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Article

# Transcranial Alternating Current Stimulation and Cognitive Training Enhanced Performance and Theta Activity in Adults With Cognitive Impairment

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**ABSTRACT**

**Background:** Age-related cognitive decline is rising due to longer life expectancy, necessitating new treatments as current drugs are ineffective and costly. Transcranial alternating current stimulation at the theta frequency (theta-tACS) has shown promise in enhancing cognitive function in both young and elderly adults, but its effectiveness in those with cognitive decline is not well-studied. **Method:** This study involved 27 participants with subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia, who underwent multiple sessions combining computerized cognitive training with theta-tACS to assess its efficacy. Participants were randomly assigned to either a real-tACS or sham-tACS group. Before and after treatment, they completed several cognitive tasks, and their behavioral and EEG data were collected. **Results:** Only the real-tACS group improved in the oddball task and exhibited increased event-related EEG amplitude in the theta range. **Conclusions:** These findings suggest that theta-tACS can improve cognitive performance in individuals with cognitive decline at both behavioral and psychophysiological levels, supporting its potential for alleviating cognitive decline in elderly populations.

## La Estimulación Eléctrica Transcraneal por Corriente Alterna y el Entrenamiento Cognitivo Mejoran la Ejecución y Aumentan la Actividad Theta en Adultos con Deterioro Cognitivo

***Palabras clave:***
Deterioro cognitivo subjetivo (DCS)
Deterioro cognitivo ligero (DCL)
Demencia
Estimulación eléctrica transcraneal por corriente alterna (tACS)
Atención

**RESUMEN**

**Antecedentes:** El deterioro cognitivo relacionado con la edad está aumentando debido a una mayor esperanza de vida, lo que requiere nuevos tratamientos, ya que los medicamentos actuales son ineficaces y costosos. La estimulación transcraneal por corriente alterna en frecuencia theta (theta-tACS) ha mostrado potencial para mejorar la función cognitiva tanto en adultos jóvenes como mayores, pero su efectividad en personas con deterioro cognitivo no está bien estudiada. **Método:** Este estudio incluyó a 27 participantes con deterioro cognitivo subjetivo (DCS), deterioro cognitivo leve (DCL) y demencia, quienes se sometieron a múltiples sesiones que combinaron entrenamiento cognitivo computarizado con theta-tACS para evaluar su eficacia. Fueron asignados aleatoriamente a un grupo de tACS real o un grupo de tACS placebo. Antes y después del tratamiento, completaron tareas cognitivas y se recogieron datos comportamentales y de EEG. **Resultados:** Solo el grupo de tACS real mejoró en la tarea oddball y presentó un aumento en la amplitud del EEG en el rango theta. **Conclusiones:** Estos hallazgos sugieren que theta-tACS puede mejorar el rendimiento cognitivo en personas con deterioro cognitivo, a nivel conductual y psicofisiológico, apoyando su potencial para aliviar el deterioro cognitivo en poblaciones mayores.

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Despite the hallmark of AD being episodic memory (EM) impairment (McKhann et al., 2011), neurodegeneration affects brain regions related to other cognitive domains (including attention, working memory -WM- and executive functioning) even from preclinical stages of the disease (Hafkemeijer et al., 2013; Saykin et al., 2006). In fact, behavioral declines in these processes have been consistently observed both in SCD (Cespón et al., 2018a; Cid-Fernández et al., 2021; Viviano et al., 2019) we investigated event-related potentials (ERPs and in MCI adults (Kirova et al., 2015; Zurrón et al., 2018). Furthermore, it has been suggested that these declines might be an indicator of incipient dementia (Viviano et al., 2019).

According to earlier studies, increased synchronized oscillations in the theta frequency band (4–8 Hz) have been linked to better working memory (WM) (Hsieh & Ranganath, 2014; Sauseng et al., 2010), executive function/complex attention, learning and memory (Hasselmo, 2005; Wang, 2010). More specifically, brain oscillations in the theta, gamma and alpha frequency bands have been associated with WM (Al Qasem et al., 2022). Theta is thought to drive synchronization of distant brain regions during WM, gamma activity nested in the theta peak seems to represent the items maintained in WM, while alpha oscillations play a role in inhibitory control (Abubaker et al., 2021; Klimesch et al., 2007; Riddle et al., 2020; Roux & Uhlhaas, 2014). In this vein, mounting evidence points to changes in the relationships between various brain areas as a cause of age-related memory and cognitive decline, possibly as a result of anatomical and functional dysconnectivity between brain regions that typically function in a coordinated or synchronous manner (Antal et al., 2017; Hsu et al., 2017; Kim et al., 2021).

Furthermore, recent promising research has demonstrated the effectiveness of tACS in improving functional synchronization between brain areas (e.g., Reinhart & Nguyen, 2019) and specific cognitive functions. This was demonstrated not only in healthy adults (Abubaker et al., 2021; Fröhlich, 2015; Hanslmayr et al., 2019; Lee et al., 2023), but also in adults with cognitive impairment (Al Qasem et al., 2022; Kim et al., 2021; Wischnewski et al., 2023) by interacting with ongoing oscillatory cortical activity, with lasting behavioral effects. Theta-gamma rhythms dissociate during memory maintenance in elderly persons with WM and coupling can be restored by delivering tACS in the theta range (theta-tACS) (Reinhart & Nguyen, 2019). Moreover, several studies have demonstrated that theta-tACS delivered over left frontal regions can improve working memory performance both in healthy young (Alekseichuk et al., 2016) and old (Reinhart & Nguyen, 2019) individuals, as well as other related cognitive domains (e.g., multitasking), also in young (Hsu et al., 2017) and in old (Jones et al., 2022; Zanto et al., 2021) adults. Furthermore, it seems that theta-gamma coupling is related to WM declines in healthy aging, but also in MCI and AD (Abubaker et al., 2021; Goodman et al., 2018). However, to the date there are any studies that evaluated the efficacy of theta-tACS to improve WM performance in adults with SCD or dementia.

Regarding MCI, a very recent paper demonstrated that theta-tACS applied in prefrontal locations is in fact able to enhance attentional activity in participants with amnestic MCI, while it did not produce any effects regarding multitasking performance (Jones et al., 2023). In addition, recent reviews have suggested that tACS is more effective when it is applied over an active brain network rather than when it is applied in a resting-state condition (Cespón et al., 2018b; Wang et al., 2020) physical exercise and non-invasive brain stimulation in healthy elderly and cognitively impaired subjects (including patients with mild cognitive impairment (MCI, while it has been suggested online tACS procedures may enable greater entrainment between ongoing brain oscillations and outside electrical oscillations than offline tACS protocols (Klink et al., 2020; Lee et al., 2023) we aim to provide an overview of frequency-specific tACS effects on a range of cognitive functions in healthy adults. This may help to transfer stimulation protocols to real-world applications. We conducted a systematic literature search on PubMed and Cochrane databases and considered tACS studies in healthy adults (age > 18 years. In addition, multi-session interventions seem to be more effective than single-session interventions (Liu et al., 2020; Sanches et al., 2021).

