

UNITED STATES ARMY AEROMEDICAL RESEARCH LABORATORY



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# **A Systematic Review of the Transcranial Stimulation Literature for Performance Enhancement**

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N/A

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<b>1. REPORT DATE (DD-MM-YYYY)</b> 08-02-2023	<b>2. REPORT TYPE</b> Technical Report	<b>3. DATES COVERED (From - To)</b> 2018-2022
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<b>4. TITLE AND SUBTITLE</b> A Systematic Review of the Transcranial Stimulation Literature for Performance Enhancement	<b>5a. CONTRACT NUMBER</b>
	<b>5b. GRANT NUMBER</b>
	<b>5c. PROGRAM ELEMENT NUMBER</b>

<b>6. AUTHOR(S)</b> D'Alessandro, M. <sup>1</sup> , Feltman, K. <sup>1</sup> , Wilkins, J. <sup>1,2</sup> , & Boggs, J. <sup>1</sup>	<b>5d. PROJECT NUMBER</b>
	<b>5e. TASK NUMBER</b>
	<b>5f. WORK UNIT NUMBER</b>

<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> U.S. Army Aeromedical Research Laboratory P.O. Box 620577 Fort Rucker, AL 36362	<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b> USAARL-TECH-TR--2023-15
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<b>9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b> U.S. Army Medical Research and Development Command Military Operational Medicine Research Program 504 Scott Street Fort Detrick, MD 21702-5012	<b>10. SPONSOR/MONITOR'S ACRONYM(S)</b> USAMRDC MOMRP
	<b>11. SPONSOR/MONITOR'S REPORT NUMBER(S)</b>

<b>12. DISTRIBUTION/AVAILABILITY STATEMENT</b> DISTRIBUTION STATEMENT A. Approved for public release: distribution is unlimited.
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<b>13. SUPPLEMENTARY NOTES</b> <sup>1</sup> U.S. Army Aeromedical Research Laboratory, <sup>2</sup> Oak Ridge Institute for Science and Education
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<b>14. ABSTRACT</b> The purpose of this report is to update a previous review on the neuromodulation technologies of transcranial magnetic stimulation and transcranial electrical stimulation (Kelley et al., 2019). Ongoing work within the U.S. Army is investigating means of sustaining or enhancing Soldier performance. As neuroenhancement is a rapidly evolving field, it is imperative to stay up-to-date on the current state of the science. As such, this report includes studies performed between 2018 and 2022 that met our specific inclusion criteria. This report specifically focuses on studies that investigate the potential role for the neuromodulation technologies of transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (tES) to enhance cognitive function. In particular, we are interested in several specific aspects of cognition that relate directly to the daily function of the Soldier including working memory, attention, inhibition, cognitive control, and reasoning/decision making. Here, we have discussed the feasibility and practicality aspects of implementing this technology in the military setting as well as the current limitations and remaining questions within the research field of transcranial stimulation pertaining to enhancing cognitive performance.
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<b>15. SUBJECT TERMS</b> Transcranial electrical stimulation (tES), transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS)
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<b>16. SECURITY CLASSIFICATION OF:</b>			<b>17. LIMITATION OF ABSTRACT</b> SAR	<b>18. NUMBER OF PAGES</b> 72	<b>19a. NAME OF RESPONSIBLE PERSON</b> Loraine St. Onge, PhD
<b>a. REPORT</b> UNCLAS	<b>b. ABSTRACT</b> UNCLAS	<b>c. THIS PAGE</b> UNCLAS			<b>19b. TELEPHONE NUMBER (Include area code)</b> 334-255-6906

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## Executive Summary

Ongoing work within the United States Army is investigating means of sustaining or enhancing Soldier performance. The purpose of this technical report is to build upon a previous review which broadly focused on interventions for cognitive enhancement such as pharmaceutical intervention, nutrition and supplements, and transcranial stimulation (Kelley et al., 2019). Given the rapid pace of technological development and quantity of research evaluating neuromodulation techniques (transcranial electrical and magnetic stimulation), we conducted a targeted review to identify emerging trends and trajectory of feasibility for implementation in operational settings. Hence, this report includes papers published between 2018 and 2022 that met our specific inclusion criteria (see eligibility section for inclusion and exclusion criteria).

This technical report focuses on studies that investigate the potential role for neuromodulation technologies to enhance cognitive function and implications for military use. In particular, we are interested in several specific aspects of cognition that relate directly to the daily function of the Soldier, including working memory, attention, inhibition, cognitive control, and reasoning/decision-making. As Soldiers are faced with many important decision-making tasks that require cognitive inhibition and precise cognitive control, a wrong decision or lack of attention to detail could have catastrophic consequences. Multiple reviews have previously detailed both the potential and limitations of transcranial electrical stimulation (tES) to improve cognitive enhancement (Chase et al., 2021). Here, we discuss the feasibility and practicality aspects of implementing this technology in the military setting as well as the current limitations and remaining questions within the research field of transcranial stimulation pertaining to enhancing cognitive performance.

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## **Acknowledgements**

The authors would like to thank Mr. Tony Waterman, the U.S. Army Aeromedical Research Laboratory Librarian, for his assistance with this project.

This research was supported in part by an appointment to the Research Participation Program at the U.S. Army Aeromedical Research Laboratory administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and the U.S. Army Medical Research and Development Command.

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## Introduction

In training and on the battlefield, Soldiers must have a positive and focused mentality to accomplish the objective/mission. Military operations require sustained attention, where a brief disruption of attention or focus could have devastating consequences. A multitude of distractions can arise in the military environment that can impact how a Soldier manages attention, in turn, decreasing mental function and cognitive performance. For example, fatigue can diminish cognitive resources during extended or frequent missions that can have significant decrements in performance (Abd-Elfattah et al., 2015). In addition to the already diminished available cognitive resources the Soldier may have from experiencing fatigue, the multi-domain operational field can place a significant demand on the Soldier, increasing the likelihood of mistakes and errors due to excessive cognitive workload.

In the operational setting, cognitive challenges are constant, especially when multitasking is required. Furthermore, these challenges may occur over an extended duration while fatigue inevitably sets in. In a degraded cognitive state, the Soldier is presented with great challenges to perform at optimal capacity. Therefore, cognitive enhancement could sustain performance despite suboptimal conditions known to elicit deficits in performance and cognition. However, there are several challenges in obtaining this desired outcome. Primarily, the United States military has an extensive history of utilizing stimulants (dating back to World War II) to maintain wakefulness and attentiveness (Bower & Phelan, 2003). While stimulant use has been well-documented to improve the aforementioned, it has not come without negative side effects that pose ethical and medical challenges as well as potentially impacting readiness post-enhancement (Levy, 1993).

Furthermore, another challenge presents as military personnel must perform in austere, extreme environments and often with additional physical burden (e.g., weight of personal protective equipment or tactical gear, physical exertion). Therefore, any additional gear required for the Soldier to carry must have a valid justification for its use and serve an important and mission-directed purpose. Hence, it is of utmost importance to identify both training and technological advancements or approaches to facilitate optimal and enhanced performance in challenging environments while mitigating the need for the addition of cumbersome equipment. A significant effort of current research aiming to increase cognitive performance is investigating neuroenhancement techniques that would enhance mental function and acuity while not creating any extra burden for the Warfighter. Neuroenhancement focuses on improving the neural processes involved in executive functioning beyond the maximum natural capability of the individual (Brunyé et al., 2020). Nonpharmacologic neuromodulation techniques such as transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (tES) have demonstrated the potential to increase neuroenhancement and provide long-term cognitive benefits (Frank et al., 2018; Grover et al., 2022; Naish et al., 2018). Current literature suggests that neuromodulation technologies such as tES and TMS may facilitate cognitive enhancement, which may further increase the chance of mission success. Although there are many techniques that may directly facilitate neuromodulation and enhance cognitive performance such as vagus and trigeminal nerve stimulation, this review specifically focuses on current transcranial interventions. This review highlights the recent literature on transcranial stimulation aimed at targeting various anatomical regions (primarily the dorsolateral prefrontal cortex) as well as other brain regions responsible for regulating and executing executive functions.

## **Neuromodulators and Neuromodulation**

Neuromodulation, the introduction of exogenous entities in the nervous system to alter affect and behavior, is tightly regulated by the prefrontal cortex (PFC) (Cools & Arnsten, 2022). The PFC plays a dynamic role in how sensory information is perceived and provides our baseline for abstract thought processes. The PFC generates executive functions such as working memory, attention, inhibition/cognitive control, and reasoning/decision-making (Friedman & Robbins, 2022). Interestingly, the PFC is highly sensitive to subtle alterations of its neurochemical environment. Research has demonstrated that small electrical stimuli delivered via TMS and tES can alter hormonal regulation (Mehrsafar et al., 2020), neurotransmitter activity and synthesis (Alvarez-Alvarado et al., 2021; Cuypers & Marsman, 2021; Heimrath et al., 2020; Premoli et al., 2014), general nervous system activity (Fertonani & Miniussi, 2017; Rodrigues et al., 2021; Schestatsky et al., 2013; Stagg et al., 2018), and behavior (Gebodh et al., 2021; Liu et al., 2018; Schestatsky et al., 2013; Y. Wang et al., 2020). However, the precise mechanisms underlying the aforementioned effects remain to be elucidated.

### **TMS**

TMS and repetitive transcranial magnetic stimulation (rTMS) have been proven to be a safe, minimally invasive methodology to produce cortical stimulation by passing an electric current through a magnetic coil to create a brief, yet high-intensity magnetic field with both excitatory and inhibitory capabilities (Hallett, 2007). Although the physiological mechanisms underlying the effects of TMS and rTMS remain unknown, a significant body of research has demonstrated the functional application of these stimulation methods to enhance cognitive function and performance (Bagherzadeh et al., 2016; Curtin et al., 2019; Klimesch et al., 2003; Klomjai et al., 2015; Luber & Lisanby, 2014). Although proven to be effective to enhance cognitive performance, proper implementation of TMS requires specialized training. Furthermore, the devices are relatively large (which may impose limitations for use in the field) and TMS has been associated with a larger side effect profile compared to other minimally invasive neuromodulation techniques (Rossi et al., 2021).

### **tES**

tES has been shown to have the capability to successfully modulate neuronal membrane potentials within many different areas of the cerebral cortex. tES can be classified into three subcategories: transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS) (Paulus, 2011). tDCS involves the utilization of a weak electrical current via the use of two electrodes, a positive anode, and a negative cathode, which are placed on the participant's scalp. Electrical current flows between the two electrodes to make a complete circuit. The positive anodal current is thought to facilitate behavioral responses corresponding to the cortical region at which it is placed. In contrast, the negative cathodal current is thought to produce a behavioral inhibition response (Thair et al., 2017). tACS utilizes alternating electrical currents, which produce a sinusoidal waveform to change between positive and negative voltage every half-cycle. Hence, the current flow is different than that of tDCS, as the current is not flowing in only one direction but alternating between the anodal and cathodal electrodes in the first half of the cycle and then moves in the reverse direction during the second half of the cycle (Elyamany et al., 2021). tRNS

involves the utilization of a randomly fluctuating current (between .1 and 640 hertz [Hz]) over a large frequency spectrum to produce cortical stimulation (Nikolin et al., 2020).

## Methods

Literature searches, limited to academic journals, were conducted using PubMed and EBSCO databases in January and February 2022.

*Table 1. Keywords Included in Literature Search*

<b>Interventions</b>	<b>Cognitive Functions</b>
tDCS	Cognition
TMS	Memory
tES	Attention
	Decision-making
	Judgment
	Spatial Abilities
	Visual Perception

## Eligibility

The inclusion criteria followed that of our previous literature review (Kelley et al., 2019) and were intentionally conservative to increase homogeneity and capture a high level of study quality (Table 2).

