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Efficacy of tACS in the enhancement of working memory performance in healthy adults: a systematic meta-analysis

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Abstract

Background: Transcranial alternating current stimulation (tACS)—a noninvasive brain stimulation technique that modulates cortical oscillations in the brain—has demonstrated the capacity to enhance working memory (WM) abilities in healthy individuals. The efficacy of tACS on the improvement of WM performance in healthy individuals is not yet fully understood.

Objective/Hypothesis: This meta-analysis aimed to systematically evaluate the efficacy of tACS in the enhancement of WM in healthy individuals and to assess moderators of response to stimulation. We hypothesized that active tACS would significantly enhance WM compared to sham. We further hypothesized that it would do so in a task-dependent manner, and that differing stimulation parameters would impact response to tACS.

Materials and Methods: Ten tACS studies met inclusion criteria and provided 32 effects in the overall analysis. Random effect models assessed mean change scores on WM tasks from baseline to post-stimulation. Included studies involved varied stimulation parameters, between-subject, and within-subject study designs, and online versus offline tACS.

Results: We observed a significant, heterogeneous, and moderate effect size for active tACS in the enhancement of WM performance over sham (Cohen's d=0.5). Cognitive load, task domain, session number, and stimulation region showed a significant relationship between active tACS and enhanced WM behavior over sham.

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Conclusions: Our findings indicate that active tACS enhances WM performance in healthy individuals compared to sham. Future randomized controlled trials are needed to further explore key parameters, including personalized stimulation versus standardized EEG frequencies, maintenance of tACS effects, and whether tACS-induced effects translate to populations with WM impairments.

Keywords

tACS; cortical oscillations; working memory; cognition; metaanalysis

Introduction

Working memory (WM)—the capacity for temporary storage and manipulation or reorganization of information held online—facilitates many higher-level cognitive functions (e.g., learning, language, problem solving)[1]. As a largely frontal lobe-mediated cognitive process, WM is linked to fluid intelligence and is involved in decision-making and goal-directed behaviors that are fundamental to everyday life[2,3]. Unfortunately, this critical cognitive ability typically declines with age, even among healthy older adults, which can negatively impact quality of life, limit functional independence, and increase mortality rates among the older adult population[4,5].

Recent years have witnessed growing interest in the use of noninvasive brain stimulation (NIBS) techniques as interventions aimed at cognitive enhancement, maintenance of cognition, or slowing of age-related cognitive changes[6-12]. Most WM NIBS studies to date have employed transcranial direct current stimulation (tDCS), which applies a direct current that impacts the resting membrane potential of neurons[13]. In contrast, transcranial alternating current stimulation (tACS) is a form of NIBS that safely and painlessly alters cortical oscillations, rhythmic patterns of electrophysiological activity of the brain, in a frequency-specific manner[14,15]. Similar to tDCS, tACS influences cortical excitability and brain activity but differs from tDCS by the application of an alternating sinusoidal electrical currents (in-phase or anti-phase) using electrodes placed over the scalp[16,17]. The mechanism of action involves entrainment of endogenous neural oscillations as a function of rhythmic shifts in membrane potentials to the set frequency of stimulation[18-22], differing from tDCS. Frequency of tACS can be applied at a standard value across participants or personalized (EEG-informed) to an individual's peak frequency of interest. TACS can synchronize (or desynchronize, depending on phase) neural oscillations to modulate cortical rhythms that underlie cognitive processes, manipulate brain activity, and impact behavior[23-25]. In addition to being dependent on phase and frequency of stimulation, effects of tACS on brain oscillations have also been shown to be task/state-dependent, in that the activities one engages in at the time of stimulation directly impact the effects elicited by stimulation[23,25-27]. Additionally, evidence suggests that multiple sessions of tACS entrainment can elicit enduring neuroplastic changes and subsequent physiologic and behavioral aftereffects[16,18,28,29], underscoring the therapeutic potential of tACS[15].

Neural oscillations play an important role in a variety of cognitive functions, including WM[27]. Mounting evidence from electroencephalography (EEG) and magnetoencephalography (MEG) studies demonstrates that WM is associated with synchronous activity across multiple frequency bands independently (e.g., theta, alpha, beta, and gamma) as well as cross-frequency coupling between theta and gamma (e.g., theta-nested gamma)[30-34]. Theta oscillations are thought to be involved in the organization of sequentially ordered WM items, whereas gamma band oscillations appear to correspond to general maintenance of WM information[35,36]. Prior research has suggested that crossfrequency coupling between low (theta) and high (gamma) frequencies enables processing of information held in WM, including the sequentially ordering and maintenance of stimuli[29,30,37,38]. Disruption of theta frequency has shown to impair working memory performance[39]. A growing body of research suggests that tACS can enhance cognitive processes that underlie WM function in healthy individuals[22,31,32,40,41]. For instance, a study in healthy participants found that tACS applied at individualized theta-frequency during a WM task increased short-term memory capacity in the active versus sham group[42]. Recent research has suggested that active frontotemporal theta tACS can enhance WM performance in healthy older adults to levels comparable to that of young adults[32]. There is also evidence that specific frequency bands are relevant to different features of WM, such as the positive association between gamma band frequency (>40 Hz) and performance at higher cognitive loads on WM tasks in healthy individuals[30,31,43,44]. The ability to manipulate cortical oscillations to a standardized frequency or personalized to an individual makes tACS a promising tool to alter brain activity that underlies cognition.

However, while studies employing tACS to enhance WM have shown promise, there exists variability in the response to tACS that is not yet well understood[45]. Moreover, the efficacy of tACS for enhancing WM in healthy individuals has not yet been explored in sufficiently large cohorts to be considered definitive. Therefore, the aim of this meta-analysis was to assess the efficacy of tACS on the enhancement of WM performance (e.g., accuracy or reaction time) in healthy participants. Potential moderators of treatment effects such as stimulation parameters (including frequency of stimulation, number of sessions, duration, stimulation region, subject-specific frequency versus standard frequency), WM task demands (e.g., cognitive load), verbal versus spatial tasks, and participant demographics were also explored, in order to determine potential moderator effects on tACS response. We hypothesized that active tACS versus sham would significantly enhance WM task performance and improve behavioral outcomes. We also hypothesized that tACS-induced effects on behavioral performance would be demonstrated in a task-dependent manner.

Materials and Methods

This systematic meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[46,47].

Literature search strategy

One reviewer (N.N.) carried out literature searches to identify studies assessing tACS in the context of WM performance in healthy individuals. Articles were identified through a computerized literature search using the following databases: Embase, PubMed, Web of Science, Cochrane Central Register of Controlled Trials, and clinicaltrials.gov. The following search terms were included for titles, abstracts, and keywords: “transcranial alternating current stimulation” OR “tACS” OR “oscillatory activity” AND “working memory” OR “executive function” OR “cognition”. The search was limited to published research articles between January 1960 and March 2022 written in English. Using this approach, we identified 509 articles from Embase, PubMed, Web of Science, Cochrane Central Register of Controlled Trials, and 24 records from ClinicalTrials.gov. The PRISMA flow diagram displays the procedures for study identification as seen in Figure 1. Additional thorough manual reviews of the articles were performed as described below.

