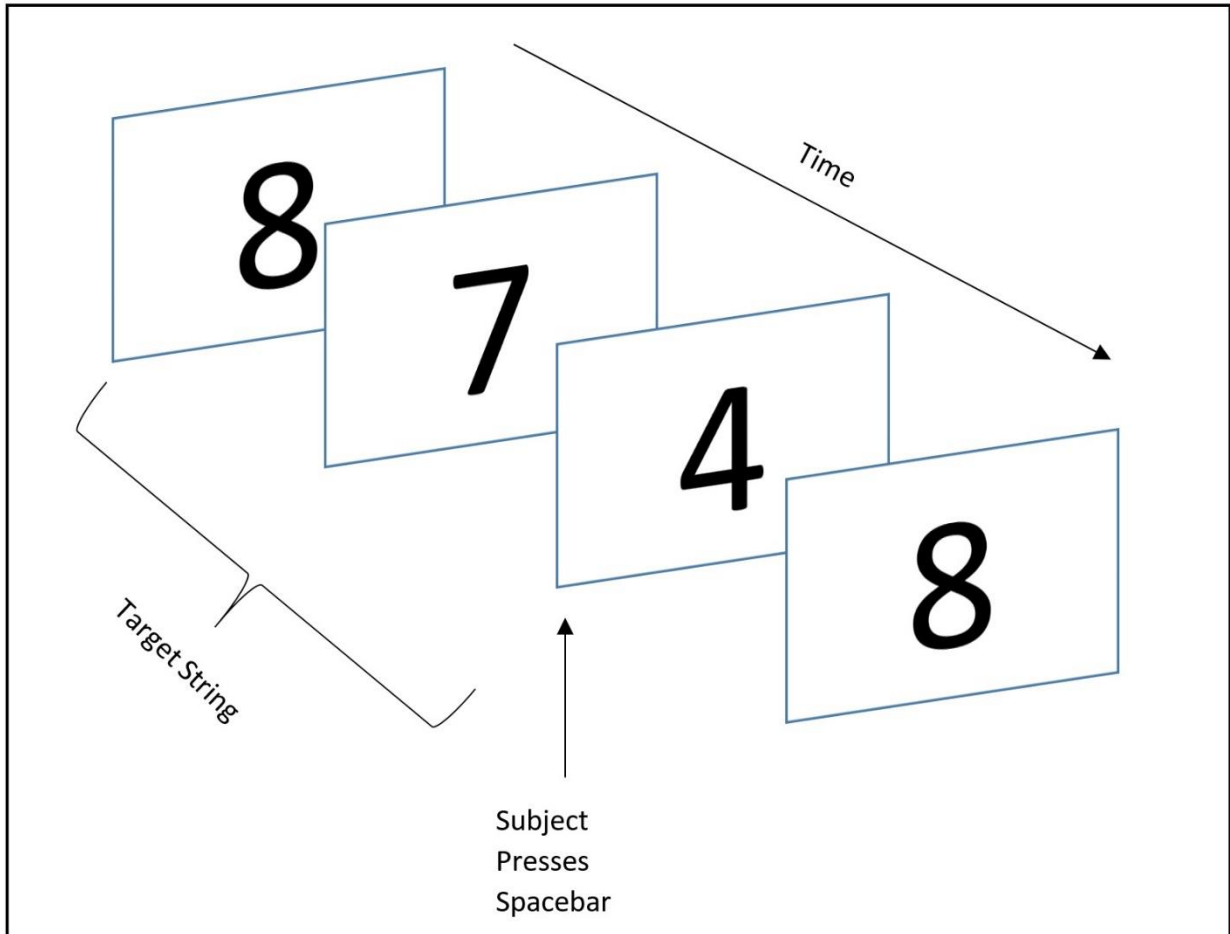
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