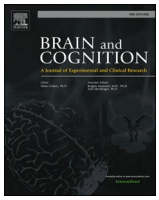
Brain and Cognition 173 (2023) 106105

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c



Effects of transcranial direct current stimulation and transcranial random noise stimulation on working memory and task-related EEG in major depressive disorder

O.W. Murphy [a,b,*], K.E. Hoy [a,b], D. Wong [c], N.W. Bailey [a,d,e], P.B. Fitzgerald [d,e], R.A. Segrave [f]

[a] Central Clinical School, Monash University, Clayton, VIC, Australia
[b] Bionics Institute, East Melbourne, VIC, Australia
[c] School of Psychology and Public Health, La Trobe University, Bundoora, VIC, Australia
[d] Monarch Research Institute Monarch Mental Health Group, Sydney, NSW, Australia
[e] School of Medicine and Psychology, Australian National University, Canberra, ACT, Australia
[f] BrainPark, Turner Institute for Brain and Mental Health, Monash University, Clayton, VIC, Australia

ARTICLE INFO

Keywords:
Transcranial direct current stimulation (tDCS)
Transcranial random noise stimulation (tRNS)
EEG
Depression
Working memory

ABSTRACT

Objective: To compare effects of transcranial direct current stimulation (tDCS) and transcranial random noise stimulation with a direct-current offset (tRNS + DC-offset) on working memory (WM) performance and task-related electroencephalography (EEG) in individuals with Major Depressive Disorder (MDD).
Methods: Using a sham-controlled, parallel-groups design, 49 participants with MDD received either anodal tDCS (N = 16), high-frequency tRNS + DC-offset (N = 16), or sham stimulation (N = 17) to the left dorsolateral prefrontal cortex (DLPFC) for 20-minutes. The Sternberg WM task was completed with concurrent EEG recording before and at 5- and 25-minutes post-stimulation. Event-related synchronisation/desynchronisation (ERS/ERD) was calculated for theta, upper alpha, and gamma oscillations during WM encoding and maintenance.
Results: tDCS significantly increased parieto-occipital upper alpha ERS/ERD during WM maintenance, observed on EEG recorded 5- and 25-minutes post-stimulation. tRNS + DC-offset did not significantly alter WM-related oscillatory activity when compared to sham stimulation. Neither tDCS nor tRNS + DC-offset improved WM performance to a significantly greater degree than sham stimulation.
Conclusions: Although tDCS induced persistent effects on WM-related oscillatory activity, neither tDCS nor tRNS + DC-offset enhanced WM performance in MDD.
Significance: This reflects the first sham-controlled comparison of tDCS and tRNS + DC-offset in MDD. These findings directly contrast with evidence of tRNS-induced enhancements in WM in healthy individuals.

1. Introduction

Major Depressive Disorder (MDD) is a highly prevalent and often debilitating mental illness which is associated with significant rates of morbidity and mortality (Kessler et al., 2005, 2009). Impairments in working memory (WM) are amongst the most common neuropsychological symptoms of MDD and may contribute an exacerbation of affective symptoms and poorer treatment outcomes (Dunkin et al., 2000; Joormann & Gotlib, 2010; Snyder, 2013). Current first-line antidepressant medications and psychotherapies are relatively ineffective at treating these cognitive symptoms (Herrera-Guzmán et al., 2010; Raskin et al., 2007), highlighting the need for the development of alternative therapeutic tools for alleviating the cognitive symptoms of MDD.

Transcranial electrical stimulation (tES) techniques such as transcranial direct current stimulation (tDCS) and transcranial random noise stimulation (tRNS) have both been shown to enhance WM performance in healthy individuals via modulation of underlying neural activity (Andrews et al., 2011; Fregni et al., 2005; Friehs & Frings, 2019; Mulquiney et al., 2011; Murphy et al., 2020). Although improvements in WM following delivery of tDCS to the dorsolateral prefrontal cortex (DLPFC) to individuals with MDD have been reported (e.g. Boggio et al., 2007; Loo et al., 2012; Moreno et al., 2015; Oliveira et al., 2013), meta-analyses and large-scale clinical trials have found that effects of tDCS on WM performance and underlying brain activity in MDD are often modest

* Corresponding author at: Central Clinical School, Monash University, Clayton, VIC, Australia.
E-mail address: omurphy@bionicsinstitute.org (O.W. Murphy).

https://doi.org/10.1016/j.bandc.2023.106105
Received 19 June 2023; Received in revised form 25 September 2023; Accepted 31 October 2023
Available online 12 November 2023

in size and variable between studies and individuals (Hill et al., 2016; Martin et al., 2018). tRNS is another form of tES which delivers an alternating current with a randomly fluctuating frequency and intensity (Fertonani et al., 2011; Terney et al., 2008). tRNS can be delivered with a DC-offset which results in electrodes maintaining a consistent polarity but with a randomly fluctuating current intensity (Ho et al., 2015). Delivery of tRNS + DC-offset thereby combines features of both tDCS and tRNS, whereby the consistent polar charge of electrodes mirrors that of tDCS (i.e., net polarisation of neuronal membrane potentials), whilst the randomly fluctuating current intensity also introduces random noise into the neural system in a manner analogous to tRNS. Research in healthy individuals has demonstrated that tRNS without an offset can induce more pronounced neurophysiological and behavioural effects than anodal tDCS (e.g. Fertonani et al., 2011; Inukai et al., 2016). Furthermore, the delivery of tRNS with a DC-offset has been shown to facilitate cortical excitability to a greater degree than tRNS without an offset (Ho et al., 2015). Our research team previously provided the first evidence that tRNS + DC-offset can induce more pronounced and consistent WM enhancements than anodal tDCS in healthy individuals (Murphy et al., 2020). However, we are not aware of any previous sham-controlled research directly comparing the effects of tDCS and tRNS in people with MDD.

A greater understanding of how tES influences underlying neurophysiological activity and modulates cognitive processing could provide valuable markers for future treatment protocol and improve the reliability of cognitive outcomes. Electroencephalography (EEG) has been widely used to characterise the neurophysiological correlates of WM functions in healthy individuals, which includes reliable and robust modulation of oscillatory activity within the theta (4–8 Hz), upper alpha (10–12.5 Hz), and gamma (30–100 Hz) frequency ranges, with the modulation of each associated with WM task accuracy (Jensen & Tesche, 2002; Jensen et al., 2002; Roux et al., 2012). There is growing evidence for abnormal modulation of oscillatory activity during WM processing in MDD, particularly for modulation of upper alpha activity during the maintenance phase of WM processing (Bailey et al., 2014; Murphy et al., 2019; Segrave et al., 2010). Crucially, in a previous study utilising baseline data from participants in the current study, we observed that individuals with MDD displayed altered modulation of frontal-midline theta, and occipital gamma and upper alpha during WM processing (Murphy et al., 2019). Given evidence that tDCS and tRNS can modulate oscillatory activity within these frequency ranges (Boonstra et al., 2016; Hoy et al., 2015; Miller et al., 2015), examination of EEG-derived measures of oscillatory activity may provide valuable insights into the neurophysiological mechanisms underlying the cognitive effects of tES in MDD. Moreover, the effects of tES on task-related EEG have frequently been reported in the absence of significant changes in task performance (Hill et al., 2017; Nikolin et al., 2018), indicating that EEG-derived measures may prove more sensitive than cognitive measures alone.

In the current study we sought to compare the acute effects of delivering a single session of anodal tDCS, tRNS + DC-offset, or sham stimulation on WM performance and WM-related oscillatory activity in individuals with MDD. We hypothesised that both tDCS and tRNS + DC-offset would significantly improve WM performance when compared to sham stimulation, and that tRNS + DC-offset would be superior to tDCS in improving WM performance. Given evidence that MDD is associated with reductions in upper alpha power during WM maintenance (Bailey et al., 2014; Murphy et al., 2019), combined with evidence that tES can modulate alpha activity in healthy individuals (Boonstra et al., 2016; Hsu & Tseng et al., 2014; Murphy et al., 2020), we hypothesised that both tDCS and tRNS + DC-offset would increase upper alpha power during WM maintenance when compared to sham stimulation, and that these enhancements would be more pronounced following tRNS + DC-offset as compared to tDCS. We also performed exploratory analyses to examine potential effects of tES on theta and gamma activity during WM encoding and maintenance, however we did not construct specific hypotheses for these analyses due to the paucity of previous evidence regarding MDD-related changes in theta and gamma activity during WM processing.

2. Methods

2.1. Participants

Forty-nine adults with MDD were recruited into the study. All participants were aged between 18 and 65 years, right-handed, fluent in English, and had normal or corrected-to-normal vision. Participants were screened for contraindication to tES (i.e., epilepsy, stroke, traumatic brain injury, neurological illness, frequent or severe headaches, pregnancy, medical infusion devices, or metal implants in the brain or skull). A structured clinical interview (see Section 2.3. Clinical Interview) was conducted to confirm the presence of a current Major Depressive Episode, and to screen for other Axis 1 psychiatric disorders. Participants were excluded if they reported recreational drug use within one month prior to testing, a history of substance abuse or dependence, or were currently taking medications which have been shown to interfere with the effects of non-invasive brain stimulation (i.e. benzodiazepines, antipsychotics, or mood stabilisers) (Brunoni et al., 2013; Stagg & Nitsche, 2011). At the time of testing, 26 participants were taking antidepressant medication and 23 were medication-free (Table 1). Written informed consent was obtained from all participants prior to engaging in the study. The experimental protocol was approved by the Alfred Human Research Ethics Committee and the Monash University Human Ethics Committee and was prospectively registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12612001061820).

2.2. Design and procedure

The study utilised a sham-controlled, single-session, parallel-groups design. Each participant completed a single experimental session conducted at the Monash Alfred Psychiatry Research Centre, Melbourne.

Table 1
Participant Characteristics.

	Sham	tDCS	tRNS	F-statistic	*p*-value
Sample (*n*)	17	16	16		
Gender (F/M)	10/7	9/7	10/6		
Age (years)	28.34 ± 10.56	28.58 ± 7.24	28.47 ± 10.56	0.003	0.997
Years of education	14.00 ± 1.84	14.19 ± 1.60	13.69 ± 1.54	0.368	0.694
WAIS-IV WMI	106.00 ± 12.63	106.69 ± 13.82	107.94 ± 11.80	0.097	0.908
HAM-D	17.35 ± 2.26	16.69 ± 2.33	17.00 ± 2.94	0.287	0.752
QIDS	13.94 ± 2.25	13.19 ± 1.87	14.13 ± 2.66	0.763	0.472
STAI - State	41.47 ± 13.07	43.06 ± 9.40	41.81 ± 9.03	0.100	0.905
STAI - Trait	51.35 ± 12.07	57.50 ± 6.42	58.94 ± 10.78	2.646	0.082
Medications					
None	10	6	7		
SSRI	6	3	6		
SNRI	1	3	1		
Tricyclic	0	1	1		
Atypical	0	3	1		

Note: Values for mean ± SD. Degrees of freedom = 48 for all comparisons. WAIS-IV WMI = Wechsler Adult Intelligence Scale, Fourth Edition – Working Memory Index; HAM-D = Hamilton Depression Rating Scale; QIDS = Quick Inventory of Depressive Symptomology; STAI = State-Trait Anxiety Inventory; SSRI = Selective Serotonin Reuptake Inhibitor; SNRI = Serotonin and Norepinephrine Reuptake Inhibitor; Tricyclic = Tricyclic Antidepressant; Atypical = Atypical Antidepressant.