This sham-controlled study evaluated the efficacy of a multi-session intervention combining computerized cognitive training (CCT) and prefrontal theta-tACS in participants with SCD, MCI, and probable dementia. The CCT activities targeted attention (13/23) and working memory (11/23), with additional tasks addressing planning (4/23) and response inhibition (2/23). After the intervention, we assessed performance and theta activity during an oddball task, expecting improved outcomes and increased theta amplitudes. Resting-state EEG (rsEEG) was analyzed for enhanced theta power. Transfer effects to other executive functions were tested with the Stimulus-Response Compatibility (SRC) and Stop-Signal (S-S) tasks, anticipating gains in cognitive control and response inhibition.

## Method

### Participants

Thirty elderly adults took part in this study and were randomly assigned to the real-tACS group ($n$ = 15) and to the sham-tACS group ($n$ = 15). All volunteers were randomly selected from our databases, as they were enrolled in the longitudinal Compostela Aging Study (Facal et al., 2019). All the participants had a previous diagnosis of subjective cognitive decline (SCD) or mild cognitive impairment (MCI), and all of them were right-handed. The sample size was estimated based on the scarce previous literature (Borghini et al., 2018) using G*Power 3.1 (Faul et al., 2007), indicating that a total sample of 15 participants was required to achieve an actual power of 0.96. As the actual sample size is 15 participants in the real-tACS group and 12 in the sham-tACS group, the power of the present study is 0.94.

Participants gave written informed consent prior to their participation. All the procedures conformed to the Declaration of Helsinki for research involving human subjects and were approved by the Clinical Research Ethics Committee (Ref. 2017/498) of the Xunta de Galicia (Galician Government, Spain).

Before undergoing the CCT+tACS intervention, the participants underwent a new comprehensive neuropsychological assessment to update their diagnosis. Twenty-one participants confirmed a SCD or MCI diagnosis, but six subjects had developed probable AD dementia (ADD). These subjects were equally distributed between groups (three in the real-tACS group and three in the sham-tACS group).

**Table 1**
*Mean Values and Standard Deviations (in parentheses) of the Demographic and Neuropsychological Measures of the Two Groups of Participants: p-Values Obtained from the Chi-Squared Test, the Mann-Whitney Tests or the t-Tests Used to Compare Both Groups are Reported*

| | Sham-tACS group (*n* = 12) | Real-tACS group (*n* = 15) | *p-value* |
|---|---|---|---|
| **Demographic characteristics** | | | |
| Gender (females/males) | 10 / 2 | 10 / 5 | .964 |
| Age (years) | 69.8 (7.9) | 70.7 (7.4) | .904 |
| Educational level | 1.67 (1.0) | 1.67 (0.9) | .981 |
| **Neuropsychological assessment** | | | |
| T@M | 38.8 (12.3) | 36.9 (9.6) | .471 |
| SCIP-S (immediate recall) | 17.1 (5.65) | 14.0 (4.1) | .336 |
| SCIP-S (delayed recall) | 6.2 (3.2) | 4.2 (3.5) | .383 |
| MPMT | 5.1 (2.8) | 5.8 (3.1) | .331 |
| PRMQ | 59.7 (6.1) | 61.2 (8.6) | .340 |
| ToH (movements) | 26.6 (6.2) | 26.1 (5.1) | .378 |
| ToH (seconds) | 122.2 (61.7) | 102.0 (53.6) | .957 |
| short-AIADLQ | 73.7 (21.4) | 73.6 (21.2) | .712 |

*Note.*T@M: test de alteración de memoria (memory alteration test); SCIP-S: screening del deterioro cognitivo en psiquiatría (cognitive decline screening in psychiatry); MPMT: The prospective memory test; PRMQ: Prospective-retrospective memory questionnaire (Spanish version); ToH (movements or seconds): number of movements or time (in seconds) needed to solve levels 1, 2 and 3 of the tower of Hanoi; short-AIADLQ: short version of the Amsterdam instrumental activities of daily living questionnaire (Spanish version).

From the initial sample, two subjects from the sham-tACS group did not finish the experimental procedure due to personal issues. After completing all the experimental procedure, another participant from the sham-tACS group was excluded because she was diagnosed with a neurological condition different from AD (i.e., Parkinson's Disease). Thus, the final sample comprised 15 participants in the real-tACS group and 12 participants in the sham-tACS group, with no differences in general cognitive functioning, memory, and executive functions. Table 1 presents the demographic, clinical, and cognitive scores that are most relevant to the two groups.

All participants had normal or corrected vision, no psychiatric or neurological disorders beyond probable ADD, and provided written informed consent.

## Instruments

### *S-S and SRC Tasks*

In the pre-T and post-T sessions, we used the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition Ltd.) to present both the S-S and the SRC (called the Multitasking Test in CANTAB) tasks.

The S-S task measures the ability to inhibit a prepotent response. Participants had to respond to an arrow (Go stimulus) by pressing the right or left button (on screen) depending on the direction in which the arrow points. They were also instructed to withhold the response if they heard an auditory signal (beep; Stop signal) after the arrow presentation, that appeared in a small percentage of trials.

For the S-S task, median reaction times (RT) to hits in the Go condition (Go hit RT, in milliseconds), the Stop-signal RT (SSRT, in milliseconds; time required between the Go stimuli and the Stop signal that allows the subject to effectively withhold the response 50% of the time, i.e., the time before which all action become ballistic and the subject is no longer able to cancel their action selection) were analysed. In addition, d' was computed as a global measure for behavioural execution (i.e., d′ = Z (hit rate) – Z (false alarm rate)) (Macmillan et al., 1990).The SRC task assesses interference between stimulus features and responses. Arrows appear on the right or left of the screen, pointing left or right. Participants respond either to the arrow's location or its direction, depending on the block, using left or right buttons. Trials can be congruent (arrow on the right pointing right) or incongruent (arrow on the left pointing right), with incongruent trials being more cognitively demanding.

For the SRC task, mean RTs for hits in the congruent trials (congruent hit RT, in milliseconds), mean RTs for hits in the incongruent trials (incongruent hit RT, in milliseconds) were analysed. As in the S-S task, d' was also computed for the SRC task.

### *Oddball Task*

The visual oddball task in pre-T and post-T sessions was implemented in Presentation (Neurobehavioral Systems, Inc.). Participants viewed 312 visual stimuli in 2 blocks, with a short rest between. Stimuli included numbers (two, four, six, eight), letters (a, e, c, u), and triangles (varied orientations), each appearing with equal probability (33.3%). Participants pressed a button with their right index finger for numbers (targets). Stimuli were shown for 200 ms with a random intertrial interval of 1300-1600 ms.

For this task, the RT to hits and to false alarms (FAs), as well as d' were analysed. In addition, event-related spectral activity measures were also collected through an EEG recording during performance of the task.