*Table 2. Study Inclusion and Exclusion Criteria*

<b>Criteria</b>	<b>Included</b>	<b>Excluded</b>
Date Published	2018 – 2022	Prior to 2018
Study Design	Within-subjects, sham-controlled	Non-random or non-counterbalanced stimulation order
	Between-subjects, with control group	Non-random assignment*
Test Population	Age: 18 to 50 years	Age: Under 18 years, over 50 years
	Race: Any	Race: None
	Gender: Males and females	Gender: None
	Health status: Healthy	Health status: Unhealthy or abnormal
	Nationality: Any	Nationality: None
Intervention	tDCS (including, high definition [HD]-tDCS, tRNS, tACS) TMS (including, rTMS) tES	
Study Condition	Normal	Sleep deprived
Language	English	Non-English
Outcome Measures	Valid and reliable	Not validated
	Neuropsychological tests of cognition	Not tested for reliability
		Not neuropsychological tests of cognition

Measures of memory, attention, spatial reasoning/abilities, math reasoning, decision-making, visual perception, and judgment

Measures of mood, personality constructs, language, imaging studies

*Note.* Several studies met the majority of our search criteria but were excluded if the purpose was not to examine enhancement (e.g., testing whether cathodal tDCS hampered performance) and the officially accepted paper was not accessible through our search parameters (Koo et al., 2018). \*One study (Au et al., 2021) used pseudorandom assignment, but was included in the final results.

### Procedure

The analysis was carried out according to the guidelines for systematic reviews and meta-analyses previously outlined (Littell et al., 2008) and (Lipsy & Wilson 2001).

The research team first searched the databases using combinations of the predetermined keywords (e.g., intervention method AND cognitive function). Next, titles and abstracts were reviewed to determine further eligibility. Following this step, full texts were retrieved and reviewed for eligibility. The review process and results are provided in Table 3.

*Table 3.* Literature Search and Review Results

Search Results (February 2022)	1410
Duplicated citations	326
Judged irrelevant or ineligible by title and abstract	974
Full-texts retrieved	110
Included studies	97

Prior to extracting study details, articles were categorized based on stimulation type. The categories included: tDCS ( $n = 51$ ), HD-tDCS ( $n = 8$ ), tACS ( $n = 15$ ), tRNS ( $n = 7$ ), rTMS ( $n = 3$ ), TMS ( $n = 9$ ), and a combination of stimulation approaches ( $n = 4$ ).

### Results

The results are summarized by stimulation type, tDCS [including HD-tDCS], tACS, tRNS, rTMS, and TMS, as well as combination studies where multiple stimulation techniques were used. Given the large number of tDCS studies, these results were further summarized by targeted cognitive function.

#### tDCS

Of the 59 studies using tDCS (including HD-tDCS), 26 studies were excluded during the extraction phase, resulting in 33 studies included in this review. Results are reported below by targeted function. Note that some studies targeted multiple cognitive functions and thus are reported in multiple locations.

## Working Memory.

Eleven studies targeted working memory, summarized in Table 4 below. Of these 11 studies, only six resulted in significant findings for tDCS enhancing working memory. Of these six, four studies found improvement with active tDCS stimulation compared to sham stimulation (Karthikeyan et al., 2021; Luque-Casado et al., 2019; Zivanovic et al., 2021), and one study found improvement compared to baseline (Assecondi et al., 2021). Hussey and colleagues (2020) had an interesting approach as they combined tDCS and sham stimulation with either acute aerobic exercise or absence thereof, resulting in four groups (exercise active stimulation, exercise sham, seated active stimulation, and seated sham) and conducted a statistical comparison between the groups to assess effects (Hussey et al., 2020). Results from this study suggest that exercise and state of health may contribute to the enhancement effects of tDCS and warrant further investigation in different subpopulations.

Working memory tasks included the versions of the *n*-back task (refer to Table 4 for specific versions) (Assecondi et al., 2021; Au et al., 2021; Boudewyn et al., 2019; Hussey et al., 2020; Ikeda et al., 2019; Karthikeyan et al., 2021; Zhu et al., 2020; Zivanovic et al., 2021), digit span memory tasks (Luque-Casado et al., 2019; Wang et al., 2018), and interference digit span task (Marko & Riecansky, 2021). Similar to previous reviews, the studies reviewed here included a variety of stimulation parameters. Eight studies specifically targeted the left dorsolateral prefrontal cortex (IDL PFC) (Boudewyn et al., 2019; Hussey et al., 2020; Ikeda et al., 2019; Karthikeyan et al., 2021; Luque-Casado et al., 2019; Marko & Riecansky, 2021; Wang et al., 2018; Zivanovic et al., 2021). Of these eight, three found improved performance using both online ( $n = 1$ ) (Karthikeyan et al., 2021) and offline ( $n = 2$ ) (Luque-Casado et al., 2019; Zivanovic et al., 2021) stimulation parameters. The duration of stimulation among these three studies ranged from 10 to 20 minutes (min), with intensities of 1 milli-amp (mA), 1.5 mA, and 1.8 mA. Moreover, Luque-Casado et al. (2019) only found effects of tDCS after performing a cluster analysis where “responders” were identified. In this study, responders were identified as a subgroup of participants who experienced an increase in motor evoked potentials in response to anodal tDCS. The “responders” improved performance in the digit span backwards task compared to sham stimulation, but not to baseline performance.

Two studies (Zhu et al., 2020; Zivanovic et al., 2021) targeted the posterior parietal cortex (PPC). Zivanovic et al. (2021) targeted both the left and right PPC with tDCS applied at 1.8 mA and 1.5 mA across three experiments, for a duration of 20 minutes. Performance improvements were found with stimulation to the left PPC, as well the IDL PFC, with large effect sizes reported ( $\eta_p^2 > .14$ ). Zhu et al. (2020) applied tDCS at 1.5 mA for 20 minutes, offline, and also found improved performance with the left PPC targeted. Zhu et al. (2020) also compared low performers to high performers and found that those identified as “low performers” at baseline had greater performance improvement ( $\eta_p^2 = .09$ ). Additionally, “high performers” had no difference in performance on some of the tasks between active stimulation and sham stimulation. Low performers, previously classified by Tseng and colleagues, were defined as participants who have poor change detection performance which may be a direct result of not being able to produce significant neurological amplitudes that are associated with certain cognitive responses. These participants were not able to elevate visual attention and memory access processes in their PPC as efficiently as their “high performer” counterparts (Tseng et al., 2012).

Three studies included the right DLPFC (rDLPRC) as the targeted region (Asseconi et al., 2021; Au et al., 2021; Zivanovic et al., 2021). Zivanovic et al. (2021) used 1.8 mA, applied offline for 20 minutes, and found improved performance. Au and colleagues used 2 mA, offline and online across four groups, for 25 minutes, and found no performance improvements due to the stimulation (Au et al., 2021). Finally, Asseconi et al. (2021) also used 2 mA, applied online for 20 minutes, and found performance improvements. Importantly, Asseconi et al. (2021) compared individuals with low working memory capacity to those with high working memory capacity. Individuals were classified in either low- or high-capacity groups based on their working memory capacity, specifically, their composite memory scores which were obtained from the results of the *n*-back tasks completed at baseline. The authors found those with low capacity who received active stimulation and strategy training improved performance in the *n*-back task (Cohen's *d* > .9). Alternatively, those with high capacity only improved performance when receiving sham stimulation and strategy training (Cohen's *d* > .9). Finally, Zhu et al. (2020) also targeted the left inferior frontal gyrus (lIFG). tDCS was applied at 1.5 mA for 20 minutes offline. Performance improvements, compared to baseline, were found, similar to their findings when the left PPC was targeted, including the same pattern for low versus high performers ( $\eta_p^2 > .14$ ).

Table 4. tDCS Working Memory Studies

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Karhikeyan et al., 2021	Within-subjects 3 Conditions 1. Control 2. Anodal 3. Sham	32 16 males (M) 26 years (yrs.)	Not mentioned	Single	F3 (anode)	Fp2 (cathode)	1 mA/10 minutes (min)  Online (started 20 min into task)	Visuospatial 2-back task	Anodal stimulation improved accuracy, sensitivity, and specificity of responses	None
Ikeda et al., 2019	Within-subjects 2 Conditions 1. tDCS-Sham 2. Sham-tDCS	24 M 21.3 yrs. (1.26)	All right-handed	Double	F3 (anode)	F4 (cathode)	2 mA/26 min total (2x, 13 min)  Offline	n-back task	No significant effects found	None
Hussey et al., 2020	Between-subjects 4 Groups 1. Exercise and stimulation 2. Exercise and sham 3. Seated and stimulation 4. Seated and sham	4 groups. 24 per group 96 total 36 M  1. 22.58 yrs. 2. 22.21 yrs. 3. 23.54 yrs. 4. 20.83 yrs.	All right-handed; excluded if had health issues preventing strenuous exercise due to exercise condition	Not mentioned	F3 (anode, array of 5 circular electrodes)	Right bicep (cathode, array of 5 circular electrodes)	2 mA/30 min  Online for 2 tasks, offline for 1 task	n-back task	Group who received tDCS adopted a conservative response strategy under 4-back condition while less conservative under 2-back condition	None
Lucque-Casado et al., 2019	Within-subjects 2 Conditions 1. Anodal tDCS 2. Sham tDCS	30 23 M 21.6 yrs. (2.7)	Caucasian	Single	Left DLPFC, localized using guided procedure (anode)	Contralateral supraorbital area (cathode)	1.5 mA/15 min  Offline	Digit span backward memory task	No effects found at group level; cluster analysis identifying “responders;” “responders” improved performance compared to sham, but not compared to baseline	None
Wang et al., 2018	Mixed 3 Conditions	23 total	All right-handed	Double	F3 (anode)	Right supraorbit	2 mA	Forward and backward	No effects found for either group	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
	1. 10 min anodal tDCS 2. 20 min anodal tDCS 3. Sham  2 Groups 1. Online 2. Offline	1. 13 8 M 22.7 yrs. (1.8)  2. 8 4 M 22.3 yrs. (1.9)  <i>Withdrawals not indicated</i>				al (cathode)	1. 10 & 20 min; Offline 2. 20 min; Online	s digit span memory tasks		
Asseconi et al., 2021	Between-subjects  4 Groups 1. Active tDCS and working memory (WM) strategy 2. Active tDCS and no strategy 3. Sham and WM strategy 4. Sham and no strategy	65 total 27 M 20.6 yrs. (3.8)	All right-handed	Single	F4 (anode)	Fp1 (cathode)	2 mA/20 min  Online	Adaptive spatial <i>n</i> -back task  Fixed-load visual <i>n</i> -back task	Participants with low WM capacity who received active stimulation and strategy, performance improved ; participants with high WM capacity performance improved with sham stimulation and strategy	None
Zhu et al., 2020	Between-subjects  3 Groups 1. L PPC 2. L IFG 3. Sham	17 each group 51 total 20 M 18.9 yrs. (1.4)	N/A	Single	Left IFG group anode located between F7-Cz & T3-Fz; Left PPC group anode P3	Contralateral cheek (cathode)	1.5 mA/20 min  Offline	Auditory and Visual 3-back	Stimulation to left IFG and left PPC decreased reaction times (RTs) from pre-stimulation to post-stimulation; both groups had decreased RTs post-stimulation compared to sham; analysis	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Au et al., 2021 <sup>±</sup>	Mixed 4 Groups 1. Offline pre-training 2. Online 3. Offline post-training 4. Sham	82 total 1. 19 (7 M) 2. 21 (7 M) 3. 22 (7 M) 4. 20 (8 M)  20.40 yrs. (1.68)	All right-handed	Single	F4 (anode)	Fp1 (cathode)	2 mA/25 min  1. Offline 2. Online 3. Offline 4. Sham	<i>n</i> - back	of low performers versus high performers found  Group who received tDCS post-training performed worse than the sham group; found stronger performance gains after the weekday relative to weekday in post-training group only ( $\eta_p^2 = 0.058$ )	1 month follow-up; no group differences remained
Boudewyn et al., 2019	Within-subjects	20 3 M 21 yrs.	N/A	Single	F3 (anode)	Fp2 (cathode)	2 mA/25 min  Online	<i>n</i> - back	Lower error rates following active stimulation were significantly correlated with higher hit rates on the N-back task that was completed concurrently with tDCS.	None
Zivanovic et al., 2021	Within-subjects across 3 experiments  1. Offline IDLPFC, left parietal prefrontal cortex (IPPC), and sham	1. 21 total 9 M 26.76 yrs. (4.83)  2. 21 total 9 M	All right-handed	Single	1. F3, P3 (anode) 2. F4, P4 (anode) 3. F3, P3 (anode)	Contralateral cheek (cathode) for all experiments	1 & 2. 1.8 mA; Offline (online during non-exp. task) 3. 1.5 mA; Online	Verbal 3-back and Spatial 3-back	1. Found improved spatial hit rate and effect size for L PPC, but shorter RTs for both tasks for L DLPFC	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
	2. Offline right dorsolateral prefrontal cortex (1 DLPFC), right posterior parietal cortex (RPPC), and sham 3. Online IDLPFC, IPPC, and sham	26.43 yrs. (4.78) 3. 21 total 10 M 24.90 yrs. (2.49)					All experiments 20 min		2. Found improved verbal hits and d' for R DLPFC, and shorter RTs for both tasks 3. No effects	
Marko et al., 2021	Between-subjects 3 Groups 1. PFC 2. Temporal parietal cortex (TPC) (control) 3. Sham (control)	121 total 49 M 23.1 yrs. (3.8)	All right-handed	Double	1. Between F3 & AF3 (anode) 2. Between T8 & P6 (anode)	Between T7 & P5 (cathode)	2 mA/25 min Online	Interference digit span task	PFC stimulation increased scores during and post-stimulation compared to baseline ( $\eta_p^2 = 0.077$ )	None