Eligibility: inclusion/exclusion

Articles were eligible for inclusion if the studies they reported met the following criteria: (1) enrolled healthy human subjects; (2) involved administration of tACS either online or offline (e.g., during or before behavioral assessments); (3) assessed WM performance before, during or after stimulation; (4) had more than two participants. Between-subject studies with active versus sham trials and baseline data were included, in addition to within-subject crossover study designs. The rationale for requiring pre- and post-stimulation data was to increase the validity and stability of working memory performance across studies that assessed different cognitive aspects of working memory and included heterogeneous stimulation protocols. The following factors excluded articles from meta-analysis: (1) case studies of a single participant; (2) studies involving clinical populations; (3) review articles; (4) studies involving non-alternating waveforms of transcranial electrical stimulation (tES); (5) studies that involved pharmacological or other additional interventions; or (6) studies that assessed tACS only in motor or sensory contexts. Common reasons for excluding articles were duplication within the literature search, tACS applications in non-cognitive domains, studies involving other brain stimulation techniques, review articles, or limited statistical reporting (e.g., conference abstracts).

Literature data extraction

Manuscripts (titles, abstracts, and full texts) were independently screened by four of the authors (N.N., D.M., S.E., and A.P.). Any disagreements during the selection process were resolved through collaborative discussion and consensus. The final selected studies are summarized in Table 1 and study demographics in Table 2. For articles that met inclusion criteria, the following information was extracted: author and publication year, study design, sample size, participant demographics (e.g., age, sex and education when reported), cognitive task, cognitive domain of the task (i.e., verbal versus spatial WM task), mean performance and SDs (accuracy and/or reaction time) at baseline, during tACS, or post-stimulation to calculate change score, and stimulation parameters including duration, frequency band, number of sessions, electrode location and size, region of stimulation (i.e., frontal versus parietal versus frontoparietal versus frontotemporal), hemisphere (i.e., bilateral versus left versus right), and personalized versus standard frequency.

Data Analyses

The Comprehensive Meta-Analysis software (CMA v3.0; www.meta-analysis.com) was used to perform analyses. To account for heterogeneity across studies due to differences in methods and sample characteristics, the random effects model approach was used for all analyses[48]. The main outcome measures, accuracy, or reaction time on WM assessments, were defined as the mean percent correct response or mean latency (ms) determined from the change score (baseline to post-stimulation). For all studies, change in performance was calculated by comparing the mean accuracy or latency achieved before versus during or after active and/or sham stimulation. If the means and standard deviations (SDs) were not reported, effect sizes were calculated from reported univariate *F*-tests, *t*-statistics, or *p*-values. In the event studies reported that active versus sham differences were not statistically significant, but did not report the direction of the effect, the direction was coded as negative to provide more conservative effect size estimates. Effect sizes were classified as small ($d \geq 0.20$), medium ($d \geq 0.5$) or large ($d \geq 0.80$), corresponding to previous conventions[49]. To determine if statistical significance was achieved, confidence intervals (CI) and *z*-transformations of the effect size were used. The criterion for statistical significance was achieved for mean effects within the 95% CI which did not span zero, providing evidence that tACS has a reproducible, robust effect on WM in healthy adults. Cochran Q-statistic, which computes the sum of the squared deviations from each study's estimate from the overall meta-analysis estimate[50], was used to assess how much of the total variability could be attributed to heterogeneity amongst the selected studies or whether variations in findings were due to chance alone[51]. Behavioral performance was analyzed across 32 effects in an overall omnibus analysis spanning different WM tasks. The following data assignments were used across all effects: paired groups (difference, *p*), paired groups (N, *t*-value), independent groups (means, SDs). The number of effects are defined as *k;* Cohen's d is defined as *d*.

To assess factors that might influence response to tACS, we explored moderator variables that might impact behavioral outcomes in sub-group moderator analyses. Performance was assessed further on behavioral tasks with multiple effects. The following categorical variables were examined: WM task domains (3 levels: identifying letters (verbal) versus spatial location versus object recognition (nonverbal), cognitive load on N-Back task (1-Back versus 2-Back versus 3-Back versus 2-Back over 1-Back), accuracy versus reaction time, study design (between-subject versus within-subject), stimulation frequency (Hz), number of sessions (1 versus 2 versus 4), stimulated hemisphere (bilateral versus left versus right), stimulation region (frontal versus parietal versus frontoparietal versus frontotemporal), and online versus offline task performance. Meta-regression was performed to explore characteristics of continuous variables, including stimulation duration, and participant demographics (mean age, education, % female versus male).

Publication bias was evaluated by visual assessment of the funnel plot, which provides a graphic scatter plot of the effect size estimates from each study plotted against the result. A relatively symmetrical funnel plot indicates absence of publication bias, whereas an asymmetrical shape indicates bias between the included studies[52]. Egger's regression was used to quantify a statistical measure of the funnel plot[53]. An adjusted rank-correlation test was calculated according to the methods of Begg and Mazumdar[54]. The classic fail-safe N was used as a measure to identify the number of additional negative studies that would be needed to negate the current findings[55].

Results

From the initial database search, we identified 10 articles[31,32,56-63] that met our inclusion criteria and provided 32 effects (*k=32)* included in the meta-analysis. All articles involved tACS, with 16 effects involving subject-specific frequency and 16 effects set at a standard frequency. The overall sample size across all effects included n=695 healthy participants that underwent tACS during WM task performance (online) or tACS in between task assessments (offline). Study details are shown in Table 1.

Effects across all tACS studies and WM tasks: Omnibus analysis

The omnibus analysis of overall effects from active tACS across all WM tasks resulted in a significant and moderate improvement in behavioral performance over sham (k=32; d=0.514; 95% CI=0.349–0.680; z=6.105; p=0.0001). Analysis of homogeneity indicated that specific study effect sizes were significantly heterogeneous (Q-stat=91.47; df=32; p=0.0001). Given the variability across tasks, study-specific effect sizes, and differences in tACS parameters, moderator analyses were performed to better account for the observed heterogeneity. The study statistics and corresponding forest plot for the omnibus analysis are provided in Figure 2.

Moderator Analyses

Effect of cognitive load: N-Back task—Assessment of cognitive load and its relationship with tACS revealed a significant difference such that 2-Back over 1-Back demonstrated the greatest effect (k=1, d=1.709, 95% CI=0.822–2.597, $p<0.0001$), followed by 2-Back (k=4, d=1.067, 95% CI=0.376–1.76, p=0.002), 1-Back (k=2, d=0.839, 95% CI=0.373–1.304, $p<0.0001$), and 3-Back (k=2 d=0.072, 95% CI=−0.53–0.67, p=0.813) (Q-stat=10.32; df=3; p=0.02). This suggests that tACS effects on WM behavior are beneficial for the more challenging 2-Back over 1-Back condition, but do not reliably influence the highest-level difficulty (i.e., 3-Back ($p>0.05$)).

Task domains: verbal, spatial, and object—Analysis of WM task domains included three levels: verbal, spatial, and object. We defined verbal tasks as those that employed language-related stimuli, including single letters. Spatial tasks tested subjects on the location of visual stimuli, while object tasks tested recognition of sequentially presented visual stimuli. Active tACS had a significant and larger improvement in verbal WM tasks (k=16; d=0.720; 95% CI=0.498–0.942) relative to tasks testing spatial location (k=6; d=0.321; 95% CI=−0.154–0.796) and object recognition (k=5; d=0.238; 95% CI=−0.095–0.571) (Q-stat=6.520; df=2; p=0.04).