The experimental session began by recording participant demographics, assessing WM ability using the Working Memory Index from the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) (Wechsler, 2008), and conducting a clinical interview. Participants were then allocated by stratified randomisation into a stimulation groups: sham, tDCS, or tRNS. Stratified randomisation was based on age, sex, and WM ability (using the WAIS-IV WMI) to ensure balancing of key characteristics across stimulation groups. Participants were blinded to stimulation condition. Cognitive and electrophysiological data were collected prior to stimulation (BASELINE), at 5-minutes (POST-1), and at 25-minutes (POST-2) after stimulation had ended (see Fig. 1 for illustration of experimental session procedure). Although not reported in this paper, combined TMS-EEG recording was also completed before and at two timepoints post-stimulation (see Supplementary Materials for details).

2.3. Clinical interview

All clinical interviews and cognitive tasks were administered by a single researcher (OWM) trained in standardised administration. The Mini International Neuropsychiatric Interview (Sheehan et al., 1998) was used to confirm the presence of a current DSM-IV defined Major Depressive Episode and screen for other Axis 1 psychiatric disorders. Depression severity was assessed using the Hamilton Depression Rating Scale, 17-item (HAM-D_{17}) (Hamilton, 1960) and the Quick Inventory of Depressive Symptomology – Clinician Rated, 16-item (QIDS-C) (Rush et al., 2003; Trivedi et al., 2004). State and trait anxiety levels were assessed using the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 2010). Baseline WM ability was assessed using the Working Memory Index from the WAIS-IV (Wechsler, 2008). Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

2.4. Transcranial electric stimulation

All stimulation conditions were delivered using an Eldith Stimulator Plus machine (NeuroConn, Germany) and a pair of rectangular 5x7 cm rubber electrodes (35 cm^2) attached to the scalp using Ten20 conductive paste (Weaver and Co., Colorado, USA). The anodal electrode was placed over the left DLPFC (F3 using the 10–20 system of electrode placement) and the cathodal electrode was placed over the right supraorbital area for all stimulation conditions (Bai et al., 2014; Hill et al., 2016; Hoy et al., 2013). Computational modelling confirmed that electric fields induced by tDCS and tRNS were maximal in the area proximal to the electrodes (see Supplementary Materials for further details). During stimulation participants completed an adaptive version of the Paced Auditory Serial Addition Task (PASAT) (Gronwall, 1977; Siegle et al., 2007), given evidence that concurrent cognitive activity during tES can induce more pronounced after-effects (Andrews et al., 2011).

Active tDCS was delivered at 1 mA (current density = 0.029 mA/cm^2) for a duration of 22-minutes (60 s ramp-up, 60 s ramp-down). The sham condition was delivered for a duration of 22-minutes and involved the delivery of active tDCS for a total of 2.5-minutes (60 s ramp-up, held constant at 1 mA for 30 s, 60 s ramp-down). This sham protocol typically produces an itching sensation under the electrodes during the initial ramping stages and has been shown to produce successful participant blinding (Boggio et al., 2008; Ferrucci et al., 2009; Murphy et al., 2020).

tRNS was delivered with an intensity of 1 mA and a 1 mA DC-offset for a duration of 22-minutes (60 s ramp-up, 60 s ramp-down). tRNS was delivered with a high frequency range (100–640 Hz) based on evidence that the resulting neuromodulatory effects are primarily caused by higher frequency oscillations (100–640 Hz) (Fertonani et al., 2011; Moret et al., 2019). When delivering tRNS, a random amplitude is generated for every sample within the pre-defined parameter space (i.e., with a 1 mA amplitude and 1 mA DC-offset). The random numbers used to determine the current amplitude were normally distributed and the probability of each frequency being selected followed a normal distribution so that all frequencies within the specified range have an equal probability of occurring at any given time during the stimulation session, thereby creating a white-noise frequency distribution (Terney et al., 2008). When delivered using these parameters, tRNS + DC-offset electrodes fluctuate in amplitude with a frequency which fluctuates randomly throughout the stimulation session, whilst maintaining a consistent polarity. This produces a unidirectional current flow from the positively-charged anode to the negatively-charged cathode. Moreover, the chosen stimulation parameters for tDCS and tRNS + DC-offset produce an equivalent average amplitude of 1 mA at each electrode over the course of the stimulation session, thereby allowing direct comparison of stimulation techniques whilst controlling for the potentially confounding effects of variability in net delivery of charge.

Participants were blinded to their stimulation condition. Immediately following tES, participants completed a side-effects questionnaire and a stimulation blinding integrity questionnaire which asked them to report whether they believed they had received active or sham stimulation.

2.5. Working memory tasks

2.5.1. Paced auditory serial addition task

An adaptive, computerised version of the PASAT was administered to participants during tES to promote engagement of fronto-parietal neurocircuitry involved in WM processing (Lazeron et al., 2003; Lockwood et al., 2004). Full details of the PASAT administration and procedure are outlined in the supplementary materials. In brief, the PASAT is a challenging mental arithmetic task in which participants are required to sum sequentially presented single-digit stimuli. We utilised an adaptive version of the PASAT (Siegle et al., 2007) which adjusts the rate of stimuli presentation based on participant performance, thereby ensuring

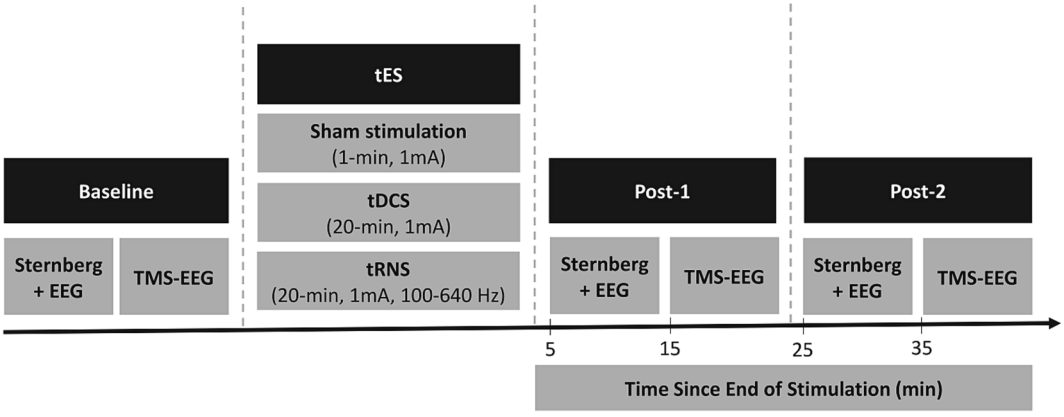


Fig. 1. Overview of experimental design and procedure.

that the task remains achievable yet cognitively challenging for all participants. Participants completed three, five-minute blocks of the PASAT, each separated by a one-minute rest period. The first block of the PASAT was begun after the initial one-minute ramping-up period for tES had ended.

2.5.2. Sternberg working memory task

Cognitive effects of tES were examined using a modified verbal Sternberg WM task presented with Neuroscan Stim2 software (Compumedics, Melbourne, Australia). The Sternberg WM task was selected as it temporally separates the encoding, maintenance, and retrieval aspects of WM processing and thereby allows examination of oscillatory activity associated with each WM phase (Jensen & Tesche, 2002; Jensen et al., 2002; Segrave et al., 2010). We used a modified version of the Sternberg WM task in which participants are presented with a memory set containing eight letters (Segrave et al., 2010). The memory set is then removed for a maintenance period, and participants are then presented with a probe letter and indicate using a button press whether the probe was present or absent in the memory set (see Fig. 2 for Sternberg WM task design and stimuli timing). Participants completed a total of 52 trials presented in two blocks with a 30 s break between blocks, resulting in a total task duration of 11 min. Participants were instructed to keep their eyes open during the maintenance period of the task, given the strong modulatory effect that closing the eyes can have on alpha power (Barry et al., 2007). Further task details are included in the supplementary materials.

2.6. Electrophysiological recording and pre-processing

A detailed methodological description of EEG setup, recording, and data pre-processing can be found in the supplementary materials. In brief, EEG was obtained from 34 Ag/AgCl scalp electrodes and four facial electrodes using Neuroscan Acquire software and a Synamps 2 amplifier (Compumedics, Melbourne Australia). Impedances were regularly checked after each EEG recording and kept below 5 kΩ throughout the experiment. Electrodes were grounded to AFz and referenced online to an electrode between Cz and CPz. EEG was sampled at 1000 Hz with an online bandpass filter of 0.1–100 Hz. Data was analysed offline in MATLAB (The Mathworks, Natick, MA) using EEGLAB for pre-processing (sccn.ucsd.edu/eeglab) (Delorme & Makeig, 2004) and fieldtrip for frequency analysis (https://www.ru.nl/donders/fieldtrip) (Oostenveld et al., 2011).

2.7. Spectral analysis

EEG data was converted into the frequency domain using Morlet Wavelet Transform (3.5 oscillation cycles with steps of 1 Hz). Neural oscillatory power was calculated within the theta (4–7 Hz), upper alpha (10–12.5 Hz), and gamma (35–45 Hz) frequency bands. These frequency ranges were selected to correspond with previous research examining oscillatory activity during WM processing and the Sternberg task (Bailey et al., 2014; Hill et al., 2017; Hsieh et al., 2011; Roberts et al., 2013). Oscillatory power during WM processing was calculated as event-related synchronisation/desynchronisation (ERS/ERD%) using the formula: [(Active - Reference)/Reference) × 100)]. ERS/ERD% values reflect relative changes in oscillatory power between a pre-defined active and reference period, with positive values indicating increased oscillatory power within the active period (i.e., neural event related synchronisation). ERS/ERD% for each frequency band was calculated separately for the encoding (1800–5800 ms) and maintenance (5800–8800 ms) periods, with the middle 600 ms period of the blank screen between the fixation cross and memory set used as the reference period. Prior to analyses, the ERS/ERD% values were averaged over trials for each participant.

2.8. TMS-EEG setup and recording

Fifty consecutive monophasic TMS pulses were delivered over the F3 EEG electrode (chosen to approximate the location of the DLPFC) using a Magstim magnetic stimulator connected to a 70 mm figure-of-eight coil (MagStim Ltd., UK). Data from TMS-EEG is not included in the present paper but the procedure is outlined here for the sake of illustrating the experimental procedure completed by participants. TMS intensity was determined individually for each participant as 120% of their resting motor threshold (RMT). RMT was determined at the beginning of each experimental session immediately after EEG setup and was defined as the lowest stimulus intensity required to elicit motor evoked potentials in the right abductor pollicis brevis muscle of >0.05 mV in at least five out of ten consecutive trials (Rossini et al., 2015). Monophasic pulses were delivered with a five second inter-pulse interval and 10% jitter (Hill et al., 2017, 2018). Concurrent EEG was recorded throughout delivery of TMS pulses the same EEG setup and recording parameters as outlined in the current study, with the exception that TMS-EEG recording utilised a higher sampling rate of 10 KHz. RMT determination and delivery of TMS pulses were conducted by an appropriately trained researcher, and administration of TMS-EEG took approximately 4.5 min to complete.