## **Attention.**

Five studies examined various aspects of attention, summarized in Table 5 below. Three of the studies used a within-subjects study design (Lewald, 2019; Lo et al., 2019; Zink et al., 2020) and two studies used a mixed-model design (Hanenberg et al., 2019; Lu, Liu, et al., 2020) and they all reported improved attentional performance with application of tDCS. Four studies used a similar study design as they counterbalanced participants to receive either sham then stimulation or stimulation then sham and then analyzed the performance differences between the conditions in each individual (Hanenberg et al., 2019; Lewald, 2019; Lo et al., 2019; Zink et al., 2020). The remaining study included in this section simply compared tDCS to sham (groups did not receive both conditions) (Lu, Liu, et al., 2020) The attention tasks utilized varied from auditory attention tasks (e.g., dichotic listening, spatial auditory attention) to vigilance tasks (e.g., Mackworth Clock Task). These five studies targeted different regions: frontal-parietal network (Zink et al., 2020), right posterior parietal cortex (Lo et al., 2019), temporal cortices (Lewald, 2019), left DLPFC (Lu, Liu, et al., 2020), and posterior superior temporal gyrus (Hanenberg et al., 2019). Additionally, different stimulation parameters were used across these studies. Stimulation intensities included 1 mA ( $n = 2$ ), 1.5 mA ( $n = 2$ ), and 2 mA ( $n = 1$ ). Duration of stimulation included 16 min ( $n = 1$ ), 20 min ( $n = 3$ ), and 32 min ( $n = 1$ ). Stimulation was applied offline ( $n = 3$ ) and online ( $n = 1$ ).

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Table 5. tDCS Attention Studies

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Zink et al., 2020	Within-subjects  2 Conditions 1. Sham first 2. Stimulation first	30 13 M 25.7 yrs. (3.4)	N/A	Not mentioned	Center of Fz-T4 & Cz-F8 (anode)	Left deltoid (cathode)	2 mA/20 min  Offline	Focused dichotic listening task	Application of stimulation resulted in improved performance only in conditions requiring high attentional control, and only when attention was focused to left ear ( $\eta_p^2 = 0.16$ )	None
Lewald, 2019	Within-subjects  2 Conditions 1. Active stimulation then sham 2. Sham then active stimulation	24 12 M 22.6 yrs.	All right-handed and fluent German speakers	Single	Between C5 & T7, and C6 & T8 (2 anodes)	Shoulders (2 cathodes)	1 mA/32 min  Timing of stimulation not specified	Spatial auditory task	Application of stimulation resulted in better performance compared to sham stimulation; those who received active stimulation first had greater improvements compared to those who received sham first in the first session, whereas there was no difference in the second session	None
Lo et al., 2019	Within-subjects  2 Conditions 1. First visit sham stimulation and second visit anodal stimulation 2. First visit anodal stimulation and second visit sham stimulation	26 13 M 24.4 yrs. (4)	All right-handed	Not mentioned	P4 (anode)	Left supraorbital bridge	1.5 mA/20 min  Offline	Attention Network Test	Orienting attention improved with active tDCS	None

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Hanenberg et al., 2019	Within-subjects  3 Conditions 1. Anodal 2. Cathodal 3. Sham  2 Groups Younger versus older (reporting younger only here)	20 10 M 24.3 yrs. (0.6)	All right-handed; all tested within normal for audiometric thresholds	Single	Btw C6 and T8 (evaluated anode & cathode separately)	Left Shoulder	1 mA/16 min Online	Auditory selective spatial attention task	Accuracy improved for targets located on the right vs. left hemispace after anodal stimulation ( $\eta_p^2 = 0.24$ )	None
Lu, Lui, et al., 2020	Mixed  2 Groups 1. Active 2. Sham	49 20 M 21.15 yrs. (1.78)	N/A	Not mentioned	F3 (single anode)	AF3, F1, F5, FC3 (4 cathodes)	1.5 mA/20 min Offline	Attention network test  Color word Stroop test	Main effect of time for executive RT, neutral RT, congruent and incongruent RT. Interaction for time and group for all conditions	None

## Memory and Learning.

Four of the tDCS studies focused on memory and/or learning. Two studies counterbalanced sham and stimulation conditions within participants and compared differences between the two conditions (Bjekic et al., 2019; Cellini et al., 2019). The other two studies included in this section compared active tDCS stimulation to sham control groups (Bystad et al., 2020; Vulic et al., 2021). The tasks to assess memory and learning ranged from fact learning to face cued word recall. All studies included in this section used a within-subjects study design. One study targeted the bilateral prefrontal cortex offline (Cellini et al., 2019), two targeted the lateral posterior cortex (Bjekic et al., 2019) in an online/offline fashion and (Vulic et al., 2021) in an online fashion) and one targeted the temporal lobe offline (Bystad et al., 2020). Different stimulation parameters were used across all studies (see Table 6 below for details). It is important to note that Vulic and colleagues found differences in responses between participants in theta-oscillatory and constant tDCS conditions. The authors simply suggest that these two stimulation conditions have different modes of action and further investigation is warranted to elucidate their exact modes of action. Interestingly, all studies except for Bystad et al. (2020), found enhanced learning and memory effects from tDCS stimulation. Although studies mentioned by authors have suggested that memory improvement from tDCS could potentially be due to enhanced excitability in the temporal cortex (Boggio et al., 2012; Ferrucci et al., 2008), the effects were found in a clinical population with Alzheimer's disease. The exact mechanism as to how these effects occurred is still not known and may be different in a non-clinical, healthy population. All studies included in this section reported large effect sizes ( $\eta_p^2 > .14$ ).

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Table 6. tDCS Memory and Learning Studies

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Cellini et al., 2019	Within-subjects  2 Conditions 1. Sham then Sleep-based short duration repetitive (SDR)-tES 2. SDR-tES then sham	17 11 M 32.24 yrs. (8.06)	Uneven sex distribution due to high attrition (30) but no sex differences found	Not mentioned	Two electrodes placed anterior and posterior to bilateral frontal positions F3 and F4 and at the mastoids	Left shoulder blade	SDR-tDCS – 4 seconds of 0.75 Hz oscillating current with maximum of 2 mA  tDCS current was intermittently applied based on real-time detection of slow oscillations during 90 min nap  Offline	Fact learning task	Greater memory retention for the SDR-tDCS condition compared to sham across two tests	Yes, delayed test 48 hours. Greater memory retention with SDR-tDCS compared to sham
Bystad et al., 2020	Mixed (Within-subjects for this review)  2 Conditions 1. Active stimulation 2. Sham	20 7 M 22 yrs.	N/A	Double	T3 (anode)	Fp2 (cathode)	2 mA/30 min across 3 sessions (30 min between sessions), 2 visits  Offline	California Verbal Learning Test	No effects found for memory and learning but did find enhancement between active and sham tDCS in executive function	None
Bjekic et al., 2019	Within-subjects  2 conditions 1. Sham/anodal 2. Anodal/sham	40 18 M 21-35 yrs.	All right-handed	Double	P3 (anode)	Contralateral cheek (cathode)	1.5 mA/20 min  Online during an unrelated computer game/offline during task	1. Face Cued Word Recall Task 2. Verbal Fluency Task	1. Higher recall of correct face-word pairs with active stimulation ( $\eta_p^2 = 0.20$ ) 2. No effects	Yes. Participants completed follow-up tests 1 and 5 days after each tDCS condition. Effects persisted at 5 days.
Vulic et al., 2021	Within-subjects  3 Conditions 1. tDCS 2. theta-oscillating (ot)-tDCS 3. Sham	36 18 M 23.78 yrs. (1.83)	All right-handed and naive to tDCS	Single	Anode was placed at P3	Return electrode was placed over contralateral cheek	20-minute blocks of stimulation. 1.5 mA for anodal tDCS and ot-DCS followed the same parameters except the current was oscillating (+/- .01 mA) around the 1.5 mA in the frequency	Face Cued Word Recall Task	Higher recall with ot-tDCS compared to sham ( $\eta_p^2 = .31$ ) and anodal tDCS compared to sham ( $\eta_p^2 = .32$ )	Yes. Participants completed follow-up tests 1 and 5 days after each tDCS condition. Effects of

<b>Authors</b>	<b>Study Design &amp; Assignment Details</b>	<b>Gender &amp; Mean Age (sd)</b>	<b>Additional Sample Details</b>	<b>Blinded</b>	<b>Active Location</b>	<b>Reference Location</b>	<b>Stimulation Description (Intensity, duration, timing [online/offline])</b>	<b>Task</b>	<b>Effects</b>	<b>Follow-up</b>
							of average human theta rhythm (5 Hz) Online			anodal tDCS persisted.

### **Reasoning and Decision-making.**

Two studies evaluated the effect of tDCS on reasoning/decision-making. Both studies compared tDCS to sham conditions (Edgcumbe et al., 2019; Wertheim et al., 2020). Edgcumbe and colleagues applied tDCS stimulation both the right and left DLPFC (1.5 mA/20 minutes) in an offline fashion while Wertheim and colleagues applied tDCS stimulation to the lDLPFC and right posterior parietal cortex (rPPC) (1 mA/20 minutes) in an online fashion during non-target tasks and offline during the target tasks. Both studies found no improvement with reasoning or decision-making tasks for tDCS applied to the lDLPFC. Interestingly, improvements were found using tDCS applied to the rDLPFC (Edgcumbe et al., 2019) and rPPC (Wertheim et al., 2020) ( $\eta_p^2 > .14$ ).