Task accuracy versus reaction time—Contrasts assessing accuracy (k=25; d=0.622; 95% CI=0.453–0.790) versus reaction time (k=7; d=−0.008; 95% CI=−0.247–0.231) revealed that accuracy was significantly and moderately enhanced from active tACS, whereas reaction time (d=0.622) slowed as a function of stimulation (p=0.0001).

Number of tACS sessions—Contrasts assessing number of sessions indicated a significant, heterogeneous result suggesting that higher number of sessions imparts greater benefit to WM behavior for active over sham stimulation (4 sessions: k=2; d=0.750; 95% CI=0.435–1.063; 2 sessions: k=14; d=0.735; 95% CI=0.454–1.016; 1 session: k=16; d=0.301; 95% CI=0.109–0.494) (Q-stat=9.211; df=2; p=0.01).

Target region of stimulation—Contrasts assessing stimulation region revealed a significant effect between parietal, frontal, frontoparietal, and frontotemporal (k=15, 5, 8, 4, respectively) where parietal received the most benefit (d=0.742), followed by frontal (d=0.479), frontoparietal (d=0.255), and frontotemporal stimulation (d=0.202) (Q-stat=9.082; df=3; p=0.03).

Non-significant Moderator Variables—Nonsignificant moderator variables, included: 1. Study design type (within-subject, k=24; between-subject, k=8) (Q-stat=0.001, df=1; p=0.973); 2. Online (k=17) versus offline (k=15) performance (Q-stat=0.782; df=1; p=0.38); 3. Waveform phase–in-phase (k=28) versus anti-phase (k=2) (Q-stat=1.559; df=1; p=0.212); 4. Frequency (Hz) between 4–40 Hz range (Q-stat=2.848; d=6; p=0.83); 5. Personalized (Hz) (k=16) versus standard frequency (k=16) (Q-stat=0.470; df=1; p=0.50); 6. Electrode type (conventional versus HD-tACS) (Q-stat=1.104; df=1; p=0.30). 7. Stimulation hemisphere (bilateral versus left versus right; k=5, 17, 10) (Q-stat=0.133; df=2; p=0.071).

Meta-regression for continuous variables—No significant differences were observed for stimulation duration (12-, 15-, 20-, 25-minutes) (z=−1.33; p=0.19). Participant demographics did not reveal significant moderation of effect size by age (z=−1.10; p=0.27) (mean age=30.56 years; range=20.5–69.6) or education (z=−1.22; p=0.22; mean education=16.7 years). Also, young (k=26) versus older adults (k=6) was not a significant moderating variable (p=0.364). Meta-regression revealed a significant moderation of effect size by percentage of female versus male participants (z=1.95; p=0.05), suggesting that studies with a higher number of females may benefit more from active tACS over sham.

Publication bias—Evaluation of publication bias revealed significant Begg (1-tailed p=0.0003) and Egger (1-tailed p=0.00018) tests, indicating the possibility of bias within this sample of literature. Trim-and-fill analyses identified five putative outlier effects. If excluded, they only minimally reduced the omnibus effect size (d=0.34)[49,64,65]. Finally, the calculation of the classic fail-safe N indicated that 573 negative or "null" results would be needed to negate the present findings. Figure 3 displays the funnel plot for all included studies.

Discussion

This systematic meta-analysis explored the efficacy of tACS on the enhancement of WM performance in healthy adults. Results revealed a significant, heterogeneous positive effect of active tACS in improving WM performance over sham. A prior meta-analysis assessed tACS on visual cognition[41] but assessed different cognitive domains with no pooled effect size. [22]This meta-analysis extends the literature by assessing the effectiveness of tACS on WM behavioral performance and factors that might modulate stimulation effects, which to our knowledge, has not been the primary focus of prior meta-analyses. In sub-analyses, we explored potential moderator variables that could impact tACS response including task-dependent effects, variations in stimulation parameters and participant demographics. Collectively, these data suggest that active tACS may enhance WM performance in healthy individuals over sham.

As we predicted, a task-dependent effect of tACS was identified on the N-Back task, suggesting cognitive load may be important for stimulation response. The load effect was specific to 2-Back over 1-Back condition (which targets attention but lacks the manipulation aspects of WM) while the 3-Back condition was not significant. This indicates that capacity of tACS-induced enhancement may depend on the nature of the task, with limits that might relate to WM network ceiling effects, given the nonsignificant 3-Back condition. Previous research has demonstrated that task-dependent effects of tES cognitive enhancements relate to the nature and cognitive load of the task being performed during stimulation[6,31,66,67]; this finding is also corroborated with state-dependent effects of tACS (i.e., physiological state and fluctuations in neural activity) that have been suggested to occur in the motor system[25]. These results also align with functional neuroimaging evidence demonstrating that neural activation of WM related brain regions correlates with the cognitive demands of a task[68,69].

Verbal and nonverbal WM tasks are supported by different neural processes[70], which could be differentially affected by tACS. Thus, we examined differences in task domain as potential moderating factors across three levels (verbal, spatial, and object stimuli). We identified significantly larger improvements on verbal compared to spatial and object recognition tasks. Prior neuroimaging studies point to hemispheric lateralization between verbal versus spatial WM in left hemisphere (LH) versus right hemisphere (RH), respectively[71]. As site specific effects may alter the impact of tACS for different WM subdomains, our results should be interpreted cautiously; very few studies in our analysis compared performance on the same behavioral task paired with stimulation at different sites.

Given the bihemispheric network of brain regions that are known to subserve WM, we examined hemisphere and stimulation region as moderator variables. Stimulation region was a significant moderator for active tACS—parietal lobe had the strongest effect on WM behavior followed by frontal, frontoparietal, and frontotemporal. Hemisphere of stimulation (LH, RH, bilateral) did not significantly moderate tACS effects. The parietal region is understood to be an essential node in the WM network[72] with involvement in short-term storage and retrieval of phonologically coded verbal information[73]. Patients with superior parietal lesions exhibit deficits when WM tasks require manipulation of information and show normal performance on rehearsal/retrieval processes, which indicates the critical nature of the parietal lobe during manipulation of WM information[72]. Our results suggest that parietal tACS is associated with improvement in several WM functions. This indicates that stimulation to other brain regions may be less effective. These findings underscore the importance of determining appropriate and optimal targets for WM task enhancement via tACS.

Across all effects, accuracy and reaction time were impacted by active stimulation over sham; accuracy significantly improved, whereas reaction time, a proxy for processing speed, slowed in response to stimulation. This is broadly consistent with prior research exploring tACS for cognitive remediation in healthy older adults, wherein accuracy, but not reaction time, has been shown to be enhanced by active stimulation[32]. This is also consistent with prior studies employing tDCS[6,74]. However, the finding could represent a speed-accuracy tradeoff whereby, due to the WM benefits induced by stimulation, individuals are able to respond with fewer errors, but at the cost of responding more slowly[75].