2.9. Statistical analysis

All statistical analyses were performed using either MATLAB or IBM SPSS Statistics, version 26 (IBM Corp, Armonk, NY). Blinding integrity and side-effect frequency were compared between groups using Chi-square tests.

2.9.1. Cognitive data

Sternberg WM task accuracy and response time were used to examine effects on WM performance. Mixed ANOVAs were used to examine effects of tES on accuracy and response time, with CONDITION (sham, tDCS, and tRNS + DC-offset) as the between-subjects factor and TIME (BASELINE, POST-1, and POST-2) as the within-subjects factor. Any significant interaction effects between CONDITION and TIME were further explored using: i) separate repeated measures ANOVAS for each stimulation condition to examine changes over TIME (BASELINE, POST-1, and POST-2), and ii) one-way ANOVAs to compare differences in change-from-baseline scores (Δ-scores) (i.e., POST-1 – BASELINE = Δ-POST-1; POST-2 – BASELINE = Δ-POST-2) between stimulation conditions at each time-point (Δ-POST-1, Δ-POST-2). Any main effects

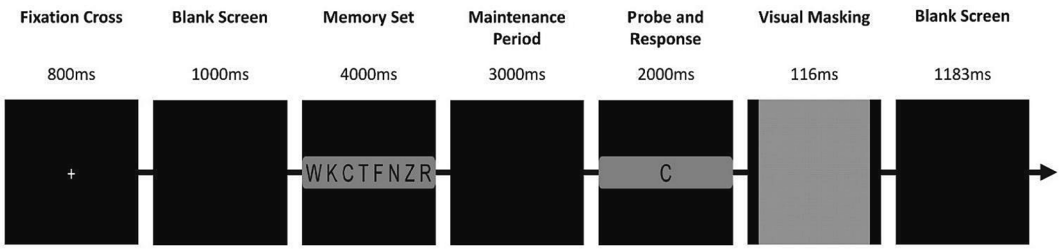


Fig. 2. Sequence and timing of stimuli for the Sternberg WM task.

for the repeated measure and one-way ANOVAS were further examined using pairwise comparisons with Bonferroni correction. Normality of the cognitive data was confirmed via inspection of skewness and kurtosis on histograms and Q-Q plots. Mauchly's test was used to evaluate the assumption of sphericity, with Greenhouse-Geisser corrections applied where appropriate.

2.9.2. EEG data

Changes in oscillatory ERS/ERD% over time were examined via nonparametric cluster-based permutation analyses using the Fieldtrip toolbox (Oostenveld et al., 2011). This technique allows examination of changes in ERS/ERD% across all EEG electrodes whilst controlling for the rate of multiple comparison (Maris & Oostenveld, 2007) and has been used previously for examining effects of tES on oscillatory activity (e.g. Hill et al., 2017, 2018). Clusters were defined as two or more neighbouring electrodes with a t-statistic < 0.05 and two-tailed Monte Carlo p-values were calculated using 2000 permutations. While cluster-based analyses within Fieldtrip are well-suited for controlling the multiple-comparison rate inherent when comparing multi-channel EEG data, these techniques do not allow mixed-model comparisons (e.g., 3x3 mixed model ANOVA with TIME and STIMULATION as independent variables). Therefore, cluster-based one-way repeated measure ANOVAs were first conducted separately for each stimulation group to examine changes in ERS/ERD% over TIME (BASELINE to POST-1 or POST-2) for each frequency range. Significant main effects were further examined using Δ-scores to explore whether changes in ERS/ERD% significantly differed between stimulation conditions.

3. Results

3.1. Demographic and clinical measures

The stimulation groups did not significantly differ in age, years of formal education, WM ability, state or trait anxiety, or depression severity (see Table 1 for demographic and clinical characteristics of the participants). One-way ANOVAs confirmed that stimulation conditions were matched at BASELINE and did not significantly differ in Sternberg WM task accuracy or response time (both $p > .05$), or theta, upper alpha, or gamma power during WM encoding and maintenance (all $p > .05$).

3.2. Effects of tES on Sternberg WM task performance

Effects of tES on WM performance were examined using separate mixed model ANOVAs for Sternberg WM task accuracy and response time.

The mixed-model ANOVA for response time on the Sternberg WM task revealed no significant main effect for stimulation condition ($F(2,46) = 0.172$, $p = .843$, $\eta_p^2 = 0.007$), and no significant interaction effect for time and stimulation condition ($F(4,92) = 1.901$, $p = .117$, $\eta_p^2 = 0.076$) (Table 2). No further comparisons were conducted for response time due to the lack of a significant interaction effect.

The mixed model ANOVA for accuracy on the Sternberg WM task revealed a significant interaction effect for time and stimulation condition ($F(4,92) = 2.705$, $p = .035$, $\eta_p^2 = 0.105$), but did not reveal a significant main effect of stimulation condition ($F(2,46) = 0.029$, $p = .971$, $\eta_p^2 = 0.001$). To further explore this significant interaction effect, repeated measures ANOVAs were conducted for each stimulation condition to examine changes in accuracy over time (Fig. 3). Accuracy for the sham group significantly increased from BASELINE to POST-1 (mean difference = 5.54, $p = .009$), and from BASELINE to POST-2 (mean difference = 5.66, $p = .034$). The tDCS group displayed significant increases in accuracy from BASELINE to POST-1 (mean difference = 5.77, $p = .035$), and from BASELINE to POST-2 (mean difference = 6.85, $p = .018$). Finally, the tRNS + DC-offset group displayed a significant increase in accuracy from BASELINE to POST-1 (mean difference = 5.41, $p = .019$), but accuracy did not differ between BASELINE and POST-2 (mean difference = 0.60, $p = .999$).

Differences in the effects of tES stimulation conditions on Sternberg WM task accuracy were further explored by comparing change-from-baseline scores between stimulation conditions. Between-group comparisons indicated that stimulation conditions did not significantly differ in their effects on accuracy from BASELINE to POST-1 ($F(2,48) = 0.010$, $p = .990$, $\eta_p^2 < 0.001$) (Fig. 4A). Significant differences were observed in the effects of stimulation condition from BASELINE to POST-2 ($F(2,48) = 3.743$, $p = .031$, $\eta_p^2 = 0.140$) (Fig. 4B). Specifically, the tDCS group displayed significantly greater improvements in accuracy from BASELINE to POST-2 when compared to the tRNS + DC-offset group (mean difference = 7.452, $p = .044$), whereas no differences were observed between the tDCS and sham group (mean difference = 1.195, $p > .999$), or the tRNS + DC-offset and sham group (mean difference = 6.257, $p = .107$) (Fig. 4B).

Table 2
Response time on the Sternberg WM task for sham, tDCS, and tRNS + DC-offset groups.

	BASELINE	POST-1	POST-2
Sham	1125.66 ± 153.55	1025.49 ± 143.55	1057.02 ± 115.78
tDCS	1103.95 ± 139.20	1040.39 ± 156.56	982.03 ± 145.38
tRNS + DC-offset	1105.38 ± 168.32	1034.83 ± 135.81	1027.91 ± 139.51

Note: Values reflect mean ± SD of response time (ms).

3.3. Effects of tES on oscillatory activity during working memory processing

3.3.1. Within-group comparisons

3.3.1.1. Sham. Examination of EEG activity for the sham group did not reveal any significant changes over time for theta, upper alpha, or gamma ERS/ERD% during the WM encoding or maintenance periods.

3.3.1.2. tDCS. Examination of EEG activity over time for the tDCS group revealed significant changes in upper alpha ERS/ERD% during the WM maintenance period. EEG recorded 5-minutes post-stimulation (POST-1) revealed a significant increase in WM maintenance period upper alpha ERS% bilaterally over parieto-occipital regions (Fig. 5). The tDCS group also displayed significant increases in WM maintenance upper alpha ERS% on EEG recorded 25-minutes post-stimulation (POST-2), which was localised over left frontal regions ($p = .026$) and bilaterally over parieto-occipital regions ($p < .001$) (Fig. 6). The tDCS group did not display any significant changes in encoding period upper alpha ERS/ERD% from BASELINE to POST-1 or POST-2, nor were any significant changes observed in encoding or maintenance period theta or gamma ERS/ERD% from BASELINE to POST-1 or POST-2 (all p's > 0.05).

3.3.1.3. tRNS. The tRNS + DC-offset group displayed a significant increase in WM maintenance period upper alpha ERS% over right-frontal regions from BASELINE to POST-2 ($p = .029$) (Fig. 7). The tRNS + DC-offset group did not display any significant changes in encoding period upper alpha ERS/ERD% from BASELINE to POST-1 or POST-2, nor were any significant changes in encoding or maintenance period theta or gamma ERS/ERD% observed from BASELINE to POST-1 or POST-2 (all $p > .05$).

3.3.2. Between-group comparisons

When compared to the sham group, the tDCS group displayed significantly larger increases in WM maintenance period parieto-occipital upper alpha ERS% from BASELINE to POST-1 ($p = .018$) (Fig. 8A), and from BASELINE to POST-2 ($p = .030$) (Fig. 8B). In contrast, changes in maintenance period upper alpha ERS/ERD% did not

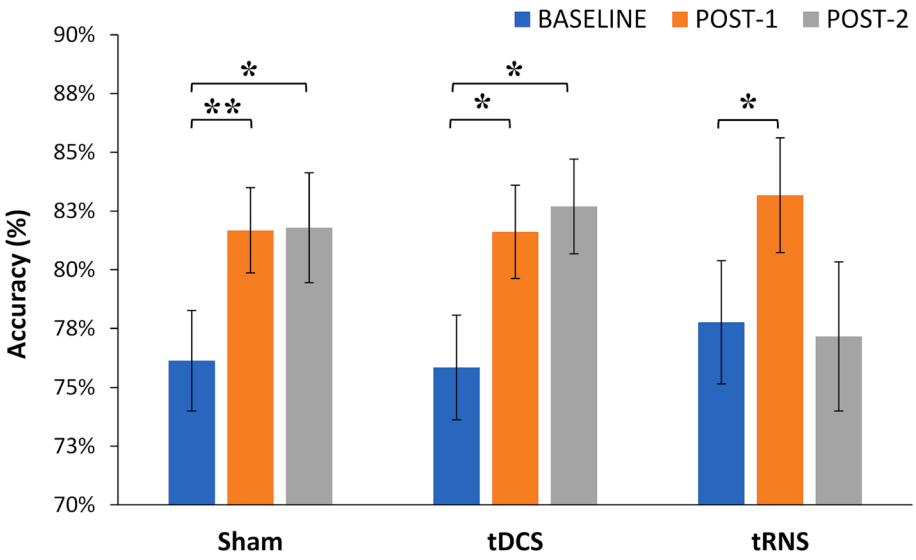


Fig. 3. Accuracy on the Sternberg WM task across the three timepoints (BASELINE, POST-1, POST-2). Error bars denote standard error of the mean. * $p < .05$. ** $p < .01$.

significantly differ between the tRNS + DC-offset and sham groups at POST-1 or POST-2 (all $p > .05$).

3.4. tES tolerability and blinding integrity

All stimulation conditions were well tolerated, and no significant, prominent, or persistent adverse effects were reported. Twenty-three of the 49 participants (46.94%) reported minor adverse effects whilst receiving tES, including: slight itching or discomfort under the electrode (15 participants), mild burning sensation (4 participants), or a mild headache (4 participants). There was no significant difference in the reporting of side-effects between the three stimulation conditions (all $p > .05$).