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Table 7. tDCS Reasoning/Decision-making Studies

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task	Effects	Follow-up
Edgcumbe et al., 2019	Between-subjects  3 groups consisting of different stimulation locations, these are detailed in the active and reference location columns	54 total 24.63 yrs.  1. 18 7 M 25.28 yrs. (4.26) 2. 18 9 M 23.78 yrs. (4.63) 3. 18 9 M 24.83 yrs. (4.60)	All participants were naïve to tDCS	Not mentioned	1. rDLPFC, F4 (anode) 2. IDLPFC, F3 (anode) 3. Sham right DLPFC return electrode over contralateral location	1. rDLPFC, F3 (cathode) 2. IDLPFC, F4 (cathode) 3. Sham left DLPFC return electrode over contralateral location	1.5 mA/20 min  Offline	Belief Bias Syllogisms  Cognitive Reflection Test  Representativeness Heuristic Task	Analytical judgment ( $\eta_p^2 = 0.15$ ) and decision making ( $\eta_p^2 = 0.11$ ) were improved with right tDCS, whereas logic index score was worsened with left tDCS ( $\eta_p^2 = 0.12$ )	None
Wertheim et al., 2020	Mixed  3 Conditions 1. rPPC 2. IDLPFC 3. Sham	51 total 14 M 21.80 yrs. (2.7)  17 in each group	All right-handed	Single	1. rPPC, P4 (anode) 2. IDLPFC, F3 (anode) 3. Sham over either region	Contralateral upper arm (cathode)	1 mA/20 min  Online during non-target tasks/Offline during target task	Spatial Reasoning Problems	Stimulation to right PPC resulted in more correct/plausible responses for deductive tasks and indeterminate deductive reasoning	None

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## **Inhibition, Cognitive Control, and Executive Functions.**

Ten studies evaluated the effects of tDCS on either inhibition, cognitive control, and/or executive function. Eight studies compared tDCS to sham stimulation conditions (Bashir et al., 2022; Dubreuil-Vall et al., 2018; Friehs & Frings, 2018; Li et al., 2019; Lu, Gong, et al., 2020; Mattavelli et al., 2022; Thomas et al., 2021; Weller et al., 2020). One study used a counterbalanced design where all participants received tDCS and sham stimulation and comparisons were made between the two conditions (Angius et al., 2019). Dousset and colleagues had multiple conditions and made comparisons across five different groups (training only, tDCS stimulation [two locations], sham stimulation, no training or stimulation) (Dousset et al., 2021). A variety of tasks, electrode placements, and stimulation conditions were used across the studies with some similarities between studies. For example, three studies used the stop signal task (Bashir et al., 2022; Friehs & Frings, 2018; Li et al., 2019), two studies used the Stroop task (Angius et al., 2019; Lu, Gong, et al., 2020), four studies used the flanker task (Dubreuil-Vall et al., 2019; Mattavelli et al., 2022; Thomas et al., 2021; Weller et al., 2020). Along with the utilization of similar tasks, several studies investigated the potential for tDCS enhancement by placing electrodes in the same anatomical region. The majority of studies within this category targeted the DLPFC and were able to find significant effects (see table below) (Angius et al., 2019; Dousset et al., 2021; Dubreuil-Vall et al., 2019; Friehs & Frings, 2018; Lu, Liu, et al., 2020; Thomas et al., 2021; Weller et al., 2020). Other regions investigated included the pars triangularis of the right inferior frontal gyrus (rIFG) (Dousset et al., 2021; Li et al., 2019), motor cortex (Bashir et al., 2022) and dorsal anterior cingulate cortex (dACC) (Mattavelli et al., 2022) albeit with different stimulation settings and conditions (online versus offline). Interestingly, all of the studies reviewed and classified in the table below demonstrated significant positive findings in support of tDCS in some aspect of cognitive enhancement. Additionally, all studies cited were able to find large effects for stimulation and sham comparisons ( $\eta_p^2 > .14$ ). Details for all the tasks, electrode placements, and stimulation conditions used in each study can be found in Table 8 below.

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Table 8. tDCS Cognitive Control/Inhibition/Executive Functions

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing [online/offline]</i> )	Task	Effects	Follow-up
Li et al., 2019	Within-subjects 3 Conditions 1. Anodal 2. Cathodal 3. Sham	26 13 M 38 yrs. (15.5)	Not mentioned	Not mentioned	F8 (anode, cathode)	Right shoulder (cathode, anode)	2 mA/ approximately 12 min total  Online	Stop Signal Task	Anodal stimulation produced faster RTs and delayed time to produce incorrect responses	None
Weller et al., 2020	Between-subjects 9 Groups 1 sham, remainder had different stimulation parameters (see stimulation description column)	162 total 35 M 23.20 yrs. (3.98)	All right-handed	Single	Groups 1 & 3, F3 (anode) Groups 2 & 4, F4 (anode) Groups 5 & 7, F3 (cathode) Groups 6 & 8, F4 (cathode)	Lateral deltoid muscle, all groups	Groups 1, 2, 5 & 6: 1 mA Groups 3, 4, 7 & 8: 2 mA  Online, all groups, 19 min, 10 s	Paced Auditory Serial Addition Task (PASAT)  Flanker Task	For PASAT, improved no. correct trials with anodal 1 mA compared to sham; when examining 1 mA anodal, performance improved with application to left PFC  No effects found on Flanker Task	For PASAT, 1 mA anodal group's performance effects remained post-training and 3-month follow-up; 1 mA to left improved post-training, but not at follow-up
Friehs & Frings, 2018	Mixed 2 Conditions 1. Active stimulation 2. Sham  Pre- and post-test	56 total 24.82 yrs. (3.78)  1. 28 10 M 25.25 yrs. (4.01) 2. 28 11 M 24.39 yrs. (3.50)	All right-handed	Single	F4 (anode)	Left deltoid (cathode)	0.5 mA/20 min  Online	Stop Signal Task (SST)	More efficient response inhibition (measured by stop signal delay RT) for anodal stimulation ( $\eta_p^2 = 0.12$ ) and fewer errors of omission ( $\eta_p^2 = 0.01$ )	None
Bashir et al., 2022	Between-subjects 2 Groups 1. Sham 2. Active	30 total (all males) 24.3 yrs. (5.03)	All right-handed	Double	C3 (anode)	AF8 (cathode)	2 mA/20 min  Timing not reported	Stop Signal Task	Stop signal task performance and response times improved from pre- to post-stimulation	None
Angius et al.,	Within-subjects	12 9 M	Performed regular aerobic exercise	Double	F3 (anode)	Fp2 (cathode)	2 mA/30 min	Stroop Task	Fewer errors following tDCS	None

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing [online/offline]</i> )	Task	Effects	Follow-up
2019	2 Conditions 1. tDCS/sham 2. Sham/tDCS	23.3 yrs. (3.0)	training (3-5 hours per week)				Offline		for incongruent words	
Dousset et al., 2021	Between-subjects  5 Groups 1. Training only 2. (Right inferior frontal gyrus) rIFG stimulation & training 3. rDLPFC stimulation & training 4. Sham stimulation & training 5. No training or stimulation	127 total  1. 26 9 M 23.3 yrs. (2.4) 2. 24 10 M 27.9 yrs. (2.5) 3. 24 13 M 22.5 yrs. (2.7) 4. 27 11 M 22.3 yrs. (2.7) 5. 26 8 M 22.5 yrs. (2.7)	Not mentioned	Single	rIFG (group 2), F8 (anode)  rDLPFC (group 3), F4 (anode)	1. rIFG 2. sub-occipital region on upper cervical spine (cathode)  3.rDLPFC, F3 (cathode)	2 mA/20 min both groups  Online during training / offline during task	Go – No – Go Task	Commission errors increased for group 2 from baseline to first session, whereas there was an overall decrease in commission errors for group 3 ( $\eta_p^2 = 0.088$ )	One week follow up, overall decrease in commission errors for group 3
Dubreuil-Vall et al., 2019	Within-subjects  2 Conditions 1. Sham vs. left active 2. Sham vs. right active	18 9 M 32.6 yrs. (15.6)	Not mentioned	Double	F4 (right)/F3 (left) (anode both)	Fp1 (right) / Fp2 (left) (cathode both)	2 mA/30 min  Offline	Eriksen Flanker Task	Left stimulation compared to sham and right resulted in decreased RTs for incongruent trials	None
Lu, Gong, et al., 2021	Mixed  2 Conditions 1. Active 2. Sham  3 Phases of experiments: pre-intervention (baseline), HD-tDCS sessions, and post-intervention	43 24 M 20.91 yrs. (1.95)	Not mentioned	Single	F3 (single anode)	AF3, F1, F5, FC3 (4 cathodes)	1.5 mA/20 min  Timing unclear	Stroop Task  Shifting attention task (SAT) Score  2-back score	Lowest Stroop effect found for sham (main effect of time)  For SAT score, main effect of time; interaction group x time (active group improved after all sessions compared to baseline, sham only at post-tDCS)	None  For 2-back, main

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing</i> [online/offline])	Task	Effects	Follow-up
Thomas et al., 2021	Within-subjects 5 experiments with different conditions 1. Anodal vs. sham tDCS 2. Cathodal vs. sham tDCS 3. Aerobic exercise (AE) vs. active control 4. Anodal vs. sham tDCS during AE 5. Cathodal vs. sham tDCS during AE	1. 21 10 M 25.7 yrs. (2.2) 2. 24 12 M 25.2 yrs. (1.7) 3. 24 15 M 25 yrs. (2.5) 4. 22 11 M 25.5 yrs. (2.1) 5. 24 15 M 24.9 yrs. (1.5)	Not mentioned	Double	F3, FC1, Fz, FC5, AF7 (4x1 ring) cathode and anode	Not mentioned	1 mA (anode)/-1 mA (cathode) for 20 min  Online (stimulated 15 min offline, 5 min online)	Flanker	effect of time (both groups improved) Exp.5 decreased accuracy with cathode tDCS + exercise from pre-to-post compared to sham with exercise	None
Mataveli et al., 2022	Within-subjects 3 Conditions 1. Active anodal 2. Active cathodal 3. Sham HD-tDCS	20 10 M 23.5 yrs. (1.9)	Not mentioned	Single	Fz-F1-FCz (anodes)	PO9-O9-O10	1 mA/session for 20 minutes  Offline	Flanker task  Loss- and risk-aversion tasks	Flanker-Cathodal dorsal anterior cingulate cortex (dACC) stimulation resulted in a significant decrease of the Flanker "conflict effect." There was a significant interaction between stimulation type and flanker condition  For the loss- and risk-aversion tasks, cathodal dACC stimulation was associated with a significantly increased degree of loss and risk	None

<b>Authors</b>	<b>Study Design &amp; Assignment Details</b>	<b>Gender &amp; Mean Age (<i>sd</i>)</b>	<b>Additional Sample Details</b>	<b>Blinded</b>	<b>Active Location</b>	<b>Reference Location</b>	<b>Stimulation Description (<i>Intensity, duration, timing</i> [online/offline])</b>	<b>Task</b>	<b>Effects</b>	<b>Follow-up</b>
									aversion	

## tACS

Our initial search parameters yielded eleven studies, three of which met our inclusion criteria. All three studies used different tasks to assess either attention (Yaple & Vakhrushev, 2018) or inhibition/cognitive control/executive function (Battaglini, Ghiani et al., 2020; Loffler et al., 2018). For the specific tasks, Yaple & Vakhrushev (2018) used the attentional blink effect, Battaglini, Ghiani, et al. (2020) used orientation discrimination, and Loffler et al. (2018) used the visual-two choice task. Furthermore, the anatomical regions that were targeted in each of the studies differed as Yaple & Vakhrushev (2018) targeted both the parietal cortex (P4) and the DLPFC (F3), Battaglini and colleagues targeted the parietal cortex (P4), and Loffler et al. (2018) targeted the visual cortex (electrodes were placed at Cz and Oz). All three studies used the online administration of tACS but used different stimulation conditions (see Table 9 below for description). Furthermore, both of the within-subject studies (Battaglini, Ghiani, et al., 2020; Yaple & Vakhrushev, 2018) found that tACS improved cognitive performance from baseline and the between-subject study (Loffler et al., 2018) found a significant improvement in performance in the experimental groups compared to the sham controls. Looking at practicality of the effects, all studies reported large effect sizes ( $\eta_p^2 > .14$ ) for either main or interaction comparisons.