## Procedure

The present study adopted a single-blind between-subjects sham-controlled experimental design, in which participants, divided in groups of three to five people, underwent 12 daily 1hour treatment sessions (excluding weekends); six with CCT alone, and six with CCT and tACS, all at the same time of day. In each session, participants performed several computerized tasks on a 10-inch touchpad for 60 minutes. The CCT tasks required the engagement of attention, WM, and executive processes, and were selected from the NeuronUp software (NeuronUp S.L., Spain), that has previously shown to be effective in significantly improving cognitive ability in adults with cognitive decline (Cruz et al., 2021; Mendoza et al., 2018).

Furthermore, tACS was applied during CCT over the F3 electrode location of the 10-20 international system (over the left dorsolateral prefrontal cortex -DLPFC-) in the last six sessions, starting 15 minutes after CCT onset to ensure the targeted networks were fully engaged (Abellaneda-Pérez et al., 2020) respectively. The first six sessions exclusively employed NeuronUP for cognitive training, allowing older participants to familiarize themselves with the tasks and reducing the need for assistance during training. The left DLPFC was set as the stimulation target, as this brain region is an important neural hub involved in different large-scale networks that support several cognitive processes as goal-driven attention, working memory, and other higher executive functions (Clark et al., 2015; Jones & Graff-Radford, 2021; Osaka et al., 2003) neural substrates of verbal working memory were investigated with respect to differences in working memory capacity. Listening-span test (LST. The stimulation given to participants was concealed from them.

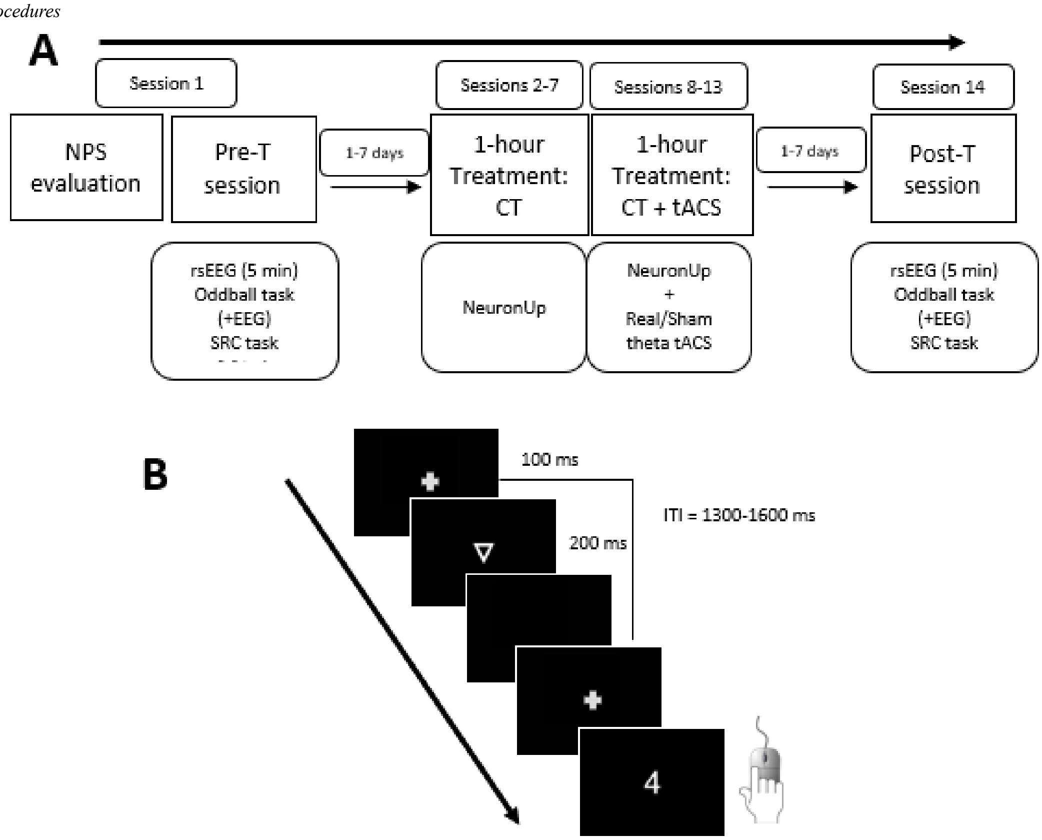
Besides, participants underwent a pre-treatment (pre-T; 1-7 days before starting treatment) and a post-treatment session (post-T; within 7 days after finishing treatment). There were no significant differences between groups in the number of days between the last day of treatment and post-T evaluation ($t$ (25) = .126, $p$ = .901; real-tACS group, mean=4.4 days, $SD$ = 1.92; sham-tACS group, mean = 4.5 days, $SD$ = 2.20). In the pre-T and post-T sessions, rsEEG was recorded for 5 minutes. In addition, participants performed three tasks: an oddball task, a stop-signal (S-S) task and a stimulus-response compatibility (SRC) task. Behavioural performance was registered for the three tasks, and EEG was also recorded during the oddball task. The experimental design is shown in Figure 1A, while Figure 1B illustrates the oddball task.

### *tACS Parameters*

During the last 6 treatment sessions, 6 Hz tACS was delivered by a battery-driven stimulator (BrainStim, EMS, Bologna, Italy) through a pair of rubber electrodes for 20 minutes (with a 20 second ramp-up and a 20 second ramp-down), starting approximately 15 minutes after initiating CCT with NeuronUp. The intensity of the stimulation was 2 mA. One of the electrodes was a round rubber electrode (2 cm diameter, area 3.14 $cm^2$, current density .64 mA/$cm^2$). Ten20 conductive paste (Weaver and Company, Aurora, CO) was used to fix the electrode to the scalp over the site of the F3 electrode (International 10-20 EEG System). Elastic straps held the second electrode, a rectangular electrode encased in a saline-soaked sponge with dimensions of 5 cm by 9.5 cm (area of 47.5 $cm^2$, and current density of .04 mA/$cm^{2)}$, to the right shoulder. Impedance level was maintained below 5 kΩ. The parameters were the same in the sham condition, with the exception that the current was shut off 20 seconds into the stimulation and brought back on during the final 20 seconds of the task. An estimation of the mean cortical e-field induced by real tACS is depicted in Supplementary Figure 1.

**Figure 1**

*Experimental Procedures*




*Note. A:* On day 1, participants underwent a comprehensive neuropsychological evaluation and the pre-treatment (pre-T) session (session 1); between 1 and 7 days after, the 1-hour treatment sessions was delivered for 12 consecutive sessions (excluding weekends; sessions 2 to 13); between 1 and 7 days after treatment, participants underwent the post-treatment (post-T) session (session 14). B: Trial procedure of the Oddball task. In each trial, a triangle, a letter or a number (target stimuli) was presented, and participants should press a button only after numbers.