Stimulation parameters including number of sessions and frequency (Hz) (standardized versus personalized (Hz)), are important factors that can impact tACS response. Consistent with previous studies[76-78], we found that number of sessions (4 versus 2 versus 1) significantly moderated response to stimulation; a higher number of sessions associated with more robust effects. This finding may relate to underlying mechanisms of neuroplasticity; studies of tES have shown that repeated sessions of stimulation may produce stable long-term changes in neuroplasticity via mechanisms like long-term potentiation (LTP) [77-79]. Stimulation frequency, including standardized versus personalized Hz, did not significantly moderate tACS effects. It has been suggested that personalized frequency may confer greater benefits in behavior over a standard frequency across participants[32]. However, our results suggest no significant difference between EEG-informed tACS versus standardized frequency across healthy participants. This may not necessarily mean that personalized tACS is less effective; across studies, different approaches are used to determine endogenous peak frequency (e.g., EEG-triggered TMS, closed loop NIBS during task/rest)[22,27,32,80-83]. Different methods may impart variability in personalization of tACS. More insight is needed to reduce potential variability of EEG-informed tACS effects across studies. Also, participant demographics may be a confounding factor; most studies included relatively young adults with high performance rates and ceiling effects compared to older adults with normal age-related decline.

Other parameters important to tACS response include duration of stimulation, online or offline task performance, in-phase versus anti-phase waveforms, and conventional versus HD-tACS. Duration of stimulation (12-, 15-, 20-, 25-minutes) was not associated with significant differences in tACS effects. This may indicate that the maximum benefit from tACS can be achieved at short stimulation session in healthy young adults. Variables such as online (during) or offline (after stimulation) performance, in-phase versus anti-phase, and conventional versus HD-tACS also were not significant moderators of response to tACS.

Demographic features such as age, sex and education have potential to influence response to stimulation and were examined as covariates using meta-regression. Mean age and education were nonsignificant factors with respect to stimulation effects. The age range across all effects was 20.5–69.6 years. We categorized subjects as young versus older adults (26 versus 6 effects, respectively) to examine potential age-related differences in tACS response but observed none. Sex was a significant covariate in response to stimulation; higher percentage of female participants in studies was associated with greater WM performance. However, this finding could be driven largely by the higher number of females in this particular sample, and not an actual biological difference in response to tACS.

This study had several limitations. Although our criteria were broad, the final number of studies that met inclusion was low and stimulation protocols varied. We acknowledge that methodological heterogeneity across tACS protocols limits the ability to identify the most beneficial strategy. In an effort to be comprehensive, we performed several moderator analyses in which only a small number of effects could be compared. One particular area where we think additional data are needed is the determination of whether stimulation at personalized tACS frequencies versus standardized frequency has an impact on stimulation effects in samples of young healthy adults. Specific regions of the WM network that are preferentially involved in particular aspects of WM may be differentially influenced by tACS (i.e., variability of functional connectivity between regions within the WM network could impact response to stimulation). Future research combining tACS with neuroimaging techniques (e.g., EEG, fMRI; structural MRI) may provide greater insights into brain processing during WM performance and aid in the optimization of targeted stimulation sites for tACS WM enhancement.

Conclusions

In summary, we identified a significant, heterogeneous effect of tACS on the enhancement of WM performance and several factors that may impact response to stimulation. Future research in this area will need to address substantive gaps in the existing data by conducting studies with larger subject samples, increasing focus on important parameter settings and protocol optimization, and further examining structure-function relationships mediating the effects of stimulation on specific WM abilities. Future studies that explore cross-frequency coupling during tACS and working memory performance may provide greater guidance towards protocol optimization. Nonetheless, this meta-analysis provides support for the use of tACS as a tool to interrogate and improve WM and foundational evidence to support the exploration of tACS as a potential intervention for clinical populations with WM deficits.

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References

[1]. Baddeley A Working memory. Curr Biol 1992;255:556–9. 10.1016/j.cub.2009.12.014.

[2]. Jaeggi SM, Buschkuehl M, Jonides J, Perrig WJ. Improving fluid intelligence with training on working memory. Proc Natl Acad Sci U S A 2008;105:6829–33. 10.1073/pnas.0801268105. [PubMed: 18443283]

[3]. Au J, Sheehan E, Tsai N, Duncan GJ, Buschkuehl M, Jaeggi SM. Improving fluid intelligence with training on working memory: a meta-analysis. Psychon Bull Rev 2015;22:366–77. 10.3758/s13423-014-0699-x. [PubMed: 25102926]

[4]. Schupf N, Tang M-X, Albert SM, Costa R, Andrews H, Lee JH, et al. Decline in cognitive and functional skills increases mortality risk in nondemented elderly. Neurology 2005;65:1218. 10.1212/01.wnl.0000180970.07386.cb. [PubMed: 16247048]

[5]. Mograbi DC, Faria C de A, Fichman HC, Paradela EMP, Lourenço RA. Relationship between activities of daily living and cognitive ability in a sample of older adults with heterogeneous educational level. Ann Indian Acad Neurol 2014;17:71–6. 10.4103/0972-2327.128558. [PubMed: 24753664]

[6]. Nissim NR, O'Shea A, Indahlastari A, Kraft JN, von Mering O, Aksu S, et al. Effects of Transcranial Direct Current Stimulation Paired With Cognitive Training on Functional Connectivity of the Working Memory Network in Older Adults. Front Aging Neurosci 2019;11. 10.3389/fnagi.2019.00340.

[7]. Nissim NR, O'Shea A, Indahlastari A, Telles R, Richards L, Porges E, et al. Effects of in-Scanner Bilateral Frontal tDCS on Functional Connectivity of the Working Memory Network in Older Adults. Front Aging Neurosci 2019;11:1–10. 10.3389/fnagi.2019.00051. [PubMed: 30740048]

[8]. Ditye T, Jacobson L, Walsh V, Lavidor M. Modulating behavioral inhibition by tDCS combined with cognitive training. Exp Brain Res 2012;219:363–8. 10.1007/s00221-012-3098-4. [PubMed: 22532165]

[9]. Park S-H, Seo J-H, Kim Y-H, Ko M-H. Long-term effects of transcranial direct current stimulation combined with computer-assisted cognitive training in healthy older adults. Neuroreport 2013:122–6. 10.1097/WNR.0000000000000080.

[10]. Meinzer M, Lindenberg R, Antonenko D, Flaisch T, Flöel A. Anodal Transcranial Direct Current Stimulation Temporarily Reverses Age-Associated Cognitive Decline and Functional Brain Activity Changes. The Journal of Neuroscience 2013;33. 10.1523/JNEUROSCI.5743-12.2013.

[11]. Dhaynaut M, Cappon D, Paciorek R, Macone J, Connor A, Guehl N, et al. Effects of modulating gamma oscillations via 40Hz transcranial alternating current stimulation (tACS) on Tau PET imaging in mild to moderate Alzheimer's Disease. 2020.

[12]. Benussi A, Cantoni V, Cotelli MS, Cotelli M, Brattini C, Datta A, et al. Exposure to gamma tACS in Alzheimer's disease: A randomized, double-blind, sham-controlled, crossover, pilot study. Brain Stimul 2021;14:531–40. 10.1016/j.brs.2021.03.007. [PubMed: 33762220]

[13]. Senkowski D, Sobirey R, Haslacher D, Soekadar SR. Boosting working memory: uncovering the differential effects of tDCS and tACS. Cereb Cortex Commun 2022;3. 10.1093/texcom/tgac018.