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Table 9. tACS Studies

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
Yaple et al., 2018	Within-subjects  2 Experiments  1. 9 blocks with 3 stimulation protocols (sham, 10 Hz, and 20 Hz) repeated 3 times 2. 15 blocks for each protocol (sham, 10 Hz at 0°, 10 Hz at 180°, 20 Hz at 0° and 20 Hz at 180°)	35 total 1. 18 8M 20.66 yrs. (2.53) 2. 15 2M 20.26 yrs. (2.35)	Not mentioned	Double	1. P4 2. P4 and F3	Right deltoid for both	1. no more than 35 min at 10 and 20 Hz 2. 50 minutes- 10 Hz and 20 Hz at 0 and 180 deg  Online	Attentional blink effect  Attention	1. main effect of lag ( $\eta_p^2=2.14$ ) 2. Main effect of stim. Frequency, 20 Hz at 180 deg increased performance compared to sham, 20 Hz at 0 deg and 10 Hz at 0 deg (no effect size reported)	None
Battaglini, Ghiani et al., 2020	Within-subjects  3 Conditions 1. 10 Hz stim 2. 18 Hz stim 3. Sham	20 10 M 23.05 yrs.	All students from the University of Padova	Single	P4	C4, Pz, O2 and P8	3x45 minute session over 3 days and intensities were 10 and 18 Hz for tACS  Online	Orientation discrimination  Inhibition/cognitive control/executive function	A lower threshold for stimuli presented in the contralateral hemifield when participants were stimulated with right parietal 18-Hz tACS, as compared to 10-Hz tACS and to the sham stimulation on the same cortical area.  Stimulation condition $\eta_p^2 = .08$ ; target position $\eta_p^2 = .06$ ; stimulation condition x target position $\eta_p^2 = .26$	None
Loffler et al., 2018	Between-subjects  2 Groups 1. tACS 2. Sham	24 12 M 25.71 yrs. (2.73) 1 not	All right-handed. Five had participated in one tACS	Not mentioned	Two rubber electrodes were positioned with their	Not mentioned	Two 30 min blocks. Intensity was set to 1 mA. 40 Hz tACS was used  Online	Visual Two-Choice Task  Inhibition/cognitive control/executive function	Increase in reaction times is approx. 19 milliseconds larger for subjects who did	None

<b>Authors</b>	<b>Study Design &amp; Assignment Details</b>	<b>Gender &amp; Mean Age (<i>sd</i>)</b>	<b>Additional Sample Details</b>	<b>Blinded</b>	<b>Active Location</b>	<b>Reference Location</b>	<b>Stimulation Description (<i>Intensity, duration, timing</i> [online/offline])</b>	<b>Task &amp; Cognitive Construct</b>	<b>Effects</b>	<b>Follow- up</b>
		included in analysis	experiment at least two weeks prior		center at Cz and Oz				not receive tACS	

## tRNS

Six studies included in our analysis implemented the use of tRNS in an attempt to either enhance reasoning and decision-making (Sprugnoli et al., 2021), attention (Conto et al., 2021; Tyler et al., 2018) or inhibition/cognitive control/decision-making (Battaglini et al., 2019; Battaglini, Contemori, et al., 2020; Contemori et al., 2019). Five studies found significant effects when comparing the tRNS stimulation to sham (Battaglini et al., 2019; Battaglini, Contemori, et al., 2020; Contemori et al., 2019; Sprugnoli et al., 2021) and sham/control groups (Tyler et al., 2018). Conto and colleagues used a mixed-model study design and compared the stimulation groups to sham and also analyzed whether or not improvements in orientation judgement accuracy occurred in each group from baseline (Conto et al., 2021). Different tasks including the semantic compound remote associates problems (CRA) and visuo-semantic Rebus puzzles (Sprugnoli et al., 2021), temporal order judgements task (Conto et al., 2021; Tyler et al., 2018), contrast detection tasks (Battaglini, Contemori, et al., 2020; Battaglini, Ghiani, et al., 2020), and visual acuity and crowding procedure tasks (Contemori et al., 2019) were used to assess the effectiveness of using tRNS for performance enhancement. Anatomical regions for electrode placement included the right parietal and temporal lobes (Conto et al., 2021; Sprugnoli et al., 2021; Tyler et al., 2018), and the occipital cortex (Battaglini, Contemori, et al., 2020; Battaglini, Ghiani, et al., 2020; Contemori et al., 2019). Participants for all previously mentioned studies received online electric brain stimulation; however, different frequencies and stimulation conditions were used across the studies (see Table 10 below for further details). Regardless of the stimulation location, tasks implemented, and protocol conditions, consistently across all studies, tRNS stimulation enhanced cognitive constructs with large effects ( $\eta_p^2 > .14$ ).

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Table 10. tRNS Studies

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
Sprugnoli et al., 2021	Within-subjects  2 Conditions 1. tRNS 2. Sham	31 14 M 24.4 yrs. (3.8)	All participants were healthy native Italian speakers and 1 was left-handed. All were naïve to the neuro-stimulation techniques	Double	RP- P4 and AT-T8	Not mentioned	3 blocks of 7 minutes each and tRNS was delivered at 100-500 Hz Online	Semantic compound remote associates (CRA) problems  Visuo-semantic Rebus puzzles  Reasoning/decision-making	tRNS over the right temporal area improved both accuracy and reaction times in CRA compared to sham stimulation  No significant findings for Rebus puzzles	None
Tyler et al., 2018	Mixed  2 Experiments with 4 stimulation conditions for each:  1. Behavioral (assigned for participants who did not meet inclusion criteria based on a brain stimulation questionnaire) 2. Human middle temporal area (hMT +) stimulation 3. Parietal stimulation 4. Sham	1. 44 8 M 18-35yrs  2. 28 3 M 18-30yrs	Participants who did not meet standard inclusion criteria based on a brain stimulation survey were assigned to the behavioral group	Not mentioned	PO7/PO8 bilaterally for hMT + and sham  P3/P4 bilaterally for parietal	Not mentioned	20 min/block beginning at block 2 and going through block 5. All participants completed block 6 without stimulation. For hf-tRNS conditions, 1 mA current was applied for 20 minutes with random alternating frequency deliverance between 101 and 640 Hz  Online	Two alternative forced-choice visual Temporal Order Judgements (TOJ) task  Attention	Post-hoc comparisons showed that parietal stimulation alone caused significantly better performance on the TOJ task than the behavioral and sham but not hMT + ( $\eta_p^2 = .157$ )  Simple effects analysis demonstrated that stimulation over parietal cortices significantly affected performance across blocks ( $\eta_p^2 = .257$ )  Participants performed better on trials when the left Gabor	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
Conto et al., 2021	Mixed 3 Stimulation Conditions  1. Parietal group 2. Human middle temporal area (hMT +) stimulation 3. Sham Pre- and post-test measurements	37 17 M 22.8 yrs.	Not mentioned	Not mentioned	PO7/PO8 bilaterally for hMT and sham  P3/P4 bilaterally for parietal	Not mentioned	25 consecutive min per session. For the two active tRNS conditions, 2mA current was applied with random alternating frequency delivered at a high frequency range between 101 and 640 Hz  Online	Two two-alternative forced-choice tasks Temporal order judgements (TOJ) and orientation discrimination (OD) tasks  Attention	was presented before the right ( $\eta_p^2 = .174$ ) Significant main effect on stimulation condition ( $\eta_p^2 = .262$ ) Interaction between stimulation condition and session was found to be highly significant ( $\eta_p^2 = .46$ )  Significant main effect on training days indicating effects of training on performance depended on stimulation condition	None
Battaglin, Contemori, Penzo et al., 2019	Within-subjects 2 Stimulation Conditions 1. tRNS 2. Sham	20 7 M 25 yrs. (3.4)	N/A	Single	Oz	Vertex (Cz)	15 consecutive minutes per session. 1.5 mA current with random alternating frequency delivered at a high frequency range between 100 and 600 Hz  Online	Contrast Detection Task (Gabor Patch)  Inhibition/cognitive control/executive functions	Significant main effect of orientation ( $\eta_p^2 = .678$ ), stimulation ( $\eta_p^2 = .273$ ), spatial frequency ( $\eta_p^2 = .789$ ), orientation x stimulation ( $\eta_p^2 = .279$ ), orientation x stimulation ( $\eta_p^2 = .699$ ) and the three-way interaction of orientation x	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
									stimulation x spatial frequency ( $\eta_p^2 = .199$ )	
									There was a significant difference between diagonal sham and diagonal tRNS and confirmed the significant difference at 12 cycle per degree of visual angle (cpd) for the tRNS group over the sham for the diagonal condition	
Contemori et al., 2019	Mixed  2 Stimulation Conditions 1. tRNS 2. Sham  Each participant underwent 3 phases (pre-test, training, and post-test)	32 15 M 25 yrs.	N/A	Not mentioned	3 centimeters above theinion	Vertex	30 minutes (approx. 5 min per block) 1.5 mA current with a 0-mA offset and maximal current density of .094 mA/cm <sup>2</sup> . This stimulation had an alternating current of random intensity with zero offset and values ranging from -1.5 mA to 1.5 mA with frequencies of fluctuation distributed across a range of 100-640 Hz with zero mean	Visual acuity  Crowding procedure tasks  Inhibition/cognitive control/executive functions	Significant main effect of session and an interaction between group and sessions. After 4 days of training the stimulation group reduced crowding more significantly than the sham group	None
Battaglini, Contemori, Fertonani et al., 2019	Within-subjects  2 stimulation conditions 1. tRNS 2. Sham	68 22 M 24 yrs. (3.0)	N/A	Not Mentioned	Exp 1 & 2: V1/V2 (Oz)  Exp 3 & 4-between Fpz	Vertex for all	Online 12 minutes. tRNS consisted of a randomly alternating current of 1.5 mA with a 0-mA offset, whose frequency ranged from 100 to 600 Hz	Contrast detection (Gabor Patch)  Inhibition/cognitive control/executive	Higher sensitivity as contrast increased for stimulated group. Sensitivity	None

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing</i> [online/offline])	Task & Cognitive Construct	Effects	Follow-up
	Four separate experiments				and nasion		Online	functions	changes (SC) became more positive with increasing contrast at 6 lambda and more negative with increasing contrast at 2 lambda ( $\eta_p^2 = .58$ )  tRNS reduced SC at 6 lambda ( $\eta_p^2 = .25$ )	

## TMS and rTMS

From the initial search which yielded twelve articles focusing on the potential use of TMS for cognitive enhancement, only five satisfied all the parameters of the inclusion criteria and were included in this report. Considering some of the studies included random and intermittent protocols, TMS and rTMS were grouped together and will be referred to as TMS for the remainder of the report. Two studies compared TMS to sham stimulation (Bakulin et al., 2020; Jung & Lambon Ralph, 2021). Wu and colleagues, using a mixed-model study design, found significant effects for intermittent transcranial brain stimulation (iTBS) comparing subjects' baselines to performance after intervention, as well as significant results comparing the intervention condition to sham stimulation (Wu et al., 2021). One rather extensive study utilized eight different stimulation conditions and compared baseline subject performance to multiple intervention stimulation conditions (Momi et al., 2020). Interestingly, Tambini and colleagues (2018) used an active condition rather than a sham TMS to ensure that non-specific effects did not occur and compared this group's results to the active TMS group. Three studies assessed the potential for TMS for working memory enhancement (Bakulin et al., 2020; Tambini et al., 2018; Wu et al., 2021). One study investigated the potential impact of TMS on reasoning and decision-making (Jung & Lambon Ralph, 2021), while another investigated the construct of inhibition/cognitive control/executive function (Momi et al., 2020). Targeted brain regions for TMS included the DLPFC (Bakulin et al., 2020; Wu et al., 2021), the anterior temporal lobe (ATL) (Jung & Lambon Ralph, 2021), the posterior inferior parietal cortex (pIPC) (Tambini et al., 2018), and the left inferior parietal lobule (IPL) and left middle frontal gyrus (IMFG) (Momi et al., 2020). Different tasks, stimulation conditions, and online/offline protocols were used across studies in addition to multiple individual experiments within the studies (see Table 11 below for further details). It is important to note that different delivery protocols of TMS evoked different significant and non-significant outcomes in the studies. For example, Wu and colleagues (2021) discovered that intermittent transcranial brain stimulation promoted a stronger cognitive effect than 20 Hz random transcranial magnetic stimulation intervention and sham control groups. All significant comparisons reported large effect sizes ( $\eta_p^2 > .14$ )

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Table 11. TMS and rTMS Studies