Based on non-invasive brain stimulation techniques, safety protocols were implemented (Antal et al., 2017) encompassing transcranial direct current (tDCS. Participants completed a standardized questionnaire evaluating the feelings brought on by tACS immediately following the conclusion of each experimental session (Antal et al., 2017; Fertonani et al., 2015) encompassing transcranial direct current (tDCS. On a 5-point scale, participants were asked to rate the strength of various sensations, including itching/irritation, pain, burning, heat, an iron taste, and fatigue (0 = *none*; 1 = *mild*; 2 = *moderate*; 3 = *considerable*; 4 = *strong*). In addition, participants were asked to guess at the conclusion of the post-T session, whether they had experienced genuine or "placebo" (i.e., sham) stimulation during the therapy sessions. For each experimental session, individuals were forced to choose one response (either "Real stimulation", "Sham", or "I don't know") for this.

### *EEG Recording and Processing*

The EEG was recorded with 27 active electrodes (ActiCap, GmbH, Germany) placed according to the International 10–10 System. The nose tip served as the reference, and Fp1 was the ground electrode. Vertical (VEOG) and horizontal (HEOG) electrooculograms were recorded near the eyes. Impedance was kept below 10 kΩ, and the EEG was digitized at 500 Hz (16-bit DC amplifier, BrainAmp, Brain Products GmbH, Herrsching, Germany). A digital bandpass filter (0.1-80 Hz) was applied offline, and bad data segments were rejected using the Artifact Subspace Reconstruction (ASR) algorithm and independent component analysis (ICA). The EEG was segmented into 4-second epochs, and theta power (4-8 Hz) was extracted for F3 and F4 electrodes. Signal processing was done with EEGLAB (Delorme & Makeig, 2004).

For the oddball task, the EEG was filtered (0.1-40 Hz), segmented into 1200 ms epochs (-200 to 1000 ms), and only correct target epochs were included. Epochs were corrected for baseline, excessive amplitude (>100 μV) was rejected, and ocular artifacts were corrected with ICA (Lee et al., 1999). A minimum of 40 artifact-free epochs were averaged, and the frequency was transformed using FFT to extract mean amplitude (μV) for the 4-8 Hz range (ERtheta) at F3, Fz, F4, and Pz electrodes. Processing was performed using ERPLAB (Lopez-Calderon & Luck, 2014)

### Data Analysis

Baseline differences between adults receiving real or sham tACS were analyzed using t-tests or Wilcoxon's tests for continuous variables and Chi-squared tests for dichotomous variables (see Table 1). The effect of tACS on resting-state EEG was assessed with Wilcoxon's tests on theta band power (4-8 Hz) at F3 and F4, comparing pre- and post-T sessions. Task performance effects were analyzed using t-tests for RT to hits in the oddball and SRC tasks (normal distribution), and Wilcoxon's tests for d', RT to FAs, and SSRT (non-normal distribution). Theta amplitudes (ERtheta) during the oddball task were also analyzed with Wilcoxon's tests at F3, Fz, F4, and Pz electrodes. Significant pre- vs post-T differences in the real-tACS group were further analyzed with Mann-Whitney U tests or t-tests for group comparisons. Bonferroni correction was applied for multiple comparisons, and $p \leq .05$ was considered significant. Two-sided p-values are reported.

In addition, correction for multiple outcomes (adjusted to Bonferroni's) were applied whenever the analysis yielded significant results regarding the variables measured in the SRC and S-S tasks, as (1) speed measures in these tasks correlate strongly with each other, as well as accuracy measures, and (2) there were no specific hypotheses for each of these parameters.

For sensations caused by tACS, Mann-Whitney U tests compared real vs. sham tACS groups (Supplementary Table 1). Statistical analysis was performed using IBM SPSS.

## Results

There were no differences in cognitive and demographical variables between the two groups, as shown in Table 1.

### Behavioural Results

### *Oddball Task*

The Wilcoxon's test performed on d' showed a significant effect in the real-tACS group ($p = .017$; see Table 2), indicating that this parameter was significantly larger in the post-T than in the pre-T session (see Figure 2 and Supplementary Table 2). On the other hand, the Wilcoxon test performed on d' in the sham-tACS group did not show a significant effect ($p = 1$). No significant effects emerged when considering RT to hits or RT to FAs as the dependent variable, in any of the groups (see Table 2).

The additional t-test performed on the post-T *minus* pre-T difference values regarding d' showed a significant effect ($t = 2.331$, $p = .028$), as the real-tACS group showed a larger (i.e., more positive) change ($M = .42$, $SD = .57$) than the sham-tACS ($M = -.13$, $SD = .66$) group (see Figure 5).

### *Stimulus-Response Compatibility (SRC) Task*

The Wilcoxon's tests performed on the congruent hit RT and on the incongruent hit RT in the sham-tACS group, and on the congruent hit RT in the real-tACS group showed significant effects ($p = .050$, $p = .027$, $p = .020$, respectively; see Table 2), indicating that these parameters were significantly lower in the post-T session than in the pre-T session (see Figure 2 and Supplementary Table 2). The Wilcoxon test performed on the incongruent hit RT in the real-tACS group showed a similar trend ($p = .072$). However, these effects did not remain after correcting for multiple outcomes ($p = .2$ for the congruent hit RT in the sham-tACS group, $p = .108$ for the incongruent hit RT in the sham-tACS group, and $p = .288$ for the incongruent hit RT in the real-tACS group), and only a trend regarding the congruent hit RT in the real-tACS group ($p = .080$) remained. When considering d' as the dependent variable, no significant effects were found (see Table 2 and Figure 2).

**Table 2**

*The Results of Wilcoxons's and t-Tests (Session) Applied to (1) the Behavioural Parameters Obtained in the Oddball, SRC and S-S tasks, (2) the EEG Parameters Obtained in the Oddball task, and (3) the Resting state EEG Parameters, are Reported. Reported p-Values are Bonferroni Corrected*

| **BEHAVIOURAL PARAMETERS** | **ODDBALL TASK** | | |
|---|---|---|---|
| **pre-t vs post-t comparisons** | **d'** | **Hit RTs** | **FA RTs** |
| **Real-tACS** | **W = 2.377** **$p$ = .034*** | t = 1.018 $p$ = .326 | W = -.445 $p$ = 1 |
| **Sham-tACS** | W = -0.471 $p$ = 1 | t = -.481 $p$ = .640 | W = -.051 $p$ = 1 |

| **pre-t vs post-t comparisons** | **SRC TASK** | | | **S-S TASK** | | |
|---|---|---|---|---|---|---|
| | **d'** | **Hit RT (congruent)** | **Hit RT (incongruent)** | **d'** | **Go RT (hits)** | **SSRT** |
| **Real-tACS** | W = 1.420 $p$ = .312 | **t = 2.617** **$p$ = .020*** | t = 1.946 $p$ = 0.072 | **W = 2.272** **$p$ = .046*** | W = -.594 $p$ = 1 | W = -1.995 $p$ = .092 |
| **Sham-tACS** | W = -.756 $p$ = .9 | **t = 2.214** **$p$ = .05*** | **t = 2.598** **$p$ = .027*** | **W = 2.401** **$p$ = .032*** | W = -1.689 $p$ = .182 | W = -0.533 $p$ = 1 |