[14]. Antonenko D, Faxel M, Grittner U, Lavidor M, Floël A. Effects of Transcranial Alternating Current Stimulation on Cognitive Functions in Healthy Young and Older Adults. Neural Plast 2016;2016. 10.1155/2016/4274127.

[15]. Elyamany O, Leicht G, Herrmann CS, Mulert C. Transcranial alternating current stimulation (tACS): from basic mechanisms towards first applications in psychiatry. Eur Arch Psychiatry Clin Neurosci 2021;271:135–56. 10.1007/s00406-020-01209-9. [PubMed: 33211157]

[16]. Antal A, Paulus W. Transcranial alternating current stimulation (tACS). Front Hum Neurosci 2013;7:317. 10.3389/fnhum.2013.00317. [PubMed: 23825454]

[17]. Alekseichuk I, Turi Z, Veit S, Paulus W. Model-driven neuromodulation of the right posterior region promotes encoding of long-term memories. Brain Stimul 2020;13:474–83. 10.1016/j.brs.2019.12.019. [PubMed: 31882373]

[18]. Herrmann CS. Modeling-informed tACS allows shaping oscillatory activity in specific brain networks. Brain Stimul 2017;10:387. 10.1016/j.brs.2017.01.144.

[19]. Vosskuhl J, Strüber D, Herrmann CS. [Transcranial alternating current stimulation : Entrainment and function control of neuronal networks]. Nervenarzt 2015. 10.1007/s00115-015-4317-6.

[20]. Vosskuhl J, Strüber D, Herrmann CS. Non-invasive Brain Stimulation: A Paradigm Shift in Understanding Brain Oscillations. Front Hum Neurosci 2018;12:1–19. 10.3389/fnhum.2018.00211. [PubMed: 29387003]

[21]. Fröhlich F, McCormick DA. Endogenous electric fields may guide neocortical network activity. Neuron 2010;67:129–43. 10.1016/j.neuron.2010.06.005. [PubMed: 20624597]

[22]. Klink K, Paßmann S, Kasten FH, Peter J. The modulation of cognitive performance with transcranial alternating current stimulation: A systematic review of frequency-specific effects. Brain Sci 2020;10:1–33. 10.3390/brainsci10120932.

[23]. Ruhnau P, Neuling T, Fuscá M, Herrmann CS, Demarchi G, Weisz N. Eyes wide shut: Transcranial alternating current stimulation drives alpha rhythm in a state dependent manner. Sci Rep 2016;6:1–6. 10.1038/srep27138. [PubMed: 28442746]

[24]. Neuling T, Ruhnau P, Weisz N, Herrmann CS, Demarchi G. Faith and oscillations recovered: On analyzing EEG/MEG signals during tACS. Neuroimage 2017;147:960–3. 10.1016/j.neuroimage.2016.11.022. [PubMed: 27888060]

[25]. Feurra M, Pasqualetti P, Bianco G, Santarnecchi E, Rossi A, Rossi S. State-dependent effects of transcranial oscillatory currents on the motor system: What you think matters. Journal of Neuroscience 2013;33:17483–9. 10.1523/JNEUROSCI.1414-13.2013. [PubMed: 24174681]

[26]. Nakazono H, Ogata K, Kuroda T, Tobimatsu S. Phase and frequency-dependent effects of transcranial alternating current stimulation on motor cortical excitability. PLoS One 2016;11:1–13. 10.1371/journal.pone.0162521.

[27]. Pahor A, Jaušovec N. The effects of theta and gamma tacs on working memory and electrophysiology. Front Hum Neurosci 2018;11. 10.3389/fnhum.2017.00651.

[28]. Antal A, Paulus W, Nitsche MA Principle and mechanisms of transcranial Direct Current Stimulation (tDCS). J Pain Manag 2009;2:249–58.

[29]. Tavakoli A v., Yun K Transcranial alternating current stimulation (tACS) mechanisms and protocols. Front Cell Neurosci 2017;11:1–10. 10.3389/fncel.2017.00214. [PubMed: 28154525]

[30]. Roux F, Uhlhaas PJ. Working memory and neural oscillations: Alpha-gamma versus theta-gamma codes for distinct WM information? Trends Cogn Sci 2014;18:16–25. 10.1016/j.tics.2013.10.010. [PubMed: 24268290]

[31]. Hoy KE, Bailey N, Arnold S, Windsor K, John J, Daskalakis ZJ, et al. The effect of γ-tACS on working memory performance in healthy controls. Brain Cogn 2015;101:51–6. 10.1016/j.bandc.2015.11.002. [PubMed: 26580743]

[32]. Reinhart RMG, Nguyen JA. Working memory revived in older adults by synchronizing rhythmic brain circuits. Nat Neurosci 2019. 10.1038/s41593-019-0371-x.

[33]. Lisman JE, Jensen O. The Theta-Gamma Neural Code. Neuron 2013;77:1002–16. 10.1016/j.neuron.2013.03.007. [PubMed: 23522038]

[34]. Sauseng P, Klimesch W, Heise KF, Gruber WR, Holz E, Karim AA, et al. Brain Oscillatory Substrates of Visual Short-Term Memory Capacity. Current Biology 2009;19:1846–52. 10.1016/j.cub.2009.08.062. [PubMed: 19913428]

[35]. Axmacher N, Henseler MM, Jensen O, Weinreich I, Elger CE, Fell J. Cross-frequency coupling supports multi-item working memory in the human hippocampus. Proc Natl Acad Sci U S A 2010;107:3228–33. 10.1073/pnas.0911531107. [PubMed: 20133762]

[36]. Fell J, Axmacher N. The role of phase synchronization in memory processes. Nat Rev Neurosci 2011;12:105–18. 10.1038/nrn2979. [PubMed: 21248789]

[37]. Sauseng P, Griesmayr B, Freunberger R, Klimesch W. Control mechanisms in working memory: A possible function of EEG theta oscillations. Neurosci Biobehav Rev 2010;34:1015–22. 10.1016/j.neubiorev.2009.12.006. [PubMed: 20006645]

[38]. Alekseichuk I, Turi Z, Amador de Lara G, Antal A, Paulus W. Spatial Working Memory in Humans Depends on Theta and High Gamma Synchronization in the Prefrontal Cortex. Current Biology 2016;26:1513–21. 10.1016/j.cub.2016.04.035. [PubMed: 27238283]

[39]. Alekseichuk I, Pabel SC, Antal A, Paulus W. Intrahemispheric theta rhythm desynchronization impairs working memory. Restor Neurol Neurosci 2017;35:147–58. 10.3233/RNN-160714. [PubMed: 28059806]

[40]. Jaušovec N, Jaušovec K. Increasing working memory capacity with theta transcranial alternating current stimulation (tACS). Biol Psychol 2014;96:42–7. 10.1016/j.biopsycho.2013.11.006. [PubMed: 24291565]

[41]. Bullard B, Levina V, Grover S, Reinhart R. Effects of transcranial alternating current stimulation on visual cognition: A systematic review and meta-analysis. Vision Sciences Society Annual Meeting Abstract, 2020.