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing</i> [online/offline])	Task & Cognitive Construct	Effects	Follow-up
<i>rTMS Studies</i>										
Wu et al., 2021	Mixed 3 Groups 1. High-frequency repetitive TMS (HF-rTMS) 2. Intermittent theta burst stimulation (iTBS) 3. Sham All groups were evaluated both pre- and post-TMS stimulation	60 34 M 1. iTBS 23.8 yrs. (3.42) 2. 20 Hz group 23.85 yrs. (2.79) 3. Sham 23.5 yrs. (2.99)	Not mentioned	Double	Montreal neurologic institute coordinates (MNI) [-38, 44, 26]	Not mentioned	22.5 minutes, Online  1. For HF-rTMS: delivered at 110% of the participant's resting motor threshold (RMT) via 45 trains of 2-s 20-Hz rTMS (i.e., 40 pulses per train), each of which was followed by intertrain pauses of 28s, for 22.5 min and a total of 1800 pulses. 2. For iTBS: 70% of RMT stimulus was delivered in the forms of bursts at a frequency of 5 Hz, with each burst consisting of three stimuli delivered at a frequency of 50 Hz, a total of 10 bursts, and a total of 600 stimuli per session	Visual spatial <i>n</i> -back  Wisconsin Card Sorting Test  Working memory	Accuracy of the 3-back task was significantly improved in the 1. HF-rTMS compared to sham ( $\eta_p^2 = .129$ ). There was a significant interaction for time and group for effects of iTBS ( $\eta_p^2 = .439$ )  iTBS showed higher effect sizes than 20-Hz rTMS in the ACC of the 3-back task	None
Jung et al., 2020	Within-subjects 4 Conditions 1. 10 Hz 2. 20 Hz 3. iTBS 4. Sham	21 14 M 22 yrs. (3.1)	All right-handed	Not mentioned	MNI [-57, -15, -35]	Occipital lobe	22.5 minutes, timing not reported  1. 10 Hz protocol had 3 blocks of 15 trains of 2 s stimulation repeated every 12 s (total 900 pulses) 2. 20 Hz stimulation consisted of 3 blocks of 8 trains of 2 s stimulation repeated every 28 s (total 960 pulses). 3. iTBS had 3 pulses of stimulation given at 50 Hz, a 2s train of TBS repeated every 10 s for 190 s (total 600 pulses). All protocols were delivered with 80% RMT for each individual	Category Judgement Tasks  Reasoning/decision-making	Significant main effect of protocol ( $\eta_p^2 = .62$ ) and TMS ( $\eta_p^2 = .33$ ) and interactions between the protocol ( $\eta_p^2 = .3$ ) and TMS and between the protocol, task, and TMS ( $\eta_p^2 = .29$ ).  Significant main effect of task and TMS ( $\eta_p^2 = .66$ ). Practice effects were found in RT. Category judgement times were significantly slower after 1 Hz stimulation and faster after 20 Hz stimulation compared to sham. There was a significant difference between 20 Hz and 1 Hz	None

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing</i> [online/offline])	Task & Cognitive Construct	Effects	Follow-up
<i>TMS Studies</i>										
Tambini et al., 2018	Within-subjects 2 Conditions 1. Continuous theta burst (cTBS) TMS 2. Active TMS control)	22 5 M 18-28 yrs.	Not mentioned	Not mentioned	Posterior inferior parietal cortex (pIPC) (MNI coordinates) +43, -67, +28	Medial S1	40 second or 600 pulse applications. Timing not reported.  cTBS was applied at 80% of active motor threshold (AMT) and composed of 50-Hz triplets (three single pulses separated by 20 msec) repeated at a frequency of 5 Hz (every 200 msec).	Graded Memory Assessment  Working memory	stimulation  Memory success was significantly greater for hippocampal-targeted pIPC TMS relative to control TMS ( $\eta_p^2 = .35$ ).  A decrease in object location error, or more accurate object placement, was found for pIPC TMS relative to control TMS ( $\eta_p^2 = .25$ ).  Subjective confidence in object placement was enhanced by pIPC TMS ( $\eta_p^2 = .19$ )	None
Momi et al., 2020	Within 8 Conditions (5 addressing the impact of cortico-cortical paired associative stimulation (cc-PAS) with different delays between the first and second TMS pulse and 3 control conditions (same experimental design but no TMS)	30 17 M 25.43 yrs. (3.69)	All participants were recruited through flyers at the University of Siena School of Medicine (Italy)	Not mentioned	Left middle frontal gyrus (IMFG) and Left inferior parietal lobule (I IPL)	Not mentioned	15 minutes; online  cc-PAS consisted of 180 paired TMS pulses delivered every 5 s (2 Hz) over a total period of 15 minutes. The conditioning (first TMS pulse) stimulus was set at an intensity of 90% RMT, while the test stimulus (second TMS pulse) was applied at an intensity of 120% of the ipsilateral RMT	Left No-Go (LNG) task (near transfer) and Visual Search (VS) task (far transfer)  Inhibition/cognitive control/executive functions	A significant interaction of reasoning x stimulation was found, and significant main effect of stimulation was found. For logical reasoning, after receiving P → F cc-PAS, participants were significantly faster as compared to other conditions. For relational reasoning, there were faster responses for F—P compared to simultaneous – TMS and Prefrontal TMS. Additionally, after No stim, participants were faster	None

Authors	Study Design & Assignment Details	Gender & Mean Age ( <i>sd</i> )	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description ( <i>Intensity, duration, timing</i> [online/offline])	Task & Cognitive Construct	Effects	Follow-up
Bakulin et al., 2020	Within-subjects 3 active stimulation conditions and 1 control	12 4 M 22-31 yrs.	Not mentioned	Not mentioned	IDLPFC	Occipital vertex	20 minutes; offline  Trains of HF rTMS with a frequency of 10 Hz had a duration of 4 seconds and it is of 26 seconds between them. Each session consisted of 40 trains (1600 stimuli)	Verbal working memory task  <i>n</i> -back Task  Working memory	compared to simultaneous-TMS and Prefrontal TMS  A significant increase in SSP scores and a significant decrease in high load <i>n</i> -back tasks with spatial stimuli were found after TMS + WM-. A significant overall effect on all tests was only shown for this protocol. There was a significant difference between 4 protocols for the high load <i>n</i> -back task with spatial stimuli. A significant difference was found for performance changes after TMS + WM + (maintenance) and TMS + WM -	None

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## Studies with Combined Stimulation Methods

Seven studies investigated the effects of multiple types of transcranial electric and magnetic stimulation interventions within a single study design and were therefore classified into the “studies with combined stimulation methods” section of this report. The majority of the studies within this category (Lang et al., 2019; Murphy et al., 2020; Pilly et al., 2019; Rohner et al., 2018) implemented tasks within their studies to assess working memory while two studies (Brem et al., 2018; Mosbacher et al., 2021) assessed reasoning and decision-making, and one study (Lema et al., 2021) focused on the potential effects of transcranial stimulation for attention enhancement. Six studies compared the intervention conditions to the sham stimulation condition (Lang et al., 2019; Lema et al., 2021; Mosbacher et al., 2021; Murphy et al., 2020; Pilly et al., 2019; Rohner et al., 2018). Brem and colleagues (2018) included a no-contact control group for comparison against sham and multiple stimulation conditions. Different brain regions were stimulated across the studies including the IDLPFC (Brem et al., 2018; Lema et al., 2021; Murphy et al., 2020; Rohner et al., 2018) and IPPC (Mosbacher et al., 2021 assessed both IDLPFC and IPPC) and right fusiform cortex (Lang et al., 2019). Interestingly, Pilly and colleagues (2019) placed 64 electrodes globally over the cortex to assess whole brain function in a mixed tACS/tDCS stimulus delivery paradigm. For specific additional regions stimulated in each study, reference Table 12 below. Specifics for the stimulation parameters are also detailed in the table below as there were several different types of stimulatory interventions and methodologies used within each study. Several studies (Lang et al., 2019; Pilly et al., 2019; Rohner et al., 2018) showed that tACS stimulation improved performance in working memory tasks significantly better than tDCS stimulation, but no effect sizes were reported. Lema and colleagues (2021) uncovered similar benefits of tACS compared to tDCS in the enhancement of attention reporting large effects ( $\eta_p^2 > .14$ ). Interestingly, while Mosbacher and colleagues (2021) found positive effects of tACS compared to tDCS stimulation for enhancing reasoning and decision-making, Brem and colleagues (2018) compared participants who were categorized into four separate groups (tDCS, tRNS, tACS, and a no-contact control group) and when a comparison was made between the groups, the authors reported that tDCS and tRNS stimulations significantly improved fluid intelligence while no effect for tACS or the no-contact control group was found.

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Table 12. Studies with Combined Stimulation Methods

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
Mosbacher et al., 2021	Mixed  7 different stimulation/montage combinations (anodal tDCS, alpha band tACS, and theta band tACS) targeting either the IDLPFC, IPPC, or sham	137 48 M 22.5yrs (3.8)	Not mentioned	Double	IDLPFC and IPPC	Left Shoulder	Duration: 25 min with a fade in/out phase of 30s in tDCS or 100 periods in tACS  Intensity: in TDCS, current intensity applied was fixed to 1 mA. In tACS, the current intensity and stimulation frequency were adjusted individually  Online	Novel arithmetic task based on the “pound arithmetic” by Rickard (1997)  Reasoning/ decision-making	Frontal theta band tACS reduced the repetitions needed to learn novel facts and both frontal and parietal theta band tACS accelerated the decrease in calculation times in fact learning problems.	None
Pilly et al., 2020	Within-subjects  4 Conditions 1. Episode A active stimulation 2. Episode A sham 3. Episode B stimulation 4. Episode B sham	24 9 M 23.96yrs (6.08)	All right-handed	Single	64 electrodes were globally placed to measure whole brain activity across all lobes	Right preauricular region	Total injected current was set to 2.5 mA, with maximum 1.5 mA and minimal 150 uA current at any electrode  Online	Declarative memory recall test  Working memory	Significant effect of baseline performance and a marginally significant effect of intervention type for both absolute accuracy and metamemory.	None
Rohner et al., 2018	Within-subjects  3 Conditions 1. tACS stimulation 2. tDCS stimulation 3. Sham	30 15M 26.2yrs (3)	All right-handed; scored with IQ above 85	Single	F3 & P3 (tACS)  F3 (tDCS / anode)	Top of left shoulder (cathode)	1 mA/15 min  Online	Visual 2-back letter task  Working memory	tACS resulted in a greater improvement in reaction time compared to tDCS and sham conditions	
Lema et al., 2021	Within-subjects 3 Conditions 1. tDCS	27 7 M 22.78 yrs (3.89)	All right-handed	Single	F3 (anode)	Fp2 (cathode)	2 mA/20 min for both tRNS and tDCS stimulation	Attention Network Task  Attention	tRNS stimulation increased attention in	None

Authors	Study Design & Assignment Details	Gender & Mean Age (sd)	Additional Sample Details	Blinded	Active Location	Reference Location	Stimulation Description (Intensity, duration, timing [online/offline])	Task & Cognitive Construct	Effects	Follow-up
	2. tRNS 3. Sham						Online		complex situations and overall performance compared to sham. No significant effects for tDCS were observed	
Lang et al., 2019	Between-subjects  3 Groups 1. tACS 2. tDCS 3. sham	59 28 M 1. 28.4 (6.9) 2. 25.3 (5.6) 3. 24.9 (4.7)	Not mentioned	Single	Fp1, P2, P3, PO7, P10 (p10 anode)	Directly above the active location	2mA for 10 minutes for both tACS and tDCS stimulation  Online	Face and Scene Task (FAST)  Working memory	Improved active memory performance was observed in the tACs group. tDCS had no effect	None
Murphy et al., 2020	Between  3 Groups 1. tDCS 2. tRNS 3. sham	1. 16 5 M 30.43 yrs. (12.01)  2. 16 6 M 27.60 yrs. (8.60)  3. 17 5 M 31.05 yrs. (13.06)	All right-handed	Not mentioned	F3 (anode)	Right supraorbital area (cathode)	1 mA/22 min for both tDCS and tRNS stimulation  Offline during tested task/ online during alt. task	Sternberg Working Memory Task  Working memory	Significantly increased accuracy for group who received tRNS compared to tDCS and sham groups ( $\eta_p^2 = 0.640$ )	None
Brem et al., 2018	Mixed  5 Groups 1. tDCS 2. tRNS 3. Multi focal tACS (mftACS) 4. mutli focal tDCS (mftDCS) 5. no contact control  Pre-test,	87 (46 M)  1. 28.41 (11.58) 2. 29.19 (10.39) 3. 30.73 +/- (13.17) 4. 27.88 +/- (11.58) 5. 30.88 +/- (12.3)	Not mentioned	Single	Anodal F3 for all active stimulation groups; Additional anodal placements for mftACS include F4, P3, and P4	Cathodal placements. tDCS- AF8; tRNS- F4; mftACS- Fz; mftDCS- Fz, T7, T8, Oz	1 mA for all stimulation conditions was delivered for 30 minutes over 9 sessions except for tDCS groups which stimulation was delivered for 20 min for 9 sessions  Online	3 Logical Deductive Reasoning Tests  1. Bochumer Matrizentest (BOMAT) 2. Sandia Matrices 3. Raven's Advanced Progressive Matrices (RAPM)  Reasoning/decision-making	All stimulation protocols, except for mftACS, significantly improved the participants' fluid intelligence after the training intervention	None

