



## Transcranial direct current stimulation versus caffeine as a fatigue countermeasure



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### ABSTRACT

**Background:** To assess the efficacy of using transcranial direct current stimulation (tDCS) to remediate the deleterious effects of fatigue induced by sleep deprivation and compare these results to caffeine, a commonly used fatigue countermeasure.

**Objective/Hypothesis:** Based on previous research, tDCS of the dorsolateral prefrontal cortex (DLPFC) can modulate attention and arousal. The authors hypothesize that tDCS can be an effective fatigue countermeasure.

**Methods:** Five groups of ten participants each received either active tDCS and placebo gum at 1800, caffeine gum with sham tDCS at 1800, active tDCS and placebo gum at 0400, caffeine gum with sham tDCS at 0400, or sham tDCS with placebo gum at 1800 and 0400 during 36-h of sustained wakefulness. Participants completed a vigilance task, working memory task, psychomotor vigilance task (PVT), and a procedural game beginning at 1800 h and continued every two hours throughout the night until 1900 the next day.

**Results:** tDCS dosed at 1800 provided 6 h of improved attentional accuracy and reaction times compared to the control group. Caffeine did not produce an effect. Both tDCS groups also had an improved effect on mood. Participants receiving tDCS reported feeling more vigor, less fatigue, and less bored throughout the night compared to the control and caffeine groups.

**Conclusions:** We believe tDCS could be a powerful fatigue countermeasure. The effects appear to be comparable or possibly more beneficial than caffeine because they are longer lasting and mood remains more positive.

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### Introduction

Fatigue induced by sleep deprivation from extended duty hours is common in many professions such as transportation, medicine, and military. During these long vigils, people experience degradations in response accuracy and speed, multi-tasking ability, and attentional levels that lead to forgetting or ignoring important aspects of their job [1]. Several laboratory studies over the years have examined the link between sleep deprivation and cognitive performance degradations. For example, Dinges [2] found that long shifts for nurses, especially during the night, led to an increase in procedural and medication errors. In aviation, NASA's Aviation Safety Reporting System (ASRS) regularly receives reports from

pilots blaming fatigue, sleep loss, and sleepiness in the cockpit for errors such as altitude and course deviations, fuel miscalculations, landings without proper clearances, and landings on incorrect runways [3]. The career fields commonly plagued with long duty hours are further complicated by circadian factors because employees are working around the clock which exacerbates the issue. Furthermore, high operational tempo has been shown to produce performance changes similar to those seen with blood alcohol concentrations of 0.05–0.08% [4]. Not only is cognitive performance affected by sleep deprivation but mood is also negatively affected. Feelings of fatigue, loss of vigor, sleepiness, and confusion are commonly reported in sleep deprivation research [5]. Unfortunately, the conditions in these career fields are unlikely to change anytime soon; therefore, it is necessary to investigate possible fatigue countermeasures.

One of the most commonly used fatigue countermeasure is caffeine. In fact, even the military makes caffeinated beverage

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options readily available at bases, and caffeinated gum is included in military rations [6]. Caffeine has been found to improve performance during inadequate sleep and circadian variation [7,8]. Specifically, SEAL trainees who were given caffeine after 72 hours of sleep deprivation significantly improved visual vigilance, choice reaction time, and self-reported fatigue [9]. However, the benefits from caffeine decline over time from chronic use [6]. Also, while caffeine may increase the ability to stay awake, it does not necessarily aid in making good decisions [10], a skill that is critically important to these professions that experience sleep loss. Sleep deprivation is known to interfere with short-term memory; however, few studies have been able to show improvements in memory from caffeine and the results seem to differ depending on task complexity, time of day the caffeine is administered, gender, and age [11,12]. In our own lab, we found that people who received caffeine had a correlation between bad performance and negative mood states. This phenomena was not found for the control group or tDCS group [13]. Therefore, it is essential to examine other forms of fatigue countermeasures to enhance alertness and performance.