Participants were unable to guess at better than chance level whether they had received active or sham stimulation (χ^2 (1, N = 49), = 1.289, $p = .525$), indicating that adequate blinding of stimulation conditions was maintained.

4. Discussion

We report evidence from the first sham-controlled direct comparison of tDCS and tRNS + DC-offset on cognitive and electrophysiological measures of WM in MDD. Contrary to our hypotheses, neither tDCS nor tRNS + DC-offset improved WM performance when compared to the sham stimulation. However, tDCS demonstrated greater improvements in WM accuracy than the tRNS + DC-offset condition at 25-minutes post-stimulation. When examining the neurophysiological effects of the stimulation conditions separately, both tDCS and tRNS + DC-offset significantly increased upper alpha ERS% during the WM maintenance period, whereas no significant changes in oscillatory activity were observed following sham stimulation. When comparing these oscillatory changes between stimulation conditions, tDCS induced sustained increases in upper alpha ERS% over parieto-occipital regions during the WM maintenance period, which remained significant when compared to sham stimulation. Effects of tRNS + DC-offset on oscillatory activity were not significant when compared to sham. These findings demonstrate the capacity of tDCS to induce alterations in WM-related neurophysiological activity which persist beyond the end of stimulation. However, the absence of significant improvements in or relationships to WM performance indicated that these neurophysiological effects were not sufficient to reliably enhance cognitive function in this small, cognitively high-functioning sample of individuals with MDD.

4.1. Effects of tES on working memory performance

Examination of cognitive performance indicated subtle yet significant improvements in WM accuracy for all stimulation conditions, including sham. The tDCS and sham groups demonstrated significant improvements in WM accuracy on immediate and delayed cognitive testing. WM accuracy for the tRNS + DC-offset group increased immediately following stimulation and then returned to pre-stimulation levels on delayed testing. Importantly, neither tDCS nor tRNS + DC-offset improved WM performance to a significantly greater degree than sham stimulation, indicating that these improvements reflect practice effects rather than stimulation effects. Contrary to our hypothesis, direct comparison of active stimulation conditions during the delayed testing period revealed that tDCS improved WM accuracy to a significantly greater degree than tRNS + DC-offset.

Our findings contract with several previous studies in MDD which observed increases in WM performance following a single sessions of tDCS (Boggio et al., 2007; Martin et al., 2018; Moreno et al., 2015; Oliveira et al., 2013; Wolkenstein & Plewnia, 2013). Despite some positive findings, the cognitive effects of tDCS are known to be highly variable between studies and individuals for both healthy and clinical populations (Ciullo et al., 2021; Figeys et al., 2021; Hill et al., 2016; Koo et al., 2023). This variability is influenced by a complex interaction between stimulation parameters (e.g. current density, duration, number of sessions, etc.) and individual characteristics (e.g. age, sex, baseline performance, skull thickness, presence of psychiatric illness, etc.) (Chew et al., 2015; Figeys et al., 2021; Koo et al., 2023; Li et al., 2015). Stimulation parameters, in particular the variation in current density (i.e., the ratio of injected current divided by the surface area of stimulation electrodes; mA/cm^2), may have influenced the discrepant results of our study. We delivered tDCS with a low current density (0.029 mA/cm^2) that has previously been shown to enhance WM performance in healthy individuals (e.g. Andrews et al., 2011; Fregni et al., 2005; Jeon & Han, 2012; Ohn et al., 2008), and those with MDD (Fregni et al., 2006). However, some meta-analytic evidence indicates that higher current densities may be more effective for enhancing WM performance in clinical populations such as MDD (Hill et al., 2016), raising the possibility that the density delivered in the present study was insufficient to induce reliable WM improvements. Still, large variability exists in studies of the cognitive effects of tDCS even when delivering a higher current density. For instance, several studies have reported enhanced WM performance in MDD when delivering tDCS with higher current

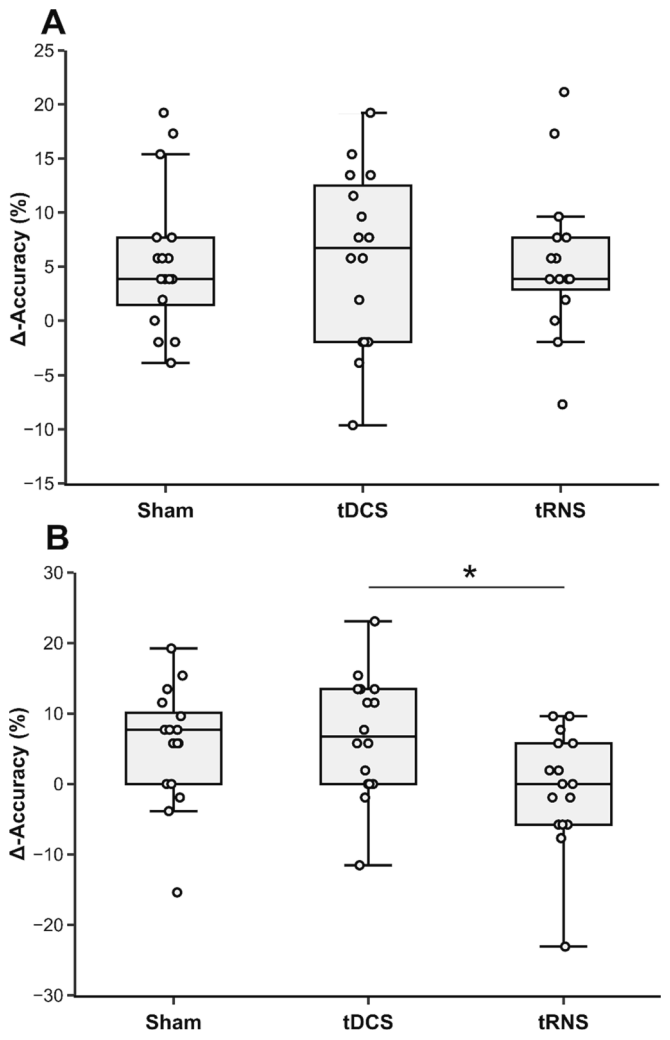


Fig. 4. Box-and-whisker plots showing change-from-baseline scores (Δ-scores) for Sternberg WM task accuracy at POST-1 (A) and POST-2 (B). Individual participant data points are overlaid (hollow circles). Boxes extend from the 25th to 75th percentiles with the median represented by a horizontal line. Significant differences between groups are highlighted with an asterisk (* $p < .05$).

densities (0.057–0.080 mA/cm^2) (Boggio et al., 2007; Loo et al., 2012; Moreno et al., 2015; Oliveira et al., 2013), whereas others have failed to replicate these findings (Brunoni et al., 2016; Loo et al., 2010; Martin et al., 2018; Wolkenstein & Plewnia, 2013). Regardless, our findings indicate that delivery of tDCS using the parameters implemented in this study is insufficient to induce reliable enhancements of WM performance in MDD.

We found that a single session of tRNS + DC-offset to the left DLPFC did not induce any significant changes in WM performance when compared to sham stimulation. To date, two sham-controlled studies have examined the effects of tRNS in MDD (Nikolin et al., 2020; Schecklmann et al., 2021). Nikolin et al. (2020) reported the results of a randomised clinical trial delivering four weeks of tRNS + DC-offset in individuals with MDD, finding that changes in depressive symptom severity did not differ between tRNS and sham. The study also did not observe significant effects of tRNS + DC-offset treatment on a battery of neuropsychological measures, including those assessing WM. Similar null findings were reported by Schecklmann et al. (2021), with a three-week course of bifrontal tRNS without a DC-offset failing to demonstrate superiority over sham stimulation as an add-on treatment for reducing clinical symptom severity in MDD. This study also did not observe any significant changes in measures of cognitive functioning, including WM. Our findings provide further evidence that a single session of prefrontal tRNS + DC-offset does not produce observable improvements in WM functioning in MDD.

Our findings are broadly consistent with research in healthy individuals by Mulquiney et al. (2011), who reported that a single session of anodal tDCS improved WM performance, whereas no significant improvements were observed following tRNS. In contrast to Mulquiney et al., however, we delivered tRNS with a DC-offset which resulted in a consistent polarity at each electrode, thereby delivering consistent polarisation of neural membrane potentials whilst also introducing noise into the neural system via random fluctuations in current intensity (Ho et al., 2015). Interestingly, we previously observed contrasting results when delivering tRNS + DC-offset in healthy individuals using the same stimulation parameters, with tRNS + DC-offset increasing WM performance to a significantly greater degree than both anodal tDCS and sham stimulation (Murphy et al., 2020). These contrasting findings may relate to state-dependent effects of tRNS, whereby stimulation protocols which demonstrate efficacy in healthy populations may induce different cognitive and neurophysiological effects when delivered in MDD (e.g. Gögler et al., 2017; Moreno et al., 2015). Hence, while we did not observe significant WM improvements following a single session of tRNS + DC-offset, further research is warranted to investigate whether tRNS may induce more pronounced effects in MDD if delivered using different stimulation parameters from those that were effective in healthy individuals.

4.2. Effects of tES on oscillatory activity during working memory processing

We found that tDCS significantly increased upper alpha ERS% over parieto-occipital regions during the WM maintenance period. Upper alpha oscillations have been functionally linked to inhibitory processes which facilitate efficient cognitive processing via suppression of non-task relevant neural regions during cognitive activity (Klimesch et al., 2007; Klimesch, 2012; Zanto et al., 2011). Within this framework, increased posterior upper alpha ERS% during the maintenance phase of the Sternberg WM task following tDCS would indicate greater functional inhibition of visual processing regions which may interfere with the active maintenance of WM stimuli (Klimesch, 2012).

Interestingly, several previous studies have reported that individuals with MDD display abnormal modulation of upper alpha activity during the maintenance phase of the Sternberg WM task, which has been interpreted as indicating dysfunctional inhibitory processes in MDD (Bailey et al., 2014; Segrave et al., 2010). Moreover, we previously observed that the current cohort of participants with MDD displayed significantly less posterior upper alpha ERS% during WM maintenance when compared to a sample of healthy controls balanced on age, gender, and WM ability (Murphy et al., 2019). Given this, increases in maintenance period upper alpha ERS% following tDCS may indicate a shift towards normalisation of altered WM-related oscillatory activity in MDD. Indeed, evidence in healthy individuals has indicated that greater alpha power over parieto-occipital regions during WM maintenance predicts higher rates of subsequent recall (Khader et al., 2010). However, the absence of improvements in WM performance, or relationship between neurophysiological changes and WM performance, indicates that these neurophysiological changes were insufficient to produce observable enhancements in WM performance in the current participant group.