[42]. Vosskuhl J, Huster RJ, Herrmann CS. Increase in short-term memory capacity induced by down-regulating individual theta frequency via transcranial alternating current stimulation. Front Hum Neurosci 2015;9:1–10. 10.3389/fnhum.2015.00257. [PubMed: 25653611]

[43]. Honkanen R, Rouhinen S, Wang SH, Palva JM, Palva S. Gamma oscillations underlie the maintenance of feature-specific information and the contents of visual working memory. Cerebral Cortex 2015;25:3788–801. 10.1093/cercor/bhu263. [PubMed: 25405942]

[44]. Howard MW, Rizzuto DS, Caplan JB, Madsen JR, Lisman J, Aschenbrenner-Scheibe R, et al. Gamma Oscillations Correlate with Working Memory Load in Humans. Cerebral Cortex 2003;13:1369–74. 10.1093/cercor/bhg084. [PubMed: 14615302]

[45]. Guerra A, Asci F, Zampogna A, D'Onofrio V, Petrucci S, Ginevrino M, et al. Gamma-transcranial alternating current stimulation and theta-burst stimulation: inter-subject variability and the role of BDNF. Clinical Neurophysiology 2020;131:2691–9. 10.1016/j.clinph.2020.08.017. [PubMed: 33002731]

[46]. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6. 10.1371/journal.pmed.1000097.

[47]. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. The BMJ 2021;372. 10.1136/bmj.n71.

[48]. Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. BMJ 2011;342:964–7. 10.1136/bmj.d549.

[49]. Cohen J Statistical Power Analysis for the Behavioral Sciences. Academic Press;1988.

[50]. Hedges L v., Olkin I Statistical Methods for Meta-Analysis. 1985. 10.2307/1164953.

[51]. Grant J, Hunter A. Measuring inconsistency in knowledgebases. J Intell Inf Syst 2006;27:159–84. 10.1007/s10844-006-2974-4.

[52]. Mavridis D, Salanti G. How to assess publication bias: Funnel plot, trim-and-fill method and selection models. Evid Based Ment Health 2014;17:30. 10.1136/eb-2013-101699. [PubMed: 24477535]

[53]. Egger M, Smith G, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34. [PubMed: 9310563]

[54]. Begg CB, Mazumdar M. Operating Characteristics of a Rank Correlation Test for Publication Bias. Biometrics 1994;50:1088–101. [PubMed: 7786990]

[55]. Orwin RG. A Fail-Safe N for Effect Size in Meta-Analysis. Journal of Educational Statistics 1983;8:157–9.

[56]. Meiron O, Lavidor M. Prefrontal oscillatory stimulation modulates access to cognitive control references in retrospective metacognitive commentary. Clinical Neurophysiology 2014;125:77–82. 10.1016/j.clinph.2013.06.013. [PubMed: 23831184]

[57]. Jaušovec N, Jaušovec K, Pahor A. The influence of theta transcranial alternating current stimulation (tACS) on working memory storage and processing functions. Acta Psychol (Amst) 2014;146:1–6. 10.1016/j.actpsy.2013.11.011. [PubMed: 24361739]

[58]. Jaušovec N, Jaušovec K. Increasing working memory capacity with theta transcranial alternating current stimulation (tACS). Biol Psychol 2014;96:42–7. 10.1016/j.biopsycho.2013.11.006. [PubMed: 24291565]

[59]. Borghini G, Candini M, Filannino C, Hussain M, Walsh V, Romei V, et al. Alpha oscillations are causally linked to inhibitory abilities in ageing. Journal of Neuroscience 2018;38:4418–29. 10.1523/JNEUROSCI.1285-17.2018. [PubMed: 29615485]

[60]. Jones KT, Arciniega H, Berryhill ME. Replacing tDCS with theta tACS provides selective, but not general WM benefits. Brain Res 2019;1720. 10.1016/j.brainres.2019.146324.

[61]. Bender M, Romei V, Sauseng P. Slow Theta tACS of the Right Parietal Cortex Enhances Contralateral Visual Working Memory Capacity. Brain Topogr 2019;32:477–81. 10.1007/s10548-019-00702-2. [PubMed: 30694422]

[62]. Biel AL, Sterner E, Röll L, Sauseng P. Modulating verbal working memory with fronto-parietal transcranial electric stimulation at theta frequency: Does it work? European Journal of Neuroscience 2022;55:405–25. 10.1111/ejn.15563. [PubMed: 34902182]

[63]. Thompson L, Khuc J, Saccani MS, Zokaei N, Cappelletti M. Gamma oscillations modulate working memory recall precision. Exp Brain Res 2021;239:2711–24. 10.1007/s00221-021-06051-6. [PubMed: 34223958]

[64]. Becker LA. Effect Size (ES). 2000.

[65]. Schäfer T, Schwarz MA. The meaningfulness of effect sizes in psychological research: Differences between sub-disciplines and the impact of potential biases. Front Psychol 2019;10. 10.3389/fpsyg.2019.00813.

[66]. Gill J, Shah-basak PP, Hamilton R. It's the Thought That Counts: Examining the Task-dependent Effects of Transcranial Direct Current Stimulation on Executive Function. Brain Stimul 2015;8:253–9. 10.1016/j.brs.2014.10.018. [PubMed: 25465291]

[67]. Santarnecchi E, Polizzotto NR, Godone M, Giovannelli F, Feurra M, Matzen L, et al. Frequency-dependent enhancement of fluid intelligence induced by transcranial oscillatory potentials. Current Biology 2013;23:1449–53. 10.1016/j.cub.2013.06.022. [PubMed: 23891115]

[68]. Nagel IE, Preuschhof C, Li S, Nyberg L. Load Modulation of BOLD Response and Connectivity Predicts Working Memory Performance in Younger and Older Adults. J Cogn Neurosci 2011;23:2030–45. 10.1162/jocn.2010.21560. [PubMed: 20828302]

[69]. Heinzel S, Lorenz RC, Brockhaus W-R, Wüstenberg T, Kathmann N, Heinz A, et al. Working Memory Load-Dependent Brain Response Predicts Behavioral Training Gains in Older Adults. The Journal of Neuroscience 2014;34:1224–33. 10.1523/JNEUROSCI.2463-13.2014. [PubMed: 24453314]

[70]. Postle B, D'Esposito M, Corkin S. Effects of verbal and nonverbal interference on spatial and object visual working memory. Mem Cognit 2005;33:203–12.

[71]. Nagel BJ, Herting MM, Maxwell EC, Bruno R, Fair D. Hemispheric lateralization of verbal and spatial working memory during adolescence. Brain Cogn 2013;82:58–68. 10.1016/j.bandc.2013.02.007. [PubMed: 23511846]

[72]. Koenigs M, Barbey AK, Postle BR, Grafman J. Superior parietal cortex is critical for the manipulation of information in working memory. Journal of Neuroscience 2009;29:14980–6. 10.1523/JNEUROSCI.3706-09.2009. [PubMed: 19940193]

[73]. Jonides J, Schumacher EH, Smith EE, Koeppe RA, Awh E, Reuter-lorenz PA, et al. The Role of Parietal Cortex in Verbal Working Memory 1998;18:5026–34.

[74]. Seo M-H, Park S-H, Seo J-H, Kim Y-H, Ko M-H. Improvement of the Working Memory by Transcranial Direct Current Stimulation in Healthy Older Adults, vol. 35. 2011.