| **EEG PARAMETERS** | **ODDBALL TASK** **Event-related power spectrum: Theta amplitudes (4-8 Hz)** | | | |
|---|---|---|---|---|
| **pre-t vs post-t comparisons** | **F3** | **Fz** | **F4** | **Pz** |
| **Real-tACS** | W = 1.846 $p$ = .13 | W = 1.819 $p$ = .138 | **W = 2.415** **$p$ = .032*** | W = .966 $p$ = .668 |
| **Sham-tACS** | W = -.314 $p$ = 1 | W = -.549 $p$ = 1 | W = -.549 $p$ = 1 | W = -.863 $p$ = .776 |

| **EEG PARAMETERS** | **RESTING-STATE EEG** | |
|---|---|---|
| **pre-t vs post-t comparisons** | **F3** | **F4** |
| **Real-tACS** | **W = 3.294** **$p$ = .002**** | **W = 2.272** **$p$ = .046*** |
| **Sham-tACS** | W = 2.197 $p$ = .056 | W = 2.118 $p$ = .068 |

*Note.* Pre-t: pre-treatment; Post-t: post-treatment, RT: reaction time, FA: false alarm, SRC: stimulus-response compatibility, S-S: Stop-signal, SSRT: stop-signal reaction time, EEG: electroencephalogram.
*$p$ < 0.05 **$p$ < 0.01

### *Stop-Signal (S-S) Task*

The Wilcoxon's tests performed on d' showed a significant effect, both in the real-tACS ($p$ = .046) and in the sham-tACS group ($p$ = .032; see Table 2), indicating that d' was significantly larger in the post-T session than in the pre-T session in both groups (see Figure 2). However, these effects did not remain significant when multiple outcomes' correction was applied ($p$ = .092 for the real-tACS group and $p$ = .064 for the sham-tACS group). When considering the RT to hits in the Go condition, or SSRT as the dependent variable, no significant effects were found.

### *Resting-State EEG Results*

The Wilcoxon's tests performed on theta power at the F3 and F4 electrode locations showed a significant session effect in the real-tACS group ($p$ = .002, and $p$ = .046, respectively; see Table 2), as power in the theta band was larger in the post-T than in the pre-T this group (see Figure 3 and Supplementary Table 2). In addition, the Wilcoxon's test performed on these parameters in the sham-tACS group showed marginally significant effects ($p$ = .056, and $p$ = .068, respectively).

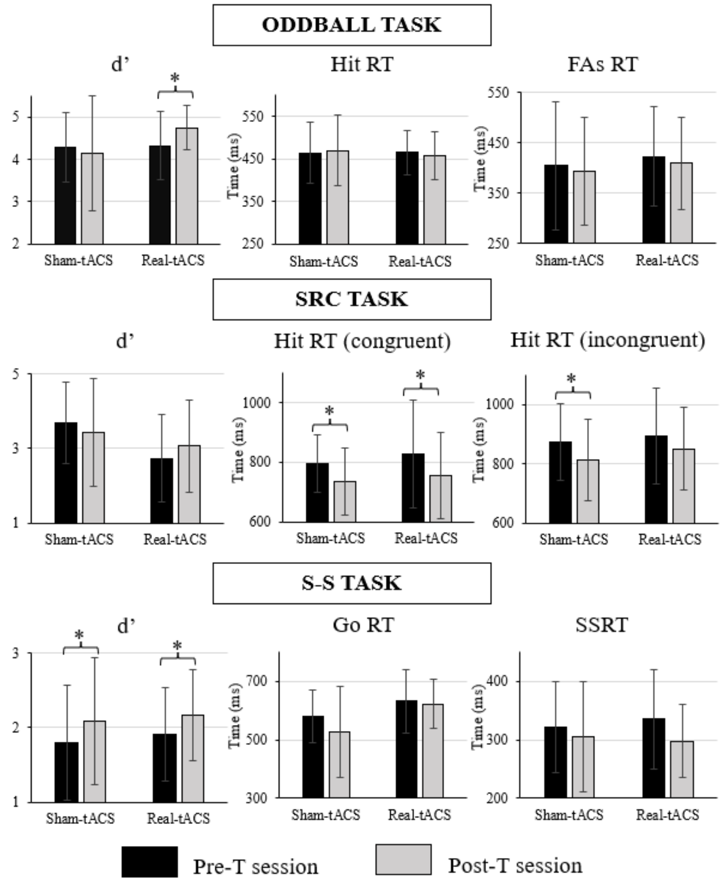
The additional Mann-Whitney's U test performed on the post-T *minus* pre-T difference values regarding theta power at the F3 and F4 locations did not show any significant effects ($U$ = 82, $p$ = .719 and $U$ = 110, $p$ = .347, respectively), indicating that the magnitude of change was rather similar between groups in both locations (see Figure 5).

### *Event-Related Theta (ERtheta) Amplitude Results (Oddball Task)*

The Wilcoxon's tests performed on the ERtheta mean amplitude at the F4 electrode location showed a significant effect in the real-tACS group ($p$ = .032; see Table 2), as this parameter was larger in the post-T session than in the pre-T session in this group (see Figure 4 and Supplementary Table 2). The same tendency can be observed in the data obtained at the F3, Fz, and Pz electrode locations in the real-tACS group (see Figure 4 and Supplementary Table 2), but the ANOVAs did not show any significant effects or interactions for ERtheta mean amplitudes at these locations (see Table 2). On the other hand, the Wilcoxon's test performed on these parameters in the sham-tACS group did not show any effects.

**Figure 2**

*Bar Diagrams Depicting the Behavioural Parameters Analyzed in Each Task*




*Note.* Upper pannel: d', hit reaction times (Hit RT), and reaction times to false alarms (FAs RT) obtained in the oddball task; Middle pannel: d', reaction times in the congruent condition (Hit RT congruent), and reaction times in the incongruent condition (Hit RT incongruent) obtained in the SRC task; and Lower pannel: d', reaction times in the Go condition (Go RT), and stop-signal reaction time (SSRT) for the S-S task.