When examining the electrophysiological effects of tRNS + DC-offset over time we observed changes consistent with our hypothesis, reflected by increases in upper alpha during WM maintenance on EEG recorded 25-miuntes post-stimulation. However, these changes did not significantly differ from sham stimulation, indicating that delivery of tRNS + DC-offset with the current parameters was not sufficient to induce substantial or persistent changes in WM-related oscillatory activity in

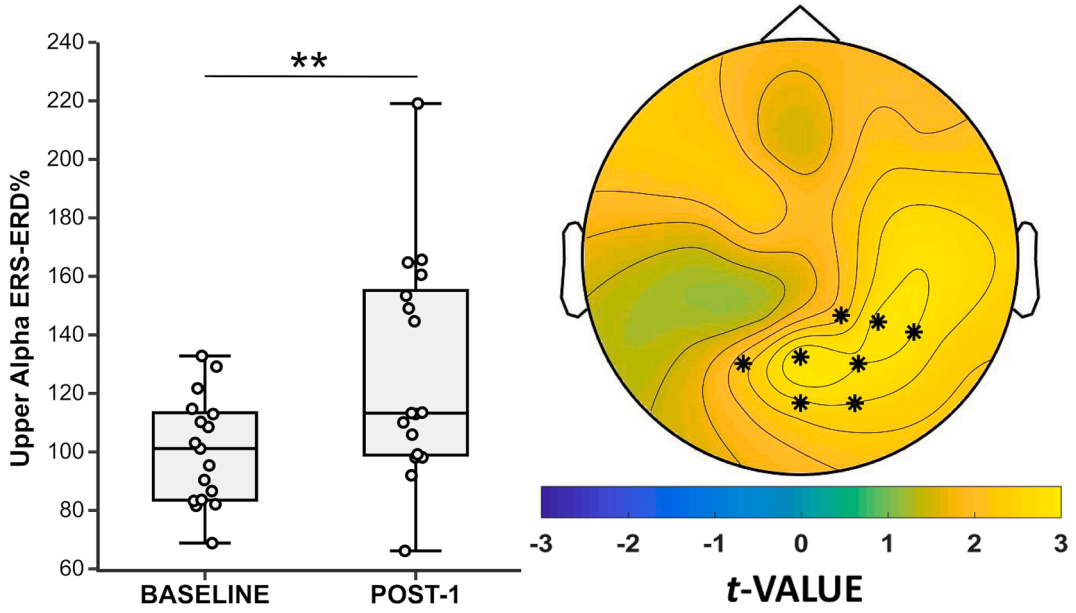


Fig. 5. Difference in maintenance period upper alpha ERS/ERD% from BASELINE to POST-1 for the tDCS group. Box-and-whisker plot displays upper alpha ERS/ERD% at BASELINE and POST-1 averaged across electrodes from the significant parieto-occipital cluster (**$p < .01$), with individual participant data points overlaid (hollow circles). Boxes extend from the 25th to 75th percentiles with the median represented by a horizontal line. Topographical map displays differences in oscillatory ERS/ERD% (POST-1 - BASELINE), with EEG electrodes forming significant clusters marked by stars ($p < .01$). *Note:* ERS-ERD% = Event-Related Synchronisation/Event-Related Desynchronisation.

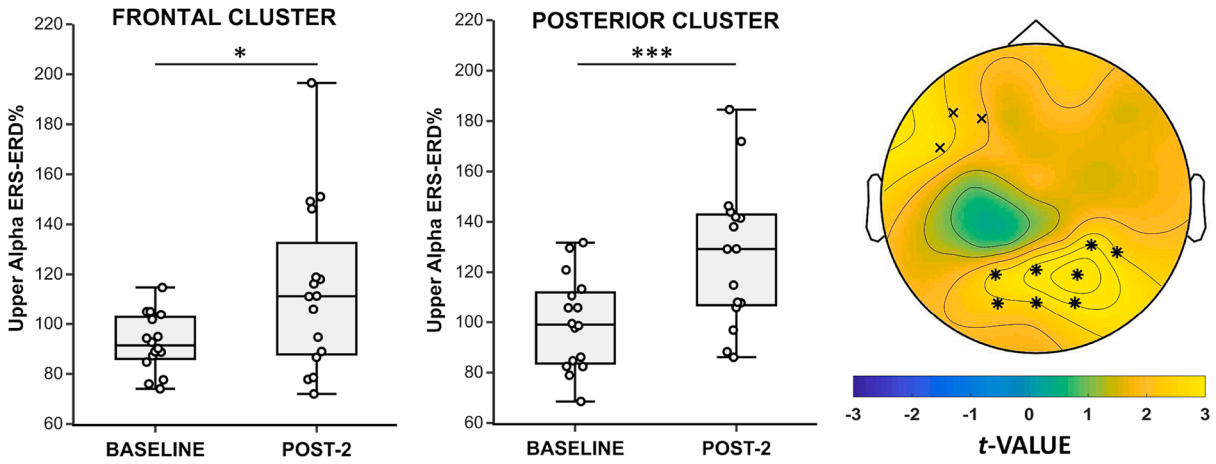


Fig. 6. Difference in maintenance period upper alpha ERS/ERD% from BASELINE to POST-2 for the tDCS group. Box-and-whisker plot displays upper alpha ERS/ERD% at BASELINE and POST-2 averaged across electrodes from the significant clusters (*$p < .05$, **$p < .01$, ***$p < .001$), with individual participant data points overlaid (hollow circles). Boxes extend from the 25th to 75th percentiles with the median represented by a horizontal line. Topographical map displays differences in oscillatory ERS/ERD% (POST-2 - BASELINE), with EEG electrodes forming significant clusters marked by black crosses ($p < .05$) and stars ($p < .01$). *Note:* ERS-ERD% = Event-Related Synchronisation/Event-Related Desynchronisation.

our current sample. This directly contrasts with previous research in healthy individuals showing that delivery of a single session of tRNS using identical stimulation parameters to the current study resulted in significant increases in WM encoding period theta and gamma ERS% when compared to both anodal tDCS and sham stimulation (Murphy et al., 2020). Given the large body of evidence demonstrating that individuals with MDD display altered patterns of neural oscillations during WM processing (Bailey et al., 2014; Murphy et al., 2019; Segrave et al., 2011), combined with evidence that effects of tES are dependent on the state of neural oscillations at the time of stimulation (e.g. Bradley et al., 2022; Hsu et al., 2016), it is perhaps unsurprising that delivering identical stimulation protocols in healthy and depressed populations may produce divergent effects. While the cognitive and neurophysiological outcomes of tES are known to be highly variable in healthy individuals, delivering these techniques in clinical conditions such as MDD raises further challenges due to the limited understanding of how tES interacts with MDD-related neural activity to produce observable cognitive improvements. Indeed, there is extremely limited information regarding the optimal tRNS stimulation parameters for modulating cognitive and neurophysiological outcomes in healthy individuals, and this evidence is entirely absent in MDD. Improving the effectiveness and reliability of tRNS as a therapeutic tool will therefore require further research examining the optimal stimulation parameters for modulating cognitive performance in MDD, as well as a greater understanding of the neurophysiological changes which underlie these cognitive improvements.

The neurophysiological effects of tRNS have been conceptualised with reference to the stochastic resonance phenomena, whereby the

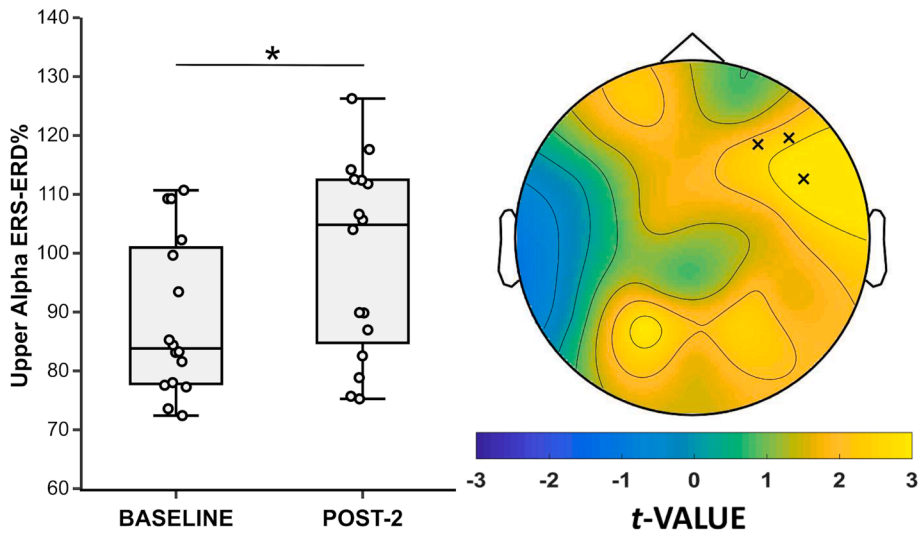


Fig. 7. Difference in maintenance period upper alpha ERS/ERD% from BASELINE to POST-2 for the tRNS + DC-offset group. Box-and-whisker plot displays upper alpha ERS/ERD% averaged across electrodes from the significant frontal cluster at BASELINE and POST-2 (*$p < .05$), with individual participant data points overlaid (hollow circles). Boxes extend from the 25th to 75th percentiles with the median represented by a horizontal line. Topographical map displays differences in oscillatory ERS/ERD% (POST-2 - BASELINE), with EEG electrodes forming significant clusters marked by black crosses ($p < .05$). *Note:* ERS-ERD% = Event-Related Synchronisation/Event-Related Desynchronisation.

introduction of random noise into a system serves to amplify the strength of signals across a range of frequencies, thereby increasing the signal-to-noise ratio of otherwise weak signals (Fertonani et al., 2011; Pavan et al., 2019). Within the context of a non-linear neural system, the effects of stochastic resonance are most prominent when the introduced random noise is sufficient to increase the amplitude of existing neural signals from sub-threshold to supra-threshold, thereby amplifying the otherwise weak signal to produce greater rates of neural firing. Consistent with this, experiments utilising tRNS to modulate auditory and visual perceptual thresholds have demonstrated that effects are most pronounced for near-threshold signals (Rufener et al., 2017; Van der Groen et al., 2018). However, there is considerable evidence that MDD is associated with abnormal oscillatory dynamics during WM processing, including reduced modulation of oscillatory power within theta, alpha, and gamma ranges (e.g. Bailey et al., 2014; Murphy et al., 2019; Segrave et al., 2011). As the effects of tRNS remain dependent on the state of the neural system during stimulation, the presence of reduced WM-related neural synchrony in MDD may limit the amplification of oscillatory power via tRNS. In our MDD participants, the neural signal may have been of insufficient strength relative to background neural noise, resulting in neural signal dynamics which are not suited for tRNS-induced amplification via stochastic resonance. Although speculative, this rationale is consistent with the state-dependence of tES effects and provides a potential mechanistic explanation for the variation in outcomes when delivering tRNS between healthy and MDD populations. It appears likely that, if tES is able to elicit more pronounced neurophysiological effects, the method will require tailoring stimulation parameters to match the altered neural dynamics associated with MDD. For example, given evidence that MDD is associated with reduced modulation of oscillatory power within theta, alpha, and gamma frequency ranges (Bailey et al., 2014; Murphy et al., 2019; Segrave et al., 2010), delivery of alternating current stimulation (tACS) at such frequencies may prove effective for entraining and facilitating oscillatory power in this population, potentially leading to more pronounced effects on cognitive functioning.