<b>Authors</b>	<b>Study Design &amp; Assignment Details</b>	<b>Gender &amp; Mean Age (sd)</b>	<b>Additional Sample Details</b>	<b>Blinded</b>	<b>Active Location</b>	<b>Reference Location</b>	<b>Stimulation Description (Intensity, duration, timing [online/offline])</b>	<b>Task &amp; Cognitive Construct</b>	<b>Effects</b>	<b>Follow-up</b>
	cognitive training combined with stimulation, and post-test									

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## Discussion

The purpose of this technical report was to provide an updated and targeted review of the research evaluating transcranial stimulation building off of the findings from USAARL's 2019 report (Kelley et al., 2019). The previous report was broader in terms of inclusion criteria for cognitive enhancement but did have a large focus on the potential benefits for tDCS to elicit cognitive enhancement (33 studies included in the analysis). In addition to tDCS, Kelley et al., 2019 reviewed other transcranial stimulation methods and reported outcomes from studies utilizing oscillating direct current stimulation, intermittent theta burst stimulation, transcranial alternating current stimulation (tACS), and repetitive transcranial magnetic stimulation (rTMS). Kelley and colleagues (2019) concluded that although the stimulation parameters in the studies varied widely, enhancement of learning tasks, perception-based tasks, visuospatial attention, and recall tasks were consistent across studies. Since the 2019 report, there has been a surge in the number of studies published that investigated the potential for transcranial stimulation to enhance cognitive performance. Therefore, the current report focused solely on transcranial electrical and transcranial magnetic stimulation and their potential to enhance cognitive performance metrics. All papers included in this analysis were published between 2018-2022. Similar to findings reported in the 2019 report, the majority of studies included here evaluated the potential for tDCS to enhance cognitive performance. Hence, to further explore the beneficial results of tDCS, we created subcategories of cognitive performance outcomes to include working memory, attention, memory and learning, reasoning and decision-making, and cognitive control/inhibition/executive functions. Furthermore, in addition to the transcranial stimulation conditions included in the 2019 report, in this report we also analyzed papers published that investigated the use of transcranial random noise stimulation (tRNS) and studies which utilized a combined methods approach (e.g., analyzing tDCS vs. tACS vs. tRNS) to enhance performance. The intent of this update was to examine utility of transcranial stimulation for cognitive enhancement, whether these interventions might benefit healthy, cognitively normal young adults, and the potential for use in the Warfighter population. Specifically, the goal was to address the following questions:

- What is the minimum length of time needed for the application of an intervention to facilitate cognitive performance enhancement?
- Which neuromodulation technique shows the most consistent findings regarding efficacy?
- How long does cognitive enhancement last after the neuromodulation intervention is discontinued?
- Can the Warfighter gain beneficial cognitive enhancement from a one-time, acute intervention or does the intervention need multiple exposure periods to generate and sustain enhanced cognitive performance?
- After re-evaluating the literature pertaining to transcranial stimulation and cognitive performance enhancement, have any of the gaps mentioned by Kelley and colleagues (2019) been closed?
- Has the research shifted course and have any additional discrepancies in findings emerged?
- Can we recommend any form of transcranial stimulation for military use at this time?

The military is constantly seeking ways to improve the Warfighter physically and mentally and to conserve the fighting strength. With a wide array of performance enhancement substances available, it is imperative to provide Warfighters with the best and most appropriate recommendations based on solid, empirical evidence. Interestingly, recent research among U.S. Army personnel has discovered that the use of performance enhancing supplements may increase during deployment. Austin and colleagues (2016) conducted a survey that included over 200 deployed Soldiers and over 1000 in-garrison and concluded that the deployed Soldiers were more likely to use performance enhancement products (Austin et al., 2016). However, there are many questions that remain relating to the effectiveness and safety of such products. As our review is focused on transcranial stimulation, several of the initial questions that arose pertained to the timing parameters (i.e., duration and timing relevant to the task) necessary for the stimulation to elicit the neuroenhancement effect (i.e., how long to apply the stimulation technique as well as when, relative to the task being performed, to conduct stimulation) to elicit the cited benefits. The studies cited in this review show considerable variability across and within modalities (i.e., tDCS, TMS, tACS, tRNS). Across the majority of studies, participants received stimulation from the TMS and tES devices for an average of approximately 20 minutes during each session. TMS studies reported the least amount of time, with an average of about 15 minutes, and tACS studies had participants wear the device for an average of about 30 minutes. It is important to note that these studies focused on the effectiveness of the intervention rather than determining the optimal time each device should be active, which is a key step to determining the length of time required to see effects. An important question that is posed for future research is: What duration of stimulation is required to enhance an individual's performance on a specific task? For example, do all individuals need 15-20 minutes of stimulation within certain parameters to achieve cognitive enhancement or can some experience the effects with as little as 5 minutes of stimulation? The 15-20-minute mark may be the time required to achieve the results (as reported by relevant research), but without a study designed to control stimulation length for each of the outcome variables, the question remains unanswered.

Similar to the findings pertaining to the capability of transcranial stimulation to enhance cognitive performance in our previous review (Kelley et al., 2019), within our categorization of stimulation techniques and conditions in this review, we still found mixed results. It is biologically plausible to suggest that the mixed results seen in our previous and current review may be simply due to study parameters and individual differences in anatomy. Consistent with our last review (Kelley et al., 2019) we noticed mixed effects for performance enhancement in tasks requiring executive functioning as well as the stimulation locations and parameters being inconsistent across studies. For example, although there were many studies that implemented transcranial stimulation specifically on the DLPFC, no study could definitively state that stimulation of the DLPFC was solely responsible for enhanced cognitive performance. There are many neural networks that the DLPFC communicates with and receives communication from, and the definitive neural mapping of its complete function is still lacking. Moreover, many of the articles cited throughout this report used a set time duration for their experimental condition. As stated previously, few studies investigated if there may be potential effects for cognitive enhancement that are directly related to the stimulation duration. For example, Yaple and Vakhrushev (2018) conducted two separate experiments which both used the same stimulation conditions. However, their first experiment included a tACS stimulation period of less than 35 minutes (targeting one brain region) while the second experiment lasted for approximately 50 minutes (targeting two regions). Interestingly, as we have previously mentioned, it appears that

there is a '15-20-minute sweet-spot' for significant results to be achieved, Yaple and Vakhrushev (2018) demonstrate just that. Furthermore, Wang and colleagues (2018) conducted two separate experiments (one in an online condition and one in an offline condition) with different tDCS stimulation durations. In the first experiment participants received a combination of sham, 10-, and 20-minute tDCS stimulation (offline). In the second experiment, participants received sham and 20-minute tDCS stimulation (online). Surprisingly, neither stimulation paradigm resulted in improvement in visual short-term memory. Hence, much more research is needed to truly establish how timing and cognitive performance enhancement are correlated.

It must also be noted that, in addition to stimulation duration, participants can perform tasks while being stimulated in addition to post-stimulation. This is an important variable to control as many "real world" and military-specific tasks would require stimulation to occur minutes, if not hours, before task engagement. Warfighter performance is mission-dependent and the tasks, whether aviating, engaging enemies, planning, or navigating terrain, may not permit Warfighters the ability to actively utilize the device without significant technological advancements. Hence, neuromodulation intervention would need to be implemented prior to task execution and the effects would need to last long enough to impact mission performance. Additionally, more research is needed to understand whether, and after how long, enhancement effects plateau for each type of stimulation.

As pointed out by Silvanto and Pascual-Leone (2008), neuro stimulation prior to task performance results in an excitatory action on the activated neuronal population, thus providing a general increase in subsequent sensory stimulation. In contrast, when stimulation is applied during the cognitive process, neurons critical to the task are further activated, while an inhibitory effect is seen on neurons not involved in the task performance (Ridding & Rothwell, 2007). As many tasks require changing and complex neuronal activation, this imbalance can cause behavioral disruption (Grosbras & Paus, 2003). There is a high degree of variance in the timing of stimulation application with more than half of the studies collecting at least some of the data while participants received stimulation. Moreover, less than half of the studies assessed enhancement effects after the initial period of data collection (e.g., hours, days, weeks after stimulation). The studies that reported post-session follow-up found the neuroenhancement effects disappeared in as little as one hour after stimulation. This may be a result of the state dependency of an individual at the time of data collection. Factors such as mood, fatigue, cognitive baseline level, and mental health can have significant moderating effects on the effectiveness of neuroenhancement (Bakulin et al., 2020; Silvanto & Pascual-Leone, 2008).

Examining the outcomes more closely, there are noticeable differences between the different types of stimulation. As previously discussed, researchers utilized either tDCS, tACS, tRNS, TMS, or a combination of the stimulation types. tDCS devices, being relatively cheap and portable, are much easier to utilize, which may explain the numerous studies conducted using tDCS in comparison to other tES modalities. Interestingly, when assessing all of the intervention modalities included in this report, tDCS was the only intervention to report null results in multiple studies. For example, looking at working memory, seven out of 14 studies (50%) reported no enhancement effects. Similarly, the remaining categories reported null results, attention (20%), memory and learning (33%), reasoning and decision-making (25%), and executive function (11%). Overall, with outstanding questions as to the underlying mechanism(s) and reliability of the reported effects, additional research is needed to evaluate whether tDCS is

an effective means of achieving sustainable neuroenhancement.

For the studies that only used tACS, only three studies met our inclusion criteria. One study looked at attention and found positive results (Yaple & Vakhrushev, 2018). Two studies found significant effects on executive functions (Battaglini, Ghiani, et al., 2020; Loffler et al., 2018). When tRNS was utilized as the sole intervention modality, all studies included in this review yielded significant results. One study found effects for reasoning and decision-making (Sprugnoli et al., 2021), two found enhancement for attention (Conto et al., 2021; Tyler et al., 2018), and three assessing executive function cited beneficial outcomes (Battaglini et al., 2019; Battaglini, Contemori, et al., 2020; Contemori et al., 2019). Lastly, TMS studies found positive results for working memory (Bakulin et al., 2020; Tambini et al., 2018; Wu et al., 2021), reasoning and decision-making (Jung & Lambon Ralph, 2021), as well as executive function (Momi et al., 2020). The combination studies yielded mixed, yet interesting results. Mosbacher and colleagues compared tACS and tDCS and found that only tACS had a positive effect on reasoning and decision-making (Mosbacher et al., 2021). The studies by Rohner and Lang found similar effects for working memory comparing tACS and tDCS where only tDCS produced significant results (Lang et al., 2019; Rohner et al., 2018). Furthermore, one study found that tRNS demonstrated improvement in attention while no effects were observed for tDCS (Lema et al., 2021). Another discovered that working memory was improved in only the group that received tRNS but not in the groups that received tDCS (Murphy et al., 2020). One study found that tRNS and tDCS had positive effects for reasoning and decision-making, but no effects were observed in the tACS condition (Brem et al., 2018). Overall, with the correct parameters, all transcranial stimulation techniques may prove promising, but more work needs to be conducted to replicate and validate these modalities for cognitive enhancement use, as much variability currently exists. Further, given the lack of operationally relevant outcomes with respect to Warfighters, there is much work to be done if tES is to be a viable intervention.

Further addressing whether any of the cited neuromodulation techniques are non-invasive and appropriate for the Warfighter, a minor limitation to this review is that device type (i.e., manufacturer, model) was not factored into the analyses and was only considered post-hoc. tES devices can be portable and durable since rechargeable or non-rechargeable batteries can provide more than enough amperage to produce the low amount of current needed. The decision to utilize one modality over another would ideally be based on the device's efficacy rather than convenience yet cost and portability of the devices are considerable factors when trying to identify those that are easily scalable in an operational setting. In studies that evaluated the potential cognitive enhancement by comparing effects with different interventions (e.g., tACS versus tDCS), several studies reported tACS as more effective in enhancing working memory (Lang et al., 2019; Pilly et al., 2019; Rohner et al., 2018). Additionally, Mosbacher and colleagues (2021) found tACS to be more effective in enhancing reasoning and decision-making. Looking at tRNS, several studies found it to be more effective for improving attention (Lema et al., 2021), and working memory (Murphy et al., 2020) than tDCS. With portability as a requirement for operational use, the TMS and tRNS technologies are less likely candidates for operational use, despite demonstrating potential benefits.