**Figure 3**

*Theta Power at the F3 and F4 Electrode Locations Obtained in the Resting-State EEG, in Both Groups (Real-tACS and Sham-tACS)*

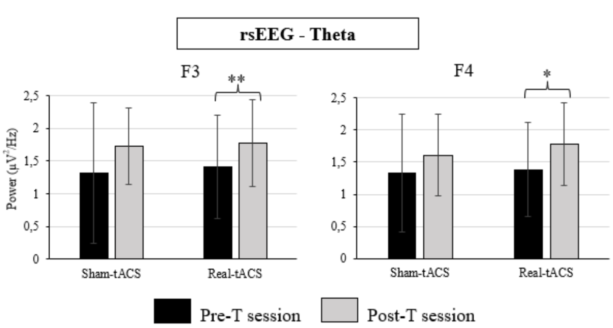
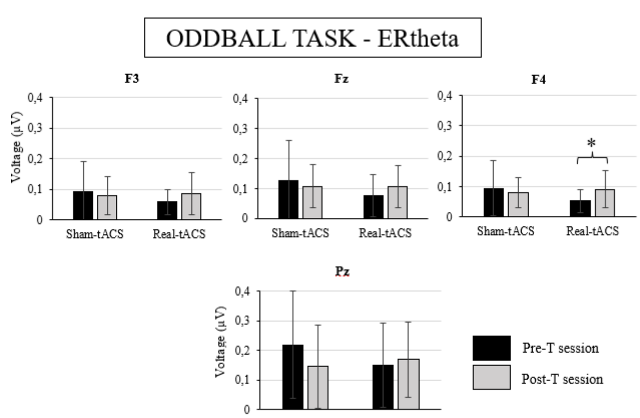



**Figure 4**

*Bar Diagrams Depicting the Mean Amplitude of Event-related EEG Activity in the Theta Range (4-8 Hz) at the F3, F4, Fz and Pz Electrode Locations Obtained in the Oddball Task in the Pre-treatment (pre-T) and Post-treatment (post-T) for Both*



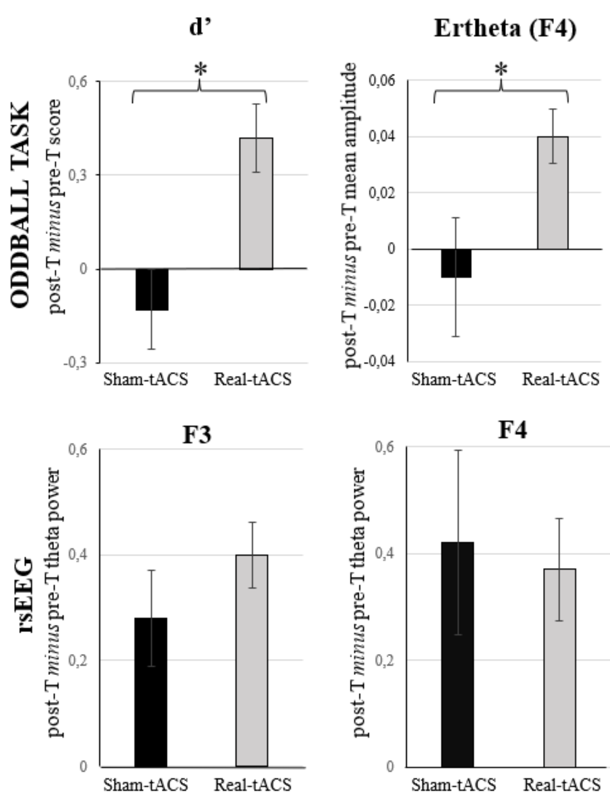
The additional t-test performed on the post-T minus pre-T difference values regarding the ERtheta values at the F4 electrode location showed a significant effect ($t$ = 2.240, $p$ = .034: see Figure 5), as the magnitude of change was larger (i.e., more positive) in the real-tACS ($M$ = .04, $SD$ = .05) than in the sham-tACS ($M$ = -.01, $SD$ = .07) group.

### Blinding Results and tACS-Induced Sensations

Participants were unable to discriminate which type of tACS (real, sham) they received. All participants responded they received real stimulation, except for one participant from the sham-tACS group and two from the real-tACS group that selected "I don't know", and one participant from the real-tACS group that selected "Sham". Furthermore, analysis comparing data collected in the real-tACS and sham-tACS groups demonstrated no differences in the perception of irritation, pain, heat, burning, itching, or the taste of iron between the real and sham tACS (all $p$ > .221). Therefore, participants in the real-tACS groups experienced indistinguishable sensations from those experienced by the sham-tACS group; thus, reducing experimental biases on participants' expectancies was achieved by concealing the sort of stimulation that was received (the data are in Supplementary Table 1).

**Figure 5**

*Bar Diagrams Depicting the Post-T Minus Pre-T Difference Scores in Each Group, for Those Parameters That Yielded Significant Results in Each Group in the Pre-T vs. Post-T Comparisons*




## Discussion

In this study, tACS combined with CCT showed to be an effective method to enhance cognitive performance of middle age and elderly participants with SCD, MCI and dementia. Participants that received online theta-tACS in the last six sessions of the 12-session intervention showed better performance (indexed by d') in the oddball task after than before treatment, while participants that received sham stimulation did not. In line with this, the magnitude of change in d' (from the pre-T to the post-T session) was more positive in the real-tACS group. In consequence, the CCT + theta-tACS combined treatment enhanced cognitive execution related to attention and working memory, and this enhancement stems from the treatment effect rather than learning or external factors. Importantly, this behavioural improvement showed a psychophysiological correlate, as only participants in the real-tACS group showed larger theta amplitude in the post-T session compared to the pre-T session during the oddball task performance, and the magnitude of change from before to after treatment was thus larger and positive in the real-tACS group. These results support our main hypothesis, demonstrating that online theta-tACS induced larger theta activity in the DLPFC region during the oddball task associated with better performance. This may indicate that theta-tACS applied over the DLPFC facilitated cognitive function by increasing theta activity in this site, supporting a causal association between tACS and cognitive performance of the participants during WM, as previously suggested (Alekseichuk et al., 2017). More importantly, these changes were present several days after finishing treatment, as the post-T evaluation was carried out 4.5 days (mean) after the last intervention session.

We also expected to find differences due to tACS application in the behavioural parameters obtained during the SRC and S-S tasks, as they require from attentional and WM engagement (the processes that received higher training during CCT). More specifically, we expected to find weaker effects compared to the Oddball task, as inhibition processes are central to these tasks but were only marginally included in this cognitive training (in two out of 23 activities). In effect, we observed that both groups improved in behavioural execution in both the SRC and S-S tasks, although these improvements were not significant after multiple comparisons correction. These results indicate that there were some behavioural improvements both in the quality of performance and in the speed of the responses in the cognitive tasks. These improvements might be due to the CCT effects, to a general learning effect, or to both combined effects. In any case, differences due to tACS application were not observed, indicating that while tACS enhanced the outcomes of those cognitive processes well trained during stimulation, it was not sufficient to enhance execution in less trained processes.

Furthermore, we expected to find larger effects of tACS on theta power measured in the resting-state EEG in the real-tACS group compared to the sham-tACS group. Both groups showed similar enhancements in theta power after treatment, indicating that CCT may have induced changes in brain oscillatory activity in the theta range. However, these results were significant in the real-tACS group, and only marginally significant in the sham-tACS group. On the other hand, the magnitude of change was not significantly different between groups, indicating that it is probable that these effects were induced by CCT. In any case, larger samples would be necessary to clarify whether these effects indicate that tACS can boost the changes in resting-state theta activity induced by CCT or are just a correlate of a general CCT effect.