4.3. Limitations and future directions

Our findings should be considered with several limitations in mind. We adopted a between groups design with different participants in each stimulation condition, as opposed to a crossover design which can minimise potential inter-individual variability in response to tES (López-Alonso et al., 2014). The advantages of the between groups design, however, were minimisation of WM task practice effects and maximisation of the integrity of participant blinding to stimulation condition, given evidence that sham tES protocols are substantially less effective for subsequent stimulation sessions and crossover trials (O'connell et al., 2012). To account for potential effects of heterogeneity in individual characteristics between groups, we utilised stratified randomisation of participants to balance groups on key factors which contribute to inter-individual variability in tES outcome, including age, sex, and WM ability (Chew et al., 2015; López-Alonso et al., 2014). Future large-scale research studies using a within-groups design will allow for greater consideration of individual characteristics which influence the outcome of tES, and thereby better inform the factors contributing to variability in the cognitive and neurophysiological response to stimulation. Although we observed significant group-level differences in WM performance, the small size may have limited the statistical sensitivity to identify more subtle changes in these measures. To investigate this possibility, we conducted post-hoc Bayesian analyses to provide a more sensitive estimate of the probability that results of binary p-value tests (i.e., significant or non-significant) reflect true group differences. These post-hoc Bayesian tests on the cognitive data provided further support for the validity of the current results. An overview of the methodology and results of these analyses is presented in the Supplementary Materials.

The experimental session included recording of EEG and TMS-EEG before and after stimulation, and it is conceivable that this may have influenced the outcomes of the study. Firstly, it is possible that the electroconductive gel used to reduce EEG electrode impedance may also increase shunting of electrical current across the scalp during tES, thereby reducing the modulatory effects of stimulation on cortical regions. Importantly, however, we feel that this is unlikely to be responsible for the absence of significant effects on cognitive outcomes in the current study, as previous studies including both tDCS and EEG have observed significant improvements in cognitive functioning (Heimrath et al., 2014; Hoy et al., 2015; Murphy et al., 2020; Zaehle et al., 2011). Moreover, any such influence of the electroconductive gel is unlikely to introduce any confounding effect on the study outcomes, as any effects on electrical fields would presumably be equivalent across the

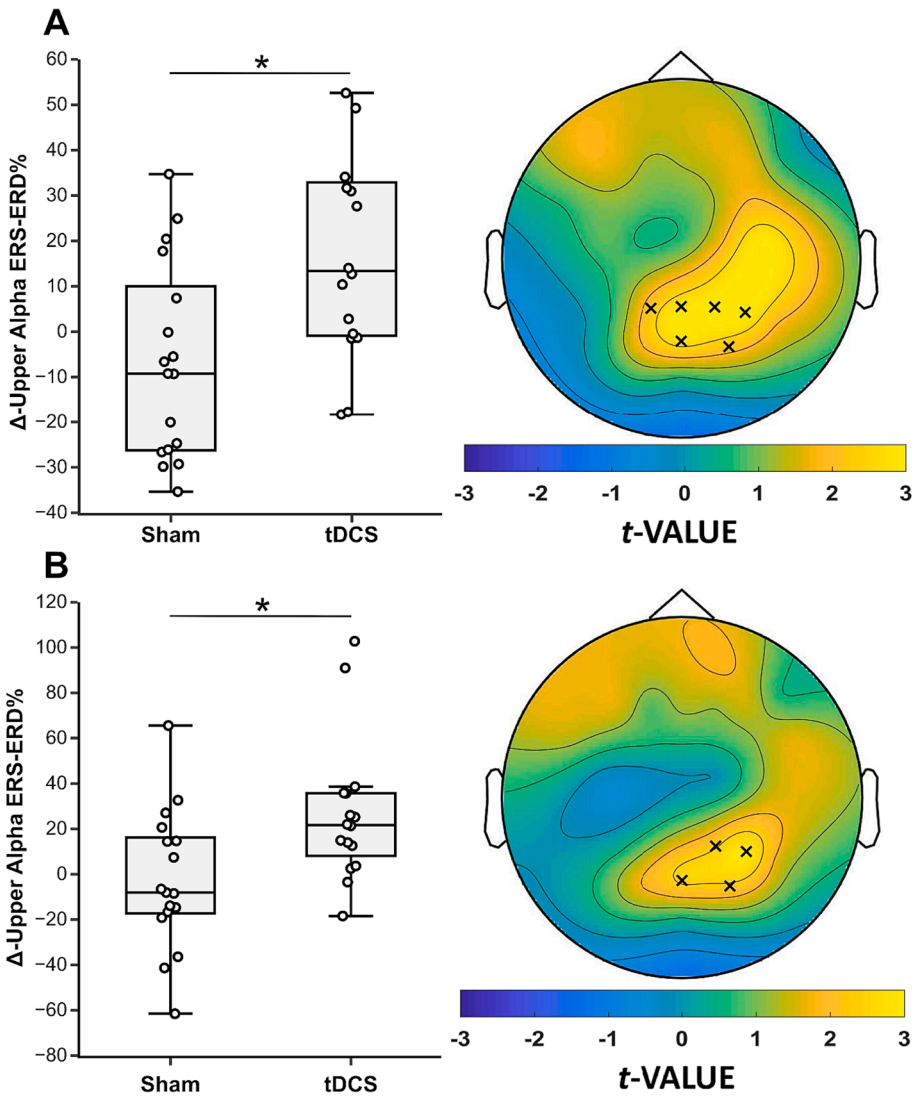


Fig. 8. Comparison of maintenance period Δ-upper alpha ERS/ERD% for the tDCS and sham conditions at POST-1 (A) and POST-2 (B). Box-and-whisker plot displays Δ-upper alpha ERS/ERD% averaged across electrodes from the significant cluster (*$p < .05$), with individual participant data points overlaid (hollow circles). Boxes extend from the 25th to 75th percentiles with the median represented by a horizontal line. Whiskers extend from the minimum to maximum values. Topographical maps display differences in oscillatory ERS/ERD% when comparing tDCS and sham at POST-1 (A) and POST-2 (B), with EEG electrodes forming significant clusters marked by black crosses ($p < .05$). *Note:* ERS-ERD% = Event-Related Synchronisation/Event-Related Desynchronisation.

stimulation conditions. Secondly, it is possible that the TMS pulses delivered during TMS-EEG could have induced subtle changes which influence the brain state prior to receiving tES (e.g., Pellicciari et al., 2016). Although conceivable, the relatively small number of pulses delivered (50 single-pulses for the TMS-EEG recording) and high inter-pulse interval (5 s) are typically considered to be insufficient to induce persistent effects on cortical excitability (Julkunen et al., 2012; Pell et al., 2011). Although subtle influences from TMS-EEG recording remain possible, the TMS-EEG procedure was held consistent across all experimental sessions and is therefore unlikely to contribute to the differential outcomes observed when delivering sham, tDCS, or tRNS + DC-offset.

Although WM impairments are a common neuropsychological symptom of MDD, the current participants performed at age-appropriate levels on standardised WM tasks at baseline (i.e., WAIS-IV WMI). This performance indicates a lack of major WM impairment under quiet test conditions and suggests a relatively high cognitively functioning sample. As cognitive enhancing effects of tDCS are more pronounced for individuals with lower abilities at baseline (Sarkar et al., 2014; Tseng et al., 2012), it remains possible that tDCS and tRNS may produce observable cognitive enhancing effects for people with MDD who are experiencing prominent cognitive impairments. It is also possible that ceiling effects on the modified Sternberg WM task may have reduced sensitivity for observing tES-induced improvements in the efficiency or accuracy of WM processing. We observed practice effects in WM task accuracy across timepoints, indicating sufficient sensitivity to observe significant changes in performance. However, the slope of these learning effects may have resulted in a smaller window for observing potential tES-induced improvements in WM performance. We used a modified Sternberg task as it allows examination of oscillatory activity within temporally separated phases of WM processing, however the inclusion of more sensitive measures of WM performance, such as the *n*-back task, may prove superior in identifying subtle improvements in cognitive functioning.

The current study delivered tES with a 1 mA current intensity (current density = 0.029 mA/cm^2) and it is possible that utilising a higher current density may have induced more pronounced outcomes. While there is some meta-analytic evidence that higher current densities (e.g., 0.058 mA/cm^2) may be more effective for enhancing WM performance in clinical populations such as MDD (Hill et al., 2016), this is contrasted

against evidence that higher current densities are also associated with more frequent side-effects and increased risk of compromised blinding of stimulation condition (Buchanan et al., 2021; O'connell et al., 2012; Wallace et al., 2016). There is also some evidence that higher current densities may also produce more inconsistent tDCS outcomes, such as an inversion in the direction of outcomes so that cathodal stimulation leads to a facilitation rather than inhibition of cortical excitability (Batsikadze et al., 2013). Despite these methodological limitations, further research is required to systematically investigate whether delivering tDCS and tRNS + DC-offset with higher current densities may produce more pronounced cognitive and neurophysiological outcomes in MDD.

5. Conclusions

In conclusion, we provide evidence that a single session of anodal tDCS to the left DLPFC induced sustained effects on WM-related oscillatory activity which persisted up to 25-minutes post-stimulation, reflected by increases in upper alpha ERS% during the WM maintenance phase. The neurophysiological effects of tDCS remained significant when compared to sham stimulation and were consistent across immediate and delayed EEG recordings. Despite this, tDCS did not enhance WM performance to a significantly greater degree than sham stimulation, indicating that these neurophysiological effects were insufficient to translate into observable cognitive improvements in this small, cognitively high-functioning sample. We also found that delivery of tRNS using the current stimulation parameters did not induce significant changes in cognitive or neurophysiological measures of WM when compared to sham stimulation. Our study supports the potential of tDCS to modulate WM-related neural activity in MDD, however further investigation is warranted to explore whether delivery of tDCS or tRNS techniques with alternative stimulation parameters or repeated sessions may produce more pronounced neurophysiological alterations and observable improvements in WM performance in MDD.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: In the last three years PBF has received equipment for research from Neurosoft, Nexstim and Brainsway Ltd. PBF has served on scientific advisory boards for Magstim and LivaNova and acted as a founder and board member for TMS Clinics Australia and Resonance Therapeutics. All other authors have no conflicts to report.

Data availability

The authors do not have permission to share data.

Acknowledgements

This work was supported by a National Health and Medical Research Council (NHMRC) fellowship held by RAS (1036201). OWM was supported by an Australian Government Research Training Program (RTP) Scholarship. PBF is supported by an NHMRC Practitioner Fellowship (1078567). KEH was supported by an NHMRC Fellowship (1135558). We are grateful to A/Prof Greg Siegle for generously providing access to the adaptive PASAT.

Appendix A. Supplementary material

Supplementary methods and results for this article can be found online at https://doi.org/10.1016/j.bandc.2023.106105.

References

Andrews, S. C., Hoy, K. E., Enticott, P. G., Daskalakis, Z. J., & Fitzgerald, P. B. (2011). Improving working memory: The effect of combining cognitive activity and anodal transcranial direct current stimulation to the left dorsolateral prefrontal cortex. *Brain Stimulation, 4*(2), 84–89.

Bai, S., Dokos, S., Ho, K.-A., & Loo, C. (2014). A computational modelling study of transcranial direct current stimulation montages used in depression. *NeuroImage, 87*, 332–344.

Bailey, N. W., Segrave, R. A., Hoy, K. E., Maller, J. J., & Fitzgerald, P. B. (2014). Impaired upper alpha synchronisation during working memory retention in depression and depression following traumatic brain injury. *Biological Psychology, 99*, 115–124. https://doi.org/10.1016/j.biopsycho.2014.03.008

Barry, R. J., Clarke, A. R., Johnstone, S. J., Magee, C. A., & Rushby, J. A. (2007). EEG differences between eyes-closed and eyes-open resting conditions. *Clinical Neurophysiology, 118*(12), Article 12. https://doi.org/10.1016/j.clinph.2007.07.028

Batsikadze, G., Moliadze, V., Paulus, W., Kuo, M.-F., & Nitsche, M. A. (2013). Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. *The Journal of Physiology, 591*(7), 1987–2000.