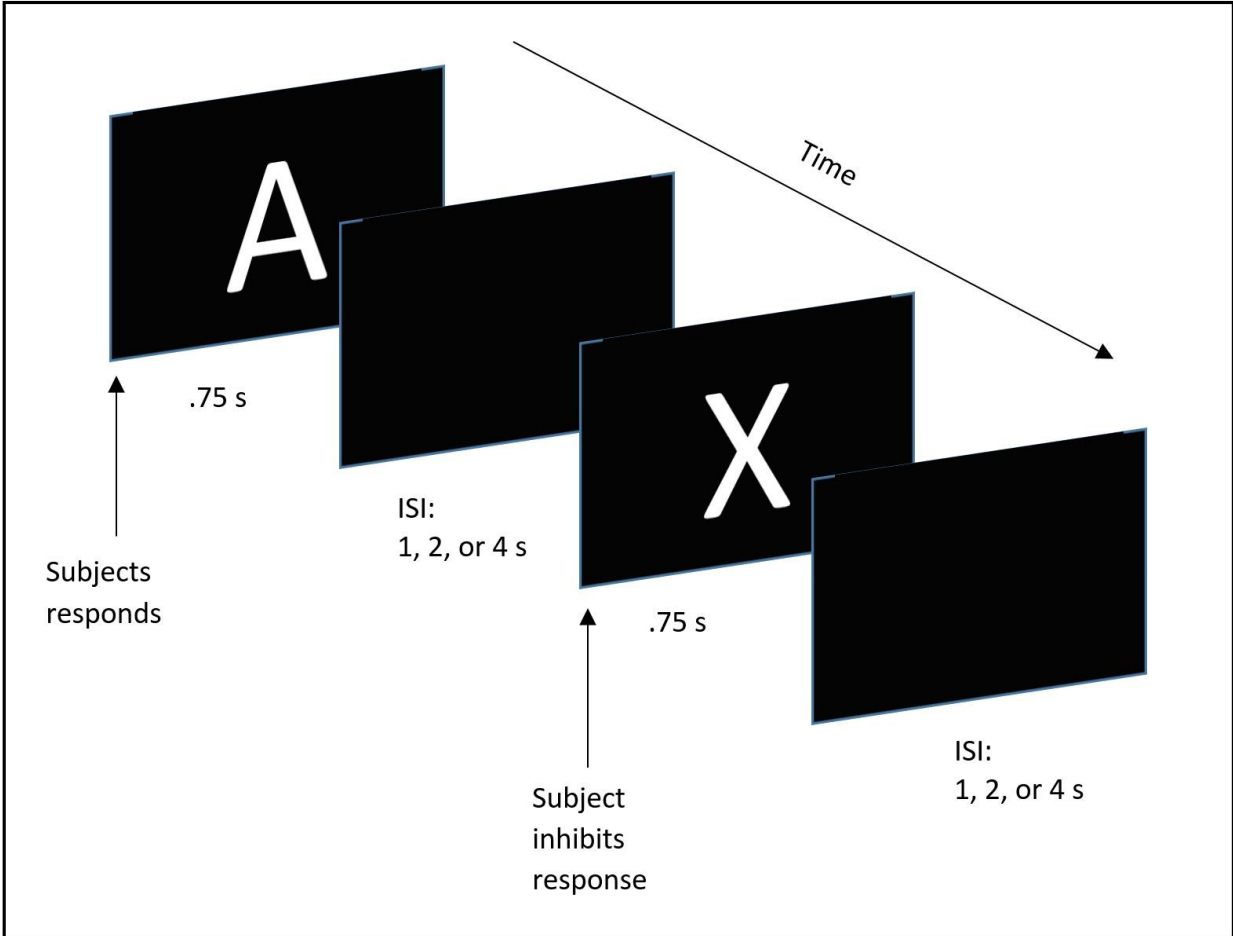
## **Appendix A. Acronyms and Abbreviations**