It has been suggested that online and offline tACS may induce different effects, being stronger for online protocols where neural activity synchronizes with tACS frequency (Klink et al., 2020). In this study tACS was delivered online during several cognitive tasks that engaged areas also involved in cognitive performance during the oddball task. This may explain the present results, as theta activity was significantly enhanced during the oddball task in the real-tACS group (but not in the sham-tACS group), while theta enhancements in the rsEEG (during which different networks are engaged) after treatment were present (and rather similar) in both groups, and thus do not seem to be restricted to the real-tACS participants.

This study has also some limitations. Firstly, the sample size is rather small, and this may have contributed to the difficulty in finding group differences in some parameters. Besides, it is worth noting that the post-T session was performed between day 1 and day 7 after finishing the treatment. This means that there were subjects that were not evaluated after treatment until 7 days after finishing it. Therefore, some effects might have decayed as the strongest effects of tES are usually found during or immediately after stimulation. On the other hand, this also indicates that the significant effects observed in this study are robust. In the last place, tACS was delivered with CCT + tACS only in 6 sessions. Recent studies found interesting long-lasting results when combining this type of treatments (CCT + gamma-tACS) for 4 weeks in adults with cognitive decline (Kehler et al., 2020; Moussavi et al., 2021). Hence, future studies need to take this into account designing longer protocols applied to larger samples.

Future studies should include larger samples that would allow to study the possible differences in treatment outcomes between participants with SCD, MCI and dementia. Furthermore, multi-session approaches need to be considered, with 10 or more sessions for tACS application. In addition, testing participants in different time points (e.g., 1 day after treatment and 1 or more weeks after treatment) would contribute to refine present knowledge about the aftereffects of this type of treatments, and this is important to design long-lasting treatment strategies.

In conclusion, this study provides behavioural evidence about the efficacy of multi-session CCT + theta-tACS (real vs sham) applied over the DLPFC to improve cognitive performance of participants with subjective or objective cognitive decline, supported by psychophysiological measures. This reinforces the starting point to improve experimental designs to maximize the efficacy of these type of treatments.

## Author Contributions

**Susana Cid-Fernández:** Methodology, investigation, software, formal analysis, data curation, writing – original draft, writing – review and editing, visualization. **Ana Nieto-Vieites**: Methodology, investigation, writing – review and editing. **Arturo X. Pereiro**: Conceptualization, methodology, writing – review and editing, funding acquisition, supervision, project administration. **Fernando Díaz**: Conceptualization, methodology, writing – original draft, writing – review and editing, funding acquisition, supervision, project administration.

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## Declaration of Interests

The authors declare that there are no conflicts of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author, Susana Cid-Fernández.

## References

Abellaneda-Pérez, K., Vaqué-Alcázar, L., Perellón-Alfonso, R., Bargalló, N., Kuo, M.-F., Pascual-Leone, A., Nitsche, M. A., & Bartrés-Faz, D. (2020). Differential tDCS and tACS Effects on Working Memory-Related Neural Activity and Resting-State Connectivity. *Frontiers in Neuroscience, 13*, Article 1440. https://doi.org/10.3389/fnins.2019.01440

Abubaker, M., Al Qasem, W., & Kvašňák, E. (2021). Working memory and cross-frequency coupling of neuronal oscillations. *Frontiers in Psychology*, *12*, Article 4506. https://doi.org/10.3389/fpsyg.2021.756661

Al Qasem, W., Abubaker, M., & Kvašňák, E. (2022). Working memory and transcranial-alternating current stimulation—state of the art: findings, missing, and challenges. *Frontiers in Psychology*, *13*, Article 822545. https://doi.org/10.3389/FPSYG.2022.822545

Alekseichuk, I., Pabel, S. C., Antal, A., & Paulus, W. (2017). Intrahemispheric theta rhythm desynchronization impairs working memory. *Restorative Neurology and Neuroscience*, *35*(2), 147–158. https://doi.org/10.3233/RNN-160714

Alekseichuk, I., Turi, Z., de Lara, G. A., Antal, A., & Paulus, W. (2016). Spatial working memory in humans depends on theta and high gamma synchronization in the prefrontal cortex. *Current Biology*, *26*(12), 1513–1521. https://doi.org/10.1016/j.cub.2016.04.035

Antal, A., Alekseichuk, I., Bikson, M., Brockmöller, J., Brunoni, A. R., Chen, R., Cohen, L. G., Dowthwaite, G., Ellrich, J., Flöel, A., Fregni, F., George, M. S., Hamilton, R., Haueisen, J., Herrmann, C. S., Hummel, F. C., Lefaucheur, J. P., Liebetanz, D., Loo, C. K., … Paulus, W. (2017). Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. *Clinical Neurophysiology*, *128*(9), 1774–1809. https://doi.org/10.1016/j.clinph.2017.06.001

Atasoy, S., Donnelly, I., & Pearson, J. (2016). Human brain networks function in connectome-specific harmonic waves. *Nature Communications*, *7*, Article 10340. https://doi.org/10.1038/NCOMMS10340

Borghini, G., Candini, M., Filannino, C., Hussain, M., Walsh, V., Romei, V., Zokaei, N., & Cappelletti, M. (2018). Alpha oscillations are causally linked to inhibitory abilities in ageing. *The Journal of Neuroscience*, *38*(18), 4418-4429. https://doi.org/10.1523/JNEUROSCI.1285-17.2018

Cespón, J., Galdo-Álvarez, S., & Díaz, F. (2018a). Event-related potentials reveal altered executive control activity in healthy elderly with subjective memory complaints. *Frontiers in Human Neuroscience*, *12*, Article 445. https://doi.org/10.3389/FNHUM.2018.00445

Cespón, J., Miniussi, C., & Pellicciari, M. C. (2018b). Interventional programmes to improve cognition during healthy and pathological ageing: Cortical modulations and evidence for brain plasticity. *Ageing Research Reviews*, *43*, 81–98. https://doi.org/10.1016/j.arr.2018.03.001

Cid-Fernández, S., Lindín, M., & Díaz, F. (2021). Event-related brain potential indexes provide evidence for some decline in healthy people with subjective memory complaints during target evaluation and response inhibition processing. *Neurobiology of Learning and Memory*, *182*, Article 107450. https://doi.org/10.1016/j.nlm.2021.107450

Clark, K., Squire, R. F., Merrikhi, Y., & Noudoost, B. (2015). Visual attention: Linking prefrontal sources to neuronal and behavioral correlates. *Progress in Neurobiology*, *132*, 59–80. https://doi.org/10.1016/J.PNEUROBIO.2015.06.006