Boggio, P. S., Bermpohl, F., Vergara, A. O., Muniz, A. L. C. R., Nahas, F. H., Leme, P. B., … Fregni, F. (2007). Go-no-go task performance improvement after anodal transcranial DC stimulation of the left dorsolateral prefrontal cortex in major depression. *Journal of Affective Disorders, 101*(1–3), 91–98. https://doi.org/10.1016/j.jad.2006.10.026

Boggio, P. S., Rigonatti, S. P., Ribeiro, R. B., Myczkowski, M. L., Nitsche, M. A., Pascual-Leone, A., & Fregni, F. (2008). A randomized, double-blind clinical trial on the efficacy of cortical direct current stimulation for the treatment of major depression. *International Journal of Neuropsychopharmacology, 11*(2), Article 2.

Boonstra, T. W., Nikolin, S., Meisener, A.-C., Martin, D. M., & Loo, C. K. (2016). Change in mean frequency of resting-state electroencephalography after transcranial direct current stimulation. *Frontiers in Human Neuroscience, 10*, 270.

Bradley, C., Nydam, A. S., Dux, P. E., & Mattingley, J. B. (2022). State-dependent effects of neural stimulation on brain function and cognition. *Nature Reviews Neuroscience*, 1–17.

Brunoni, A. R., Ferrucci, R., Bortolomasi, M., Scelzo, E., Boggio, P. S., Fregni, F., … Priori, A. (2013). Interactions between transcranial direct current stimulation (tDCS) and pharmacological interventions in the major depressive episode: Findings from a naturalistic study. *European Psychiatry, 28*(6), Article 6.

Brunoni, A. R., Tortella, G., Benseñor, I. M., Lotufo, P. A., Carvalho, A. F., & Fregni, F. (2016). Cognitive effects of transcranial direct current stimulation in depression: Results from the SELECT-TDCS trial and insights for further clinical trials. *Journal of Affective Disorders, 202*, 46–52.

Buchanan, D. M., Bogdanowicz, T., Khanna, N., Lockman-Dufour, G., Robaey, P., & D'Angiulli, A. (2021). Systematic review on the safety and tolerability of transcranial direct current stimulation in children and adolescents. *Brain Sciences, 11*(2), 212.

Chew, T., Ho, K.-A., & Loo, C. K. (2015). Inter-and intra-individual variability in response to transcranial direct current stimulation (tDCS) at varying current intensities. *Brain Stimulation, 8*(6), Article 6.

Ciullo, V., Spalletta, G., Caltagirone, C., Banaj, N., Vecchio, D., Piras, F., & Piras, F. (2021). Transcranial direct current stimulation and cognition in neuropsychiatric disorders: Systematic review of the evidence and future directions. *The Neuroscientist, 27*(3), 285–309.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), Article 1.

Dunkin, J. J., Leuchter, A. F., Cook, I. A., Kasl-Godley, J. E., Abrams, M., & Rosenberg-Thompson, S. (2000). Executive dysfunction predicts nonresponse to fluoxetine in major depression. *Journal of Affective Disorders, 60*(1), Article 1.

Ferrucci, R., Bortolomasi, M., Brunoni, A. R., Vergares, M., Tadini, L., Giacopuzzi, M., & Priori, A. (2009). Comparative benefits of transcranial direct current stimulation (tDCS) treatment in patients with mild/moderate vs. severe depression. *Clinical Neuropsychiatry, 6*(6), Article 6.

Fertonani, A., Pirulli, C., & Miniussi, C. (2011). Random noise stimulation improves neuroplasticity in perceptual learning. *Journal of Neuroscience, 31*(43), 15416–15423.

Figeys, M., Zeeman, M., & Kim, E. S. (2021). Effects of transcranial direct current stimulation (tDCS) on cognitive performance and cerebral oxygen hemodynamics: A systematic review. *Frontiers in Human Neuroscience, 15*, Article 623315.

Fregni, F., Boggio, P. S., Nitsche, M., Bermpohl, F., Antal, A., Feredoes, E., … Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research, 166*(1), 23–30. https://doi.org/10.1007/s00221-005-2334-6

Fregni, F., Boggio, P. S., Nitsche, M. A., Marcolin, M. A., Rigonatti, S. P., & Pascual-Leone, A. (2006). Treatment of major depression with transcranial direct current stimulation. *Bipolar Disorders, 8*(2), Article 2.

Friehs, M. A., & Frings, C. (2019). Offline beats online: Transcranial direct current stimulation timing influences on working memory. *Neuroreport, 30*(12), 795–799.

Gögler, N., Willacker, L., Funk, J., Strube, W., Langgartner, S., Napiórkowski, N., … Finke, K. (2017). Single-session transcranial direct current stimulation induces enduring enhancement of visual processing speed in patients with major depression. *European Archives of Psychiatry and Clinical Neuroscience, 267*(7), Article 7.

Gronwall, D. M. A. (1977). Paced auditory serial-addition task: A measure of recovery from concussion. *Perceptual and Motor Skills, 44*(2), Article 2.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry, 23*(1), Article 1.

Heimrath, K., Kuehne, M., Heinze, H.-J., & Zaehle, T. (2014). Transcranial direct current stimulation (tDCS) traces the predominance of the left auditory cortex for processing of rapidly changing acoustic information. *Neuroscience, 261*, 68–73. https://doi.org/10.1016/j.neuroscience.2013.12.031

Herrera-Guzmán, I., Gudayol-Ferré, E., Herrera-Abarca, J. E., Herrera-Guzmán, D., Montelongo-Pedraza, P., Blázquez, F. P., … Guàrdia-Olmos, J. (2010). Major depressive disorder in recovery and neuropsychological functioning: Effects of selective serotonin reuptake inhibitor and dual inhibitor depression treatments on residual cognitive deficits in patients with major depressive disorder in recovery. *Journal of Affective Disorders, 123*(1), Article 1.

Hill, A. T., Fitzgerald, P. B., & Hoy, K. E. (2016). Effects of anodal transcranial direct current stimulation on working memory: A systematic review and meta-analysis of findings from healthy and neuropsychiatric populations. *Brain Stimulation, 9*(2), 197–208. https://doi.org/10.1016/j.brs.2015.10.006

Hill, A. T., Rogasch, N. C., Fitzgerald, P. B., & Hoy, K. E. (2017). Effects of prefrontal bipolar and high-definition transcranial direct current stimulation on cortical reactivity and working memory in healthy adults. *NeuroImage, 152*, 142–157. https://doi.org/10.1016/j.neuroimage.2017.03.001

Hill, A. T., Rogasch, N. C., Fitzgerald, P. B., & Hoy, K. E. (2018). Effects of single versus dual-site High-Definition transcranial direct current stimulation (HD-tDCS) on cortical reactivity and working memory performance in healthy subjects. *Brain Stimulation*.

Ho, K.-A., Taylor, J. L., & Loo, C. K. (2015). Comparison of the effects of transcranial random noise stimulation and transcranial direct current stimulation on motor cortical excitability. *The Journal of ECT, 31*(1), 67–72.

Hoy, K. E., Bailey, N. W., Arnold, S. L., & Fitzgerald, P. B. (2015). The effect of transcranial Direct Current Stimulation on gamma activity and working memory in schizophrenia. *Psychiatry Research, 228*(2), 191–196. https://doi.org/10.1016/j.psychres.2015.04.032

Hoy, K. E., Emonson, M. R., Arnold, S. L., Thomson, R. H., Daskalakis, Z. J., & Fitzgerald, P. B. (2013). Testing the limits: Investigating the effect of tDCS dose on working memory enhancement in healthy controls. *Neuropsychologia, 51*(9), 1777–1784.

Hsieh, L.-T., Ekstrom, A. D., & Ranganath, C. (2011). Neural oscillations associated with item and temporal order maintenance in working memory. *Journal of Neuroscience, 31*(30), Article 30.

Hsu, T.-Y., Juan, C.-H., & Tseng, P. (2016). Individual differences and state-dependent responses in transcranial direct current stimulation. *Frontiers in Human Neuroscience, 10*, 643.

Hsu, T.-Y., Tseng, P., Liang, W.-K., Cheng, S.-K., & Juan, C.-H. (2014). Transcranial direct current stimulation over right posterior parietal cortex changes prestimulus alpha oscillation in visual short-term memory task. *NeuroImage, 98*, 306–313.

Inukai, Y., Saito, K., Sasaki, R., Tsuiki, S., Miyaguchi, S., Kojima, S., … Onishi, H. (2016). Comparison of three non-invasive transcranial electrical stimulation methods for increasing cortical excitability. *Frontiers in Human Neuroscience, 10*, 668.

Jensen, O., Gelfand, J., Kounios, J., & Lisman, J. E. (2002). Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. *Cerebral Cortex, 12*(8), 877–882.

Jensen, O., & Tesche, C. D. (2002). Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience, 15*(8), 1395–1399.

Jeon, S. Y., & Han, S. J. (2012). Improvement of the working memory and naming by transcranial direct current stimulation. *Annals of Rehabilitation Medicine, 36*(5), Article 585. https://doi.org/10.5535/arm.2012.36.5.585

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition and Emotion, 24*(2), Article 2.

Julkunen, P., Säisänen, L., Hukkanen, T., Danner, N., & Könönen, M. (2012). Does second-scale intertrial interval affect motor evoked potentials induced by single-pulse transcranial magnetic stimulation? *Brain Stimulation, 5*(4), 526–532.

Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Chatterji, S., Lee, S., Ormel, J., … Wang, P. S. (2009). The global burden of mental disorders: An update from the WHO World Mental Health (WMH) surveys. *Epidemiology and Psychiatric Sciences, 18*(1), 23–33.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*(6), 593–602.

Khader, P. H., Jost, K., Ranganath, C., & Rösler, F. (2010). Theta and alpha oscillations during working-memory maintenance predict successful long-term memory encoding. *Neuroscience Letters, 468*(3), Article 3.

Klimesch, W. (2012). Alpha-band oscillations, attention, and controlled access to stored information. *Trends in Cognitive Sciences, 16*(12), 606–617. https://doi.org/10.1016/j.tics.2012.10.007

Klimesch, W., Sauseng, P., & Hanslmayr, S. (2007). EEG alpha oscillations: The inhibition–timing hypothesis. *Brain Research Reviews, 53*(1), 63–88. https://doi.org/10.1016/j.brainresrev.2006.06.003

Koo, G. K., Gaur, A., Tumati, S., Kusumo, R. W., Bawa, K. K., Herrmann, N., … Lanctôt, K. L. (2023). Identifying factors influencing cognitive outcomes after anodal transcranial direct current stimulation in older adults with and without cognitive impairment: A systematic review. *Neuroscience & Biobehavioral Reviews*, Article 105047.

Lazeron, R. H., Rombouts, S. A., de Sonneville, L., Barkhof, F., & Scheltens, P. (2003). A paced visual serial addition test for fMRI. *Journal of the Neurological Sciences, 213*(1–2), Article 1–2.