A key remaining challenge is that the effects of brain stimulation are not limited to the targeted brain region, and few studies monitor the locality of neuronal activation, let alone delve into the mechanism by which the effects are elicited. Activation is rarely localized but can spread

ortho- and antidromically along neural connections. Studies in animal models demonstrate that TMS might be best conceptualized as modulating activity across bi-hemispheric cortico-subcortical networks reached from the directly targeted brain region (Valero-Cabre et al., 2007; Valero-Cabre et al., 2005). In humans, studies combining TMS with brain imaging methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) confirm such distributed network effects (Bestmann et al., 2008; Sack et al., 2007). With widespread activation and state-effects, it is difficult to ascribe causality to neurostimulation treatment.

Finally, it is important to highlight that some of the combination studies reported non-significant findings for certain stimulation conditions (Brem et al., 2018; Lang et al., 2019; Lema et al., 2021). Interestingly, several of the studies focused solely on tDCS reported non-significant findings with various explanations as to why results were not significant (Bystad et al., 2020; Ikeda et al., 2019; Wang, Wen, et al., 2018). Ikeda and colleagues (2019) simply stated that it is unclear as to why the tDCS gamma oscillation did not enhance working memory capacity (Ikeda et al., 2019). Wang and colleagues (2018) suggested that their non-significant findings could be due to the fact that their participants were young and were high-level baseline performers (Wang, Wen, et al., 2018). Moreover, Bystad and colleagues (2020) attributed their nonsignificant findings to the utilization of a novel, accelerated protocol (different from previous studies by Manenti et al., 2013 and Sandrini et al., 2013 that did show enhanced memory function after stimulation to the temporal area). However, even though Bystad and colleagues did not observe learning and memory enhancement effects, it is important to note that they did find significant enhancement through use of tDCS for executive function among their younger participants. It is also important to note that previous studies that the authors included in their paper, which claimed to have found tDCS targeting the temporal cortex and facilitating an improvement in working memory, were in a clinical population. Specifically, these effects were found in a population of Alzheimer's patients (Bystad et al., 2020). This is important to mention because the relationship between transcranial stimulation and cognitive enhancement remains to be debated in healthy individuals. Complicating the interpretation of results by using a clinical population with neurocognitive functional abnormalities only creates more speculation and adds another layer of experimental variables. For example, the period and severity of cognitive decline varies widely in Alzheimer's patients and there is currently not a truly definitive way to define it. Researchers would have to have diagnostic tests on the patients conducted in order to accurately classify the severity of cognitive decline and there may be significant variation between participants which would render the results very difficult to interpret (Malpetti et al., 2020).

Regardless of the intervention technique, the studies that supported cognitive enhancement effects reported large effect sizes ( $\eta_p^2 > .14$ ) showing that, under the right conditions and with the right population, tES may be an effective tool for temporary neuroenhancement. Further, it is clear that tES could have a practical use in the military community; the challenge is to determine standardizations for the type of stimulation, location of stimulation, duration of stimulation, optimal timing of stimulation in relation to target tasks, the duration of time that neuromodulation effects last after stimulation, and whether repeated stimulation sessions have an additive effect or only a temporary increase in baseline performance.

## Limitations and Future Directions

Less than half of the studies assessed in our review investigated the lasting effects after the initial data collection period (e.g., hours, days, and weeks after stimulation). Several of the studies included in this report conducted a post-session follow-up only to discover that neuroenhancement effects disappeared in as little as one hour after stimulation (Bjekic et al., 2019; Hanenberg et al., 2019; Lewald, 2019). One of the main factors that makes it difficult to attribute cognitive enhancement effects to neurostimulation over any period is the state dependency of an individual at the time of data collection. Factors such as mood, fatigue, cognitive baseline level, and mental health can significantly moderate the effectiveness of neuroenhancement (Bakulin et al., 2020; Silvanto & Pascual-Leone, 2008). Hence, longitudinal follow-up experiments and studies to investigate the potential for sustained cognitive enhancement from tES should be implemented.

Extensive research has been conducted using the tES and TMS methods evaluated in our current literature review targeting brain regions directly involved in cognitive and executive function (specifically prefrontal cortical regions such as the dorsolateral prefrontal cortex). However, the utilization of transcranial ultrasound (tUS) in a healthy population for enhancement of cognitive performance is relatively scarce. This was a surprising finding as tUS offers several advantages over tES and TMS, such as the ability to target specific deep cortical anatomical regions while simultaneously providing better spatial resolution (Fini & Tyler, 2017; Kubanek, 2018; Lee et al., 2016; Legon et al., 2018). Interestingly, to our current knowledge, there has only been one study, in a nonclinical healthy population, that investigated the use of tUS specifically targeting the right prefrontal cortex (RPFC) (Sanguinetti et al., 2020). When this same region has been targeted by tDCS (Boudewyn et al., 2019; Hussey et al., 2020; Ikeda et al., 2019; Luque-Casado et al., 2019) and TMS (Bakulin et al., 2020; Wu et al., 2021), it has been shown to improve several aspects of cognitive and executive function. This study, conducted by Sanguinetti and colleagues, used tUS to target the RPFC and demonstrated that the intervention could improve mood and positively alter functional neural networks related to emotional regulation (Sanguinetti et al., 2020), which is proof of concept that there is potential for tUS to provide positive mental enhancement. However, to date, no studies utilizing tUS have assessed its potential for cognitive performance enhancement and future research should explore this avenue.

Finally, one aspect that should be included in future studies and/or reviews is the interaction effects of pairing tES with commonly used medications and stimulants that can have positive or negative neuromodulation effects (i.e., caffeine and other stimulants) by themselves. With long duty hours and poor sleep habits, Soldiers commonly use a host of over the counter (OTC) products that could have a significant effect on the efficacy of tES in operational environments. In addition to the OTC products, medical conditions and prescribed medication can interact and either potentiate or dilute the desired effects. Beyond the obvious safety concerns, ecological validity can only be achieved if the research is conducted to account for the current operational environment.

## Conclusion

The findings from the updated literature review are in-line with those from the previous review. Although both reviews analyzed literature which claims transcranial stimulation can improve cognitive performance, the underlying mechanisms as to how this is achieved, and under which experimental conditions (i.e., location, duration, frequency, etc.) remain to fully reach a consensus. In both the 2019 report and the current review, tDCS was the focus of most studies. tDCS outcomes in both reviews revealed mixed results depending on the stimulation parameters and the outcome measure. For example, in the 2019 review, one study indicated that executive function was enhanced when tDCS (1 mA for 20 minutes) was applied to the dorsolateral prefrontal cortex compared to motor cortex (Gbadeyan et al., 2016) yet the same parameters and stimulation location did not improve learning outcomes in several studies (Luculano & Kadosh, 2013; Devries et al., 2009). In addition, Kelley and colleagues (2019) concluded that mixed effects were observed for creativity/object naming tasks, attention, decision-making, and working memory. These conflicting outcomes make it extremely difficult to interpret the data and make valid recommendations for future studies. In concert with our previous publication, we arrived at similar conclusions. Several of the combination studies found mixed results within their own experiments (Brem et al., 2018; Lang et al., 2019; Lema et al., 2021). Also, several studies within our tDCS category for working memory (Wang et al., 2018 and Ikeda et al., 2021), as well as one study within the memory and learning category (Bystad et al., 2020) yielded nonsignificant results for their reported outcomes. Interestingly, the explanations from the studies in our report that yielded nonsignificant findings varied. Ikeda and colleagues (2019) simply stated that it is unclear as to why the tDCS gamma oscillation did not enhance working memory capacity (Ikeda et al., 2019). Wang and colleagues (2018) suggested that their non-significant findings could be due to the fact that their participants were young and were high-level baseline performers (Wang et al., 2018). As these explanations are plausible, it is unknown whether mixed results are attributable to tES effectiveness or to limitations in study methodology. This report did not include literature on transcranial ultrasound as limited research is available for use of this modality on a healthy, non-clinical population. Although most studies reported statistically significant effects of transcranial stimulation on task performance, there are many limitations when it comes to summarizing the research and answering fundamental questions such as:

- Which stimulation type is most effective for each type of task (e.g., attention, memory, executive function)?
- Where is the best location to place each type of device to elicit neuromodulation effects?
- What is the minimum stimulation duration needed to improve task performance for each type of task?

In spite of the variation in studies, there are several generalizations that can be made. For example, the majority of studies reported improvements in performance, although some reported improvements only for subpopulations (e.g., responders, low baseline performance, younger participants). Also, the vast majority of studies included in this review had large effect sizes ( $\eta_p^2 > .14$ ), a case may be made for any of the techniques as a feasible option in future studies for cognitive performance enhancement. Arguably, the main limitation to all of the studies cited are that none of the studies included utilized applied, real-world tasks. Rather, all studies focused on discrete cognitive tasks, such as *n*-back tasks. In terms of transcranial stimulation timing,

most of the studies only found strong effects while stimulation was co-occurring with completion of the task. This might impose a significant challenge for integration into military training and operations, especially in the deployed environment, as the environment is dynamic, constantly changing, and fast-paced, which are all completely opposite conditions from those used in the reviewed literature.

Looking at the transcranial stimulation devices and usage, except for tUS, the neuromodulation equipment is small and light enough to be readily and easily transportable, although there is still the need for trained operators, time constraints to properly equip the devices, and extreme mobility limitations. Related to timing of stimulation, if a Soldier was able to receive a neuromodulation intervention prior to performing a mission and improve their cognitive performance on military relevant operational tasks for a sufficient time allowing task completion, then the use of the technology may receive buy-in from higher echelons rather than if the stimulation would need to be active while performing the task. The end goal of this line of research should be to create a minimally invasive, significant neuroenhancement effect, without compromising operational integrity or creating any additional burden to the Soldier. Further research using applied tasks is needed before recommendations for the use of neuromodulation techniques in operational settings can be made as many unknowns remain.

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## Appendix A. Acronyms and Abbreviations

Abbreviation	Meaning
ATL	Anterior Temporal Lobe
cc-PAS	Cortico-cortical Paired Associative Stimulation
CPD	Cycle Per Degree of Visual Angle
cTBS	Continuous Theta Burst
dACC	Dorsal Anterior Cingulate Cortex
exp	Experiments
FAST	Face and Scene Task
HD-tDCS	High-Definition Transcranial Direct Current Stimulation
HF-rTMS	High-Frequency Repetitive Transcranial Magnetic Stimulation
hMT	Human Middle Temporal Area
Hz	Hertz
iTBS	Intermittent Transcranial Brain Stimulation
IDLDFC	Left Dorsolateral Prefrontal Cortex
lIFG	Left Inferior Frontal Gyrus
lIPL	Left Inferior Parietal Lobule
lMFG	Left Middle Frontal Gyrus
LNG	Left No-Go Task
lPPC	Left Parietal Prefrontal Cortex
lPPC	Left Posterior Parietal Cortex
mA	Milli-Amp
mftACS	Multifocal Alternating Current Stimulation
mftDCS	Multifocal Direct Current Stimulation
N/A	Not Applicable
OTC	Over The Counter
Ot-tDCS	Theta Oscillating Transcranial Direct Current Stimulation
PASAT	Paced Auditory Serial Addition Task
PFC	Prefrontal Cortex
pIPC	Posterior Inferior Parietal Cortex
PPC	Posterior Parietal Cortex
rDLPFC	Right Dorsolateral Prefrontal Cortex
rIFG	Right Inferior Frontal Gyrus
RMT	Resting Motor Threshold
rPPC	Right Posterior Parietal Cortex
rTMS	Repetitive Transcranial Magnetic Stimulation
RTs	Reaction Times
SAT	Shifting Attention Task
SD	Standard Deviation
SDR	Short Duration Repetitive
SST	Stop Signal Test
tACS	Transcranial Alternating Current Stimulation
tDCS	Transcranial Direct Current Stimulation

tES	Transcranial Electrical Stimulation
TMS	Transcranial Magnetic Stimulation
TPC	Temporal Parietal Cortex
tRNS	Transcranial Random Noise Stimulation
tUS	Transcranial Ultrasound
U.S.	United States
uA	Microampere
VS	Visual Search
WM	Working Memory
Yrs.	Years





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