Cruz, P., Fong, K. N. K., & Brown, T. (2021). Transcranial direct current stimulation as an adjunct to cognitive training for older adults with mild cognitive impairment: A randomized controlled trial. *Annals of Physical and Rehabilitation Medicine*, *64*(5), Article 101536. https://doi.org/10.1016/j.rehab.2021.101536

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), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Facal, D., Guàrdia-Olmos, J., Pereiro, A. X., Lojo-Seoane, C., Peró, M., & Juncos-Rabadán, O. (2019). Using an overlapping time interval strategy to study diagnostic instability in Mild Cognitive Impairment subtypes. *Brain Sciences*, *9*(9), Article 242. https://doi.org/10.3390/BRAINSCI9090242

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*(2), 175–191. https://doi.org/10.3758/bf03193146

Fertonani, A., Ferrari, C., & Miniussi, C. (2015). What do you feel if I apply transcranial electric stimulation? Safety, sensations and secondary induced effects. *Clinical Neurophysiology*, *126*(11), 2181–2188. https://doi.org/10.1016/j.clinph.2015.03.015

Fries, P. (2005). A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends in Cognitive Sciences*, *9*(10), 474–480. https://doi.org/10.1016/J.TICS.2005.08.011

Fröhlich, F. (2015). Experiments and models of cortical oscillations as a target for noninvasive brain stimulation. *Progress in Brain Research*, *222*, 41–73. https://doi.org/10.1016/bs.pbr.2015.07.025

Goodman, M. S., Kumar, S., Zomorrodi, R., Ghazala, Z., Cheam, A. S. M., Barr, M. S., Daskalakis, Z. J., Blumberger, D. M., Fischer, C., Flint, A., Mah, L., Herrmann, N., Bowie, C. R., Mulsant, B. H., Rajji, T. K., Pollock, B. G., Lourenco, L., Butters, M., Gallagher, D., … Voineskos, A. N. (2018). Theta-Gamma coupling and working memory in Alzheimer's dementia and Mild Cognitive Impairment. *Frontiers in Aging Neuroscience*, *10*, Article 101. https://doi.org/10.3389/fnagi.2018.00101

Grover, S., Nguyen, J. A., & Reinhart, R. M. G. (2021). Synchronizing brain rhythms to improve cognition. *Annual Review of Medicine*, *72*, 29–43. https://doi.org/10.1146/ANNUREV-MED-060619-022857

Hafkemeijer, A., Altmann-Schneider, I., Oleksik, A. M., Van De Wiel, L., Middelkoop, H. A. M., Van Buchem, M. A., Van Der Grond, J., & Rombouts, S. A. R. B. (2013). Increased functional connectivity and brain atrophy in elderly with subjective memory complaints. *Brain Connectivity*, *3*(4), 353–362. https://doi.org/10.1089/brain.2013.0144

Hanslmayr, S., Axmacher, N., & Inman, C. S. (2019). Modulating human memory via entrainment of brain oscillations. *Trends in Neurosciences*, *42*(7), 485–499. https://doi.org/10.1016/j.tins.2019.04.004

Hasselmo, M. E. (2005). What is the function of hippocampal theta rhythm?-Linking behavioral data to phasic properties of field potential and unit recording data. *Hippocampus*, *15*(7), 936–949. https://doi.org/10.1002/HIPO.20116

Hsieh, L. T., & Ranganath, C. (2014). Frontal midline theta oscillations during working memory maintenance and episodic encoding and retrieval. *NeuroImage*, *85*, 721–729. https://doi.org/10.1016/J.NEUROIMAGE.2013.08.003

Hsu, W.-Y., Zanto, T. P., Van Schouwenburg, M. R., & Gazzaley, A. (2017). Enhancement of multitasking performance and neural oscillations by transcranial alternating current stimulation. *PLoS ONE*, *12*(5), Article e0178579. https://doi.org/10.1371/journal.pone.0178579

Jones, D. T., & Graff-Radford, J. (2021). Executive dysfunction and the prefrontal cortex. *Continuum: Lifelong Learning in Neurology, 27*(6), 1586–1601. https://doi.org/10.1212/CON.0000000000001009

Jones, K. T., Johnson, E. L., Gazzaley, A., & Zanto, T. P. (2022). Structural and functional network mechanisms of rescuing cognitive control in aging. *NeuroImage*, *262*, Article 119547. https://doi.org/10.1016/j.neuroimage.2022.119547

Jones, K. T., Ostrand, A. E., Gazzaley, A., & Zanto, T. P. (2023). Enhancing cognitive control in amnestic mild cognitive impairment via at-home non-invasive neuromodulation in a randomized trial. *Scientific Reports*, *13*, Article 7435. https://doi.org/10.1038/s41598-023-34582-1

Kehler, L., Francisco, C. O., Uehara, M. A., & Moussavi, Z. (2020). The effect of transcranial alternating current stimulation (tACS) on cognitive function in older adults with dementia. *Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2020,* 3649–3653. https://doi.org/10.1109/EMBC44109.2020.9175903

Kim, J., Kim, H., Jeong, H., Roh, D., & Kim, D. H. (2021). tACS as a promising therapeutic option for improving cognitive function in Mild Cognitive Impairment: A direct comparison between tACS and tDCS. *Journal of Psychiatric Research*, *141*, 248–256. https://doi.org/10.1016/j.jpsychires.2021.07.012

Kirova, A. M., Bays, R. B., & Lagalwar, S. (2015). Working memory and executive function decline across normal aging, Mild Cognitive Impairment, and Alzheimer's Disease. *BioMed Research International*, *2015*, Article 748212. https://doi.org/10.1155/2015/748212

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

Klink, K., Paßmann, S., Kasten, F. H., & Peter, J. (2020). The modulation of cognitive performance with transcranial alternating current stimulation: A systematic review of frequency-specific effects. *Brain Sciences, 10*(12), Article 932. https://doi.org/10.3390/brainsci10120932

Lee, T. L., Lee, H., & Kang, N. (2023). A meta-analysis showing improved cognitive performance in healthy young adults with transcranial alternating current stimulation. *npj Science of Learning*, *8*, Article 1. https://doi.org/10.1038/s41539-022-00152-9

Lee, T. W., Girolami, M., & Sejnowski, T. J. (1999). Independent component analysis using an extended infomax algorithm for mixed subgaussian and supergaussian sources. *Neural Computation*, *11*(2), 417–441. https://doi.org/10.1162/089976699300016719

Liu, C. S., Herrmann, N., Gallagher, D., Rajji, T. K., Kiss, A., Vieira, D., & Lanctôt, K. L. (2020). A pilot study comparing effects of bifrontal versus bitemporal transcranial direct current stimulation in Mild Cognitive Impairment and mild Alzheimer Disease. *Journal of ECT*, *36*(3), 211–215. https://doi.org/10.1097/YCT.0000000000000639

Lopez-Calderon, J., & Luck, S. J. (2014). ERPLAB: An open-source toolbox for the analysis of event-related potentials. *Frontiers in Human Neuroscience*, *8*, Article 213. https://doi.org/10