ASRS	Adult ADHD Self Report Scale Symptom Checklist
BDI	Beck Depression Inventory
BIS/BAS	Behavioral Inhibition/ Avoidance Scales
CISS	Convergence Insufficiency Symptom Survey
CPT	Continuous Performance Task
FVL	Future Vertical Lift
KSS	Karolinska Sleepiness Scale
MEMORE	Mediation and Moderation for Repeated Measures
MEQ	Morningness-Eveningness Questionnaire
NASA-TLX	NASA Task Load Index
POMS-SF	Profile of Mood States – Short Form
PPC	Posterior Parietal Cortex
RP	Research Pilots
RVIP	Rapid Visual Information Processing Task
SILS	Shipley Institute of Living Scale
STQ	Sleep Timing Questionnaire
tDCS	Transcranial Direct Current Stimulation
tES	Transcranial Electrical Stimulation
USAARL	U.S. Army Aeromedical Research Laboratory
WAIS-R	Weschler Adult Intelligence Scale-Revised
WHO	World Health Organization

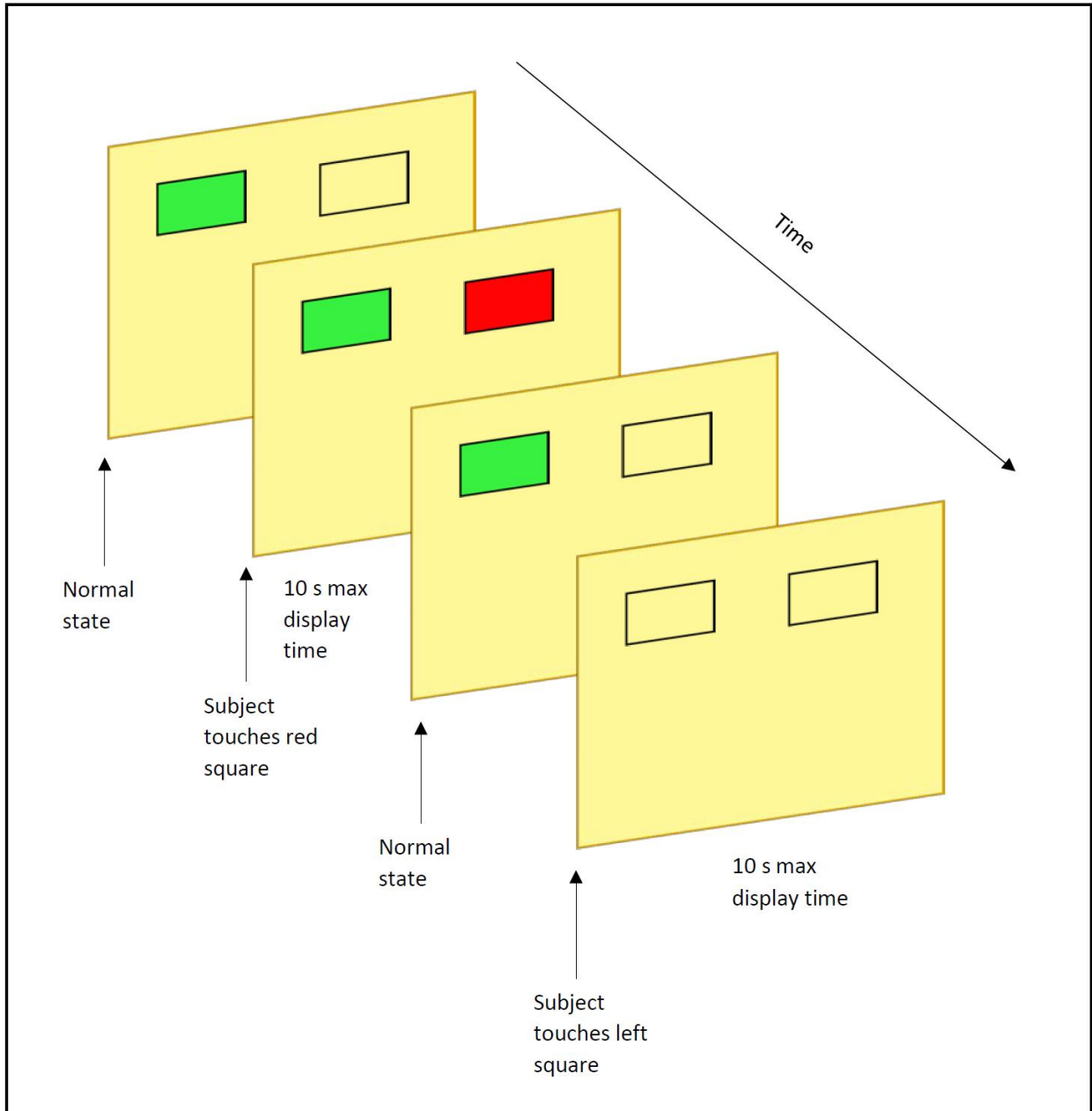
## Appendix B. Rapid Visual Information Processing Task



## Appendix C. Continuous Performance Task



## Appendix D. Visual Secondary Task





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