A form of non-invasive brain stimulation called transcranial direct current stimulation (tDCS) might provide a viable option as a fatigue countermeasure. tDCS uses a mild direct electrical current passed between electrodes on the scalp to modify neuronal membrane resting potential in a polarity dependent manner, elevating or lowering neuron excitability in a region [14,15]. For a detailed description of these technologies, design, physics, and principles of activation, see Wagner et al. [16]. The potential therapeutic effects of this technology have been examined for decades in a variety of neurological disorders such as Parkinson's disease, major depressive disorder, schizophrenia, stroke, dementia, chronic pain, etc. In recent years, there has been a rapid expansion of research showing that tDCS is effective in enhancing healthy human performance (see [17] and [18] for reviews). Specifically, tDCS has been shown to improve attention, working memory, vigilance, accuracy, and speed of response in healthy populations [18–20]. All of these cognitive abilities are also significantly affected by fatigue. Additionally, our previous sleep deprivation study indicated that tDCS could mitigate the deleterious effects of sustained wakefulness for up to 6 h post-stimulation [13]. The goal of the project reported herein was to extend our results on cognitive enhancement by examining the effect of tDCS on cognitive performance following a period of extended wakefulness. The differences in timing of the stimulation (i.e. stimulating at the beginning of the shift versus stimulation later in the shift when performance would be most degraded) were tested. We also compared these effects to those of caffeine to determine if there are any benefits of tDCS in mitigation of fatigue that are above the simple intake of caffeine. The duration of the study was lengthened beyond that reported by McIntire et al. [13] to determine the extent of the duration of the performance and behavioral benefits from tDCS.

## Material and methods

### Equipment

**tDCS Stimulator:** The MagStim DC stimulator (Magstim Company Limited; Whitland, UK) was used to provide the tDCS stimulation. This battery-powered device was controlled with a microprocessor to ensure constant current at up to 5,000  $\mu$ A. The device automatically shuts off if the impedance becomes greater than 50 k $\Omega$  to prevent electric shocks or burns.

**tDCS Electrodes:** The electrodes included an array of 5 electroencephalographic (EEG) electrodes arranged in a circular pattern purchased from Rio Grande Neurosciences. Each electrode had an inner diameter of 1.6 cm yielding a contact area of 2.01 cm<sup>2</sup> for each

electrode. At 2 mA of supplied current, there was an average current density of 0.199  $\frac{mA}{cm^2}$ . The anodal electrode was placed on the left dorsolateral prefrontal cortex while the cathode was placed on the contralateral (right) upper bicep. Electrode gel was used as the electrode to skin conduit.

**StayAlert<sup>®</sup> Gum** (MarketRight, Inc., Plano, IL): Gum was the delivery mechanism used to administer 200 mg of caffeine to participants in the caffeine group. The placebo gum was also StayAlert<sup>®</sup> gum which looked and tasted the same as the caffeinated gum.

### Subjects

Fifty active-duty military participants from Wright-Patterson Air Force Base completed this study. There were 36 male and 14 female participants with an average age of  $27 \pm 5$ . Participants were compensated for their time but were disqualified if they met any of the exclusion criteria described in McKinley et al. [21]. Sixty-seven participants enrolled in the study but eleven were dismissed because they met one or more of the study exclusion criteria. Disqualification criteria included: any neurological diagnosis, any psychological diagnosis, psychological hospitalization, hospitalization for surgery/illness within 6 months of participation, taking of psychotropic medications, a shot in the left arm within one week of participation (i.e. flu, allergy, pain), non-removable metal or tattoos around the head, uncorrectable vision impairments, pregnant or could become pregnant, smoking, treatment for drug/alcohol within 6 months of participation, head injury within 30 days of participation, history of any of the following: learning difficulty, frequent headaches, attention deficit, severe head injury, seizures, fainting, migraine headaches, high blood pressure, diabetes, or heart disease. Four participants self-withdrew in the middle of data collection because they were either too tired to complete, had a family emergency, or felt ill. Two were dismissed because they did not meet baseline training standards. The 50 remaining participants were randomly assigned into one of five groups with 10 individuals each.

### Performance tasks

**Mackworth Clock Test (Vigilance Task):** The vigilance task was developed according to the description of the task used by Kilpaläinen, Huttunen, Lohi, and Lyytinen [22]. The task was an adopted version of the Mackworth clock test with parameters adopted from Teikari [23] and run on a standard desktop computer. The participant was presented a visual display with 16 hole-like black circles arranged in a clock-like figure against a black background. Each circle changed from black to red for 0.525 s in turn, with each cycle lasting 3 s. The red light moved in a clockwise pattern by one step, which was considered the normal stimulus appearance. When the light moved twice the usual distance (i.e., skipping a circle), it was considered a critical signal and the participant was required to respond to this signal by pressing the spacebar as fast as possible on the keyboard with his preferred index finger. The response was defined as a correct hit when it occurred less than 3 s after the target signal and a false alarm if the reaction occurred outside this time range (+0.1–3.0 s). Undetected targets were defined as misses.

**Delayed Matching-To-Sample Working Memory Task:** The Delayed Matching-To-Sample (DMS) task taken from the Cambridge Neuropsychological Assessment Battery (CANTAB). The CANTAB software package housed a complete battery of tasks that can be used to probe various basic cognitive functions. The DMS task was designed to probe perceptual matching, immediate and delayed visual memory. The participant was presented with a

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