Li, L. M., Uehara, K., & Hanakawa, T. (2015). The contribution of interindividual factors to variability of response in transcranial direct current stimulation studies. *Frontiers in Cellular Neuroscience, 9*. https://doi.org/10.3389/fncel.2015.00181

Lockwood, A. H., Linn, R. T., Szymanski, H., Coad, M. L., & Wack, D. S. (2004). Mapping the neural systems that mediate the Paced Auditory Serial Addition Task (PASAT). *Journal of the International Neuropsychological Society, 10*(1), Article 1.

Loo, C. K., Alonzo, A., Martin, D., Mitchell, P. B., Galvez, V., & Sachdev, P. (2012). Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. *The British Journal of Psychiatry, 200*(1), Article 1.

Loo, C. K., Sachdev, P., Martin, D., Pigot, M., Alonzo, A., Malhi, G. S., … Mitchell, P. (2010). A double-blind, sham-controlled trial of transcranial direct current stimulation for the treatment of depression. *International Journal of Neuropsychopharmacology, 13*(1), Article 1.

López-Alonso, V., Cheeran, B., Río-Rodríguez, D., & Fernández-del-Olmo, M. (2014). Inter-individual variability in response to non-invasive brain stimulation paradigms. *Brain Stimulation, 7*(3), 372–380. https://doi.org/10.1016/j.brs.2014.02.004

Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG-and MEG-data. *Journal of Neuroscience Methods, 164*(1), Article 1.

Martin, D. M., Moffa, A., Nikolin, S., Bennabi, D., Brunoni, A. R., Flannery, W., … Loo, C. K. (2018). Cognitive effects of transcranial direct current stimulation treatment in patients with major depressive disorder: An individual patient data meta-analysis of randomised, sham-controlled trials. *Neuroscience & Biobehavioral Reviews, 90*, 137–145. https://doi.org/10.1016/j.neubiorev.2018.04.008

Miller, J., Berger, B., & Sauseng, P. (2015). Anodal transcranial direct current stimulation (tDCS) increases frontal–midline theta activity in the human EEG: A preliminary investigation of non-invasive stimulation. *Neuroscience Letters, 588*, 114–119. https://doi.org/10.1016/j.neulet.2015.01.014

Moreno, M. L., Vanderhasselt, M.-A., Carvalho, A. F., Moffa, A. H., Lotufo, P. A., Benseñor, I. M., & Brunoni, A. R. (2015). Effects of acute transcranial direct current stimulation in hot and cold working memory tasks in healthy and depressed subjects. *Neuroscience Letters, 591*, 126–131. https://doi.org/10.1016/j.neulet.2015.02.036

Moret, B., Donato, R., Nucci, M., Cona, G., & Campana, G. (2019). Transcranial random noise stimulation (tRNS): A wide range of frequencies is needed for increasing cortical excitability. *Scientific Reports, 9*(1), 1–8.

Mulquiney, P. G., Hoy, K. E., Daskalakis, Z. J., & Fitzgerald, P. B. (2011). Improving working memory: Exploring the effect of transcranial random noise stimulation and transcranial direct current stimulation on the dorsolateral prefrontal cortex. *Clinical Neurophysiology, 122*(12), 2384–2389. https://doi.org/10.1016/j.clinph.2011.05.009

Murphy, O. W., Hoy, K. E., Wong, D., Bailey, N. W., Fitzgerald, P. B., & Segrave, R. A. (2019). Individuals with depression display abnormal modulation of neural oscillatory activity during working memory encoding and maintenance. *Biological Psychology, 148*, Article 107766.

Murphy, O. W., Hoy, K. E., Wong, D., Bailey, N. W., Fitzgerald, P. B., & Segrave, R. A. (2020). Transcranial random noise stimulation is more effective than transcranial direct current stimulation for enhancing working memory in healthy individuals: Behavioural and electrophysiological evidence. *Brain Stimulation, 13*(5), 1370–1380.

Nikolin, S., Alonzo, A., Martin, D., Gálvez, V., Buten, S., Taylor, R., … Loo, C. K. (2020). Transcranial random noise stimulation for the acute treatment of depression: A randomized controlled trial. *International Journal of Neuropsychopharmacology, 23*(3), 146–156.

Nikolin, S., Martin, D. M., Loo, C. K., & Boonstra, T. W. (2018). Effects of TDCS dosage on working memory in healthy participants. *Brain Stimulation, 11*(3), Article 3.

O'connell, N. E., Cossar, J., Marston, L., Wand, B. M., Bunce, D., Moseley, G. L., & De Souza, L. H. (2012). *Rethinking clinical trials of transcranial direct current stimulation: Participant and assessor blinding is inadequate at intensities of 2mA*.

Ohn, S. H., Park, C.-I., Yoo, W.-K., Ko, M.-H., Choi, K. P., Kim, G.-M., … Kim, Y.-H. (2008). Time-dependent effect of transcranial direct current stimulation on the enhancement of working memory. *Neuroreport, 19*(1), 43–47.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9*(1), Article 1.

Oliveira, J. F., Zanão, T. A., Valiengo, L., Lotufo, P. A., Benseñor, I. M., Fregni, F., & Brunoni, A. R. (2013). Acute working memory improvement after tDCS in antidepressant-free patients with major depressive disorder. *Neuroscience Letters, 537*, 60–64. https://doi.org/10.1016/j.neulet.2013.01.023

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience, 2011*, 1.

Pavan, A., Ghin, F., Contillo, A., Milesi, C., Campana, G., & Mather, G. (2019). Modulatory mechanisms underlying high-frequency transcranial random noise stimulation (hf-tRNS): A combined stochastic resonance and equivalent noise approach. *Brain Stimulation, 12*(4), 967–977.

Pell, G. S., Roth, Y., & Zangen, A. (2011). Modulation of cortical excitability induced by repetitive transcranial magnetic stimulation: Influence of timing and geometrical parameters and underlying mechanisms. *Progress in Neurobiology, 93*(1), 59–98.

Pellicciari, M. C., Miniussi, C., Ferrari, C., Koch, G., & Bortoletto, M. (2016). Ongoing cumulative effects of single TMS pulses on corticospinal excitability: An intra-and inter-block investigation. *Clinical Neurophysiology, 127*(1), 621–628.

Raskin, J., Wiltse, C. G., Siegal, A., Sheikh, J., Xu, J., Dinkel, J. J., … Mohs, R. C. (2007). Efficacy of duloxetine on cognition, depression, and pain in elderly patients with major depressive disorder: An 8-week, double-blind, placebo-controlled trial. *American Journal of Psychiatry, 164*(6), Article 6.

Roberts, B. M., Hsieh, L.-T., & Ranganath, C. (2013). Oscillatory activity during maintenance of spatial and temporal information in working memory. *Neuropsychologia, 51*(2), Article 2.

Rossini, P. M., Burke, D., Chen, R., Cohen, L. G., Daskalakis, Z., Di Iorio, R., … George, M. S. (2015). Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an IFCN Committee. *Clinical Neurophysiology*, *126*(6), 6.

Roux, F., Wibral, M., Mohr, H. M., Singer, W., & Uhlhaas, P. J. (2012). Gamma-band activity in human prefrontal cortex codes for the number of relevant items maintained in working memory. *Journal of Neuroscience, 32*(36), Article 36.

Rufener, K. S., Ruhnau, P., Heinze, H.-J., & Zaehle, T. (2017). Transcranial random noise stimulation (tRNS) shapes the processing of rapidly changing auditory information. *Frontiers in Cellular Neuroscience, 11*, 162.

Rush, A. J., Trivedi, M. H., Ibrahim, H. M., Carmody, T. J., Arnow, B., Klein, D. N., … Manber, R. (2003). The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): A psychometric evaluation in patients with chronic major depression. *Biological Psychiatry, 54*(5), Article 5.

Sarkar, A., Dowker, A., & Kadosh, R. C. (2014). Cognitive enhancement or cognitive cost: Trait-specific outcomes of brain stimulation in the case of mathematics anxiety. *Journal of Neuroscience, 34*(50), Article 50.

Schecklmann, M., Nejati, V., Poeppl, T. B., Peytard, J., Rupprecht, R., Wetter, T. C., … Kreuzer, P. M. (2021). Bifrontal high-frequency transcranial random noise stimulation is not effective as an add-on treatment in depression. *Journal of Psychiatric Research, 132*, 116–122.

Segrave, R. A., Cooper, N. R., Thomson, R. H., Croft, R. J., Sheppard, D. M., & Fitzgerald, P. B. (2011). Individualized alpha activity and frontal asymmetry in major depression. *Clinical EEG and Neuroscience, 42*(1), 45–52.

Segrave, R. A., Thomson, R. H., Cooper, N. R., Croft, R. J., Sheppard, D. M., & Fitzgerald, P. B. (2010). Upper alpha activity during working memory processing reflects abnormal inhibition in major depression. *Journal of Affective Disorders, 127* (1–3), 191–198. https://doi.org/10.1016/j.jad.2010.05.022

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., … Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry*.

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*(2), Article 2.

Snyder, H. R. (2013). Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review. *Psychological Bulletin*, *139*(1), 1. doi: 10.1037/a0028727.

Spielberger, C. D., Gorsuch, R. L., Lushene, R. E., & Vagg, P. R. (2010). State-trait anxiety inventory (STAI). *BiB, 1970*, 180.

Stagg, C. J., & Nitsche, M. A. (2011). Physiological basis of transcranial direct current stimulation. *The Neuroscientist, 17*(1), 37–53. https://doi.org/10.1177/1073858410386614

Terney, D., Chaieb, L., Moliadze, V., Antal, A., & Paulus, W. (2008). Increasing human brain excitability by transcranial high-frequency random noise stimulation. *Journal of Neuroscience, 28*(52), 14147–14155.

Trivedi, M. H., Rush, A. J., Ibrahim, H. M., Carmody, T. J., Biggs, M. M., Suppes, T., … Dennehy, E. B. (2004). The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: A psychometric evaluation. *Psychological Medicine*, *34*(1), 1.

Tseng, P., Hsu, T.-Y., Chang, C.-F., Tzeng, O. J., Hung, D. L., Muggleton, N. G., … Juan, C.-H. (2012). Unleashing potential: Transcranial direct current stimulation over the right posterior parietal cortex improves change detection in low-performing individuals. *Journal of Neuroscience, 32*(31), 10554–10561.

Van der Groen, O., Tang, M. F., Wenderoth, N., & Mattingley, J. B. (2018). Stochastic resonance enhances the rate of evidence accumulation during combined brain stimulation and perceptual decision-making. *PLoS Computational Biology, 14*(7), Article e1006301.

Wallace, D., Cooper, N. R., Paulmann, S., Fitzgerald, P. B., & Russo, R. (2016). Perceived comfort and blinding efficacy in randomised sham-controlled transcranial direct current stimulation (tDCS) trials at 2 mA in young and older healthy adults. *PLoS One1, 11*(2), Article e0149703.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale-Fourth Edition (WAIS–IV)*. San Antonio, TX: The Psychological Corporation.

Wolkenstein, L., & Plewnia, C. (2013). Amelioration of cognitive control in depression by transcranial direct current stimulation. *Biological Psychiatry, 73*(7), Article 7.

Zaehle, T., Sandmann, P., Thorne, J. D., Jäncke, L., & Herrmann, C. S. (2011). Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: Combined behavioural and electrophysiological evidence. *BMC Neuroscience, 12*(1), Article 2.

Zanto, T. P., Rubens, M. T., Thangavel, A., & Gazzaley, A. (2011). Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. *Nature Neuroscience, 14*(5), Article 5.