[75]. Zimmerman M Speed-Accuracy Tradeoff. Encyclopedia of Clinical Neuropsychology 2017:1113–5. 10.1007/978-3-319-56782-2_1247-3.

[76]. Fregni F, Boggio PS, Nitsche MA, Rigonatti SP, Pascual-Leone A. Cognitive effects of repeated sessions of transcranial direct current stimulation in patients with depression [1]. Depress Anxiety 2006;23:482–4. 10.1002/da.20201. [PubMed: 16845648]

[77]. Monte-Silva K, Kuo MF, Hessenthaler S, Fresnoza S, Liebetanz D, Paulus W, et al. Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. Brain Stimul 2013;6:424–32. 10.1016/j.brs.2012.04.011. [PubMed: 22695026]

[78]. Boggio PS, Nunes A, Rigonatti SP, Nitsche MA, Pascual-Leone A, Fregni F. Repeated sessions of noninvasive brain DC stimulation is associated with motor function improvement in stroke patients. Restor Neurol Neurosci 2007;25:123–9. [PubMed: 17726271]

[79]. Monte-Silva K, Kuo M-F, Liebetanz D, Paulus W, Nitsche MA. Shaping the optimal repetition interval for cathodal transcranial direct current stimulation (tDCS). vol. 103. 2010. 10.1152/jn.00924.2009.

[80]. Aktürk T, de Graaf TA, Güntekin B, Hanoğlu L, Sack AT. Enhancing memory capacity by experimentally slowing theta frequency oscillations using combined EEG-tACS. Sci Rep 2022;12. 10.1038/s41598-022-18665-z.

[81]. Bjekić J, Paunovic D, Živanović M, Stanković M, Griskova-Bulanova I, Filipović SR. Determining the Individual Theta Frequency for Associative Memory Targeted Personalized Transcranial Brain Stimulation. J Pers Med 2022;12. 10.3390/jpm12091367.

[82]. Aktürk T, de Graaf TA, Erdal F, Sack AT, Güntekin B. Oscillatory delta and theta frequencies differentially support multiple items encoding to optimize memory performance during the digit span task. Neuroimage 2022;263:119650. 10.1016/j.neuroimage.2022.119650. [PubMed: 36167270]

[83]. Živanović M, Bjekić J, Konstantinović U, Filipović SR. Effects of online parietal transcranial electric stimulation on associative memory: a direct comparison between tDCS, theta tACS, and theta-oscillatory tDCS. Sci Rep 2022;12. 10.1038/s41598-022-18376-5.

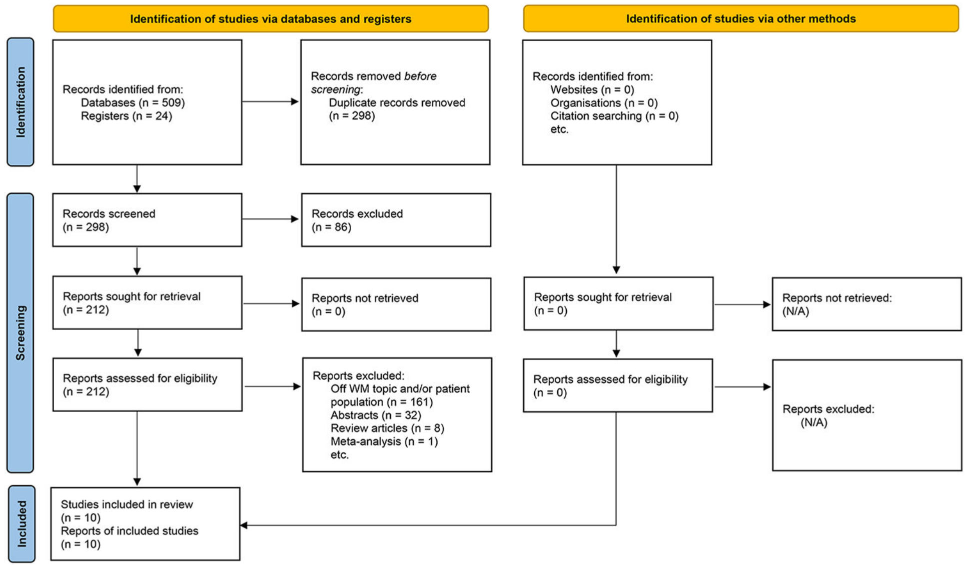

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart for the search and selection of studies.

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Meiron, 2014	1.265	0.447	0.200	0.388	2.141	2.828	0.005	
Meiron, 2014a	0.418	0.413	0.170	-0.391	1.226	1.012	0.312	
Jaušovec, 2014 (1)	1.137	0.370	0.137	0.411	1.863	3.070	0.002	
Jaušovec, 2014a (1)	-0.312	0.296	0.087	-0.891	0.268	-1.055	0.292	
Jaušovec, 2014b (1)	-0.049	0.289	0.083	-0.615	0.517	-0.170	0.865	
Jaušovec, 2014 (2)	0.719	0.324	0.105	0.084	1.354	2.220	0.026	
Jaušovec, 2014a (2)	0.635	0.316	0.100	0.015	1.256	2.008	0.045	
Jaušovec, 2014b (2)	1.709	0.453	0.205	0.822	2.597	3.775	0.000	
Jaušovec, 2014c (2)	0.785	0.330	0.109	0.138	1.432	2.377	0.017	
Jaušovec, 2014d (2)	0.672	0.320	0.102	0.046	1.299	2.103	0.035	
Jaušovec, 2014e (2)	0.897	0.342	0.117	0.227	1.566	2.623	0.009	
Jaušovec, 2014f (2)	0.785	0.330	0.109	0.138	1.432	2.377	0.017	
Jaušovec, 2014g (2)	2.208	0.535	0.286	1.159	3.257	4.125	0.000	
Jaušovec, 2014h (2)	0.672	0.320	0.102	0.046	1.299	2.103	0.035	
Hoy, 2015	0.431	0.246	0.061	-0.052	0.914	1.750	0.080	
Borghini, 2018	0.749	0.226	0.051	0.305	1.193	3.310	0.001	
Borghini, 2018a	0.749	0.226	0.051	0.305	1.193	3.310	0.001	
Jones, 2019	0.378	0.168	0.028	0.049	0.707	2.251	0.024	
Jones 2019a	-0.232	0.164	0.027	-0.554	0.090	-1.411	0.158	
Bender, 2019	0.754	0.303	0.092	0.160	1.347	2.489	0.013	
Bender, 2019a	0.714	0.299	0.090	0.127	1.300	2.384	0.017	
Reinhart, 2019	0.577	0.167	0.028	0.250	0.903	3.461	0.001	
Reinhart, 2019a	-0.099	0.155	0.024	-0.402	0.204	-0.639	0.523	
Reinhart, 2019b	0.586	0.205	0.042	0.185	0.987	2.865	0.004	
Reinhart, 2019c	-0.242	0.192	0.037	-0.617	0.134	-1.260	0.208	
Biel, 2021	0.046	0.417	0.174	-0.773	0.864	0.109	0.913	
Biel, 2021a	0.218	0.419	0.175	-0.602	1.039	0.521	0.602	
Biel, 2021b	0.693	0.430	0.185	-0.149	1.535	1.612	0.107	
Biel, 2021c	0.295	0.420	0.176	-0.528	1.118	0.703	0.482	
Biel, 2021d	0.544	0.416	0.173	-0.270	1.359	1.309	0.190	
Biel, 2021e	0.742	0.422	0.178	-0.085	1.569	1.758	0.079	
Thompson, 2021	0.337	0.144	0.021	0.054	0.619	2.338	0.019	
Omnibus effect →	0.514	0.084	0.007	0.349	0.680	6.105	0.000	

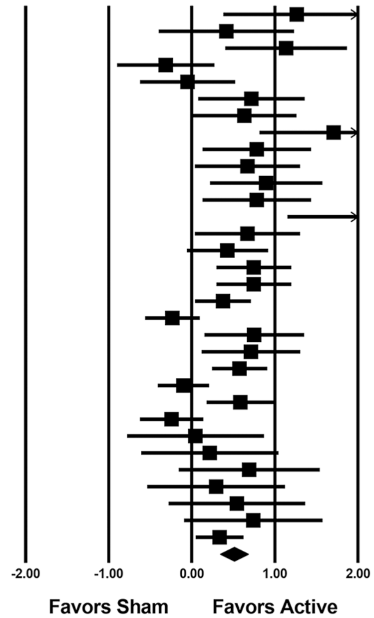

Figure 2.

Overall meta-analysis effect size (Cohen's d omnibus effect=0.514) of all included tACS studies. Corresponding forest plot demonstrates the effects of favoring active stimulation (>0) versus favoring sham stimulation (<0).

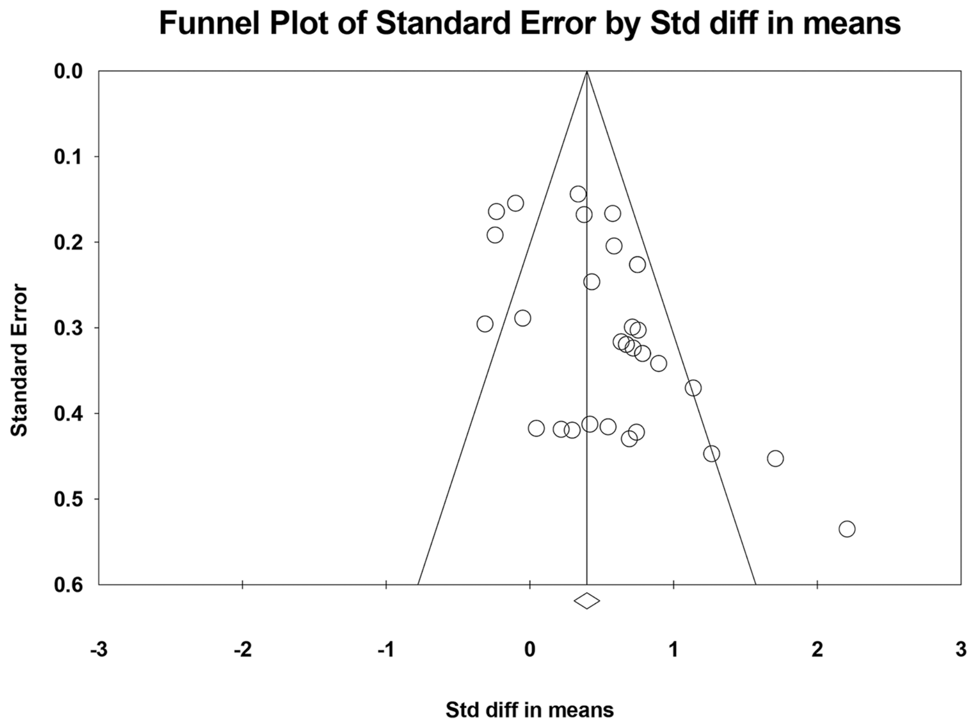

Figure 3.

Funnel plot displays tACS effects for the assessment of publication bias.

Table 1.

Data summary of included studies in the meta-analysis.

Author, year	Study Design	Session Number	Duration (mins)	Stimulation Frequency	Electrode Location (Anode, Cathode(s))	Electrode size	Concurrent Task	Task	Task Domain	Measure	Outcome
Meiron, 2014	Between-subject	1	20	4.5 Hz; theta	Bilateral DLPFC (F3/F4)	4x4cm	Online	N-Back	Verbal	Accuracy, RT	WM accuracy significantly improved
Jaušovec, 2014a	Within-subject	2	15	personalized; theta	Left parietal (P3), right eyebrow	5x7 cm; 10x7cm	Offline	Visual array comparison task	Spatial	Accuracy, RT	WM storage capacity significantly improved
Jaušovec, 2014b	Within-subject	2	15	personalized; theta	Left parietal (P3), right eyebrow	5x7 cm	Offline	Corsi block tapping task (FW/BW); Digit span (FW/BW)	Verbalspatial	Accuracy	WM storage capacity significantly improved
Hoy, 2015	Within-subject	1	20	40 Hz; gamma	Left frontal(F3), right supraorbital area	5x7 cm	Offline	N-Back	Verbal	Accuracy	Larger performance improvement in active vs sham, not statistically significant
Borghini, 2018	Within-subject	4	20	10Hz; alpha	Bilateral parietal (P3/P4)	5x7 cm	Online	Retro-cue working memory paradigm	Spatial	Accuracy	WM recall accuracy significantly improved
Jones, 2019	Within-subject	1	15	4.5 Hz; theta	Right DLPFC (F4), right parietal (P4)	5x5cm	Offline	N-Back	Object	Accuracy	Object WM significantly improved
Bender, 2019	Within-subject	2	12	4 Hz; theta	Right parietal (P4); Oz, Cz, and T8	19.6 cm^2; 4.9 cm^2 return	Online	Delayed match-to-sample	Visuospatial	Accuracy	WM storage capacity significantly improved
Reinhart, 2019	Within-subject	1	25	personalized; theta	Left frontal (F3), left temporal (T3)	12mm diameter, Ag/AgCl	Online	Change detection task	Object	Accuracy, RT	WM accuracy significantly improved
Biel, 2021	Between-subject	1	14	6 Hz; theta	Left frontal (F3), left parietal (P3); Cz, focal	2.5cm diameter	Online	Delayed Letter Recognition Task	Verbal	Accuracy, RT	Performance in demanding task significantly improved
Thompson, 2021	Within-subject	1	20	35 Hz; gamma	Bilateral parietal (P3/P4)	5x7 cm	Online	Retro-cue working memory paradigm	Visuospatial	Accuracy	WM recall accuracy significantly improved

Table 2.

Study sample demographics.

Author, year	Sample size	Age	Percent female	Education (mean year)
Meiron, 2014	24	21.5	100	12.67 Active; 12.43 Sham
Jaušovec, 2014a	12	20.6	66.6	-
Jaušovec, 2014b	12	20.5	75	-
Hoy, 2015	18	29.3	50	16.23
Borghini, 2018	25	69.1	44	16.2
Jones, 2019	38	24.5	66	-
Bender, 2019	14	21.9	85	-
Reinhart, 2019	42	68.8	52	17
Biel, 2021	24	21.3	58.3	-
Thompson, 2021	51	24.1	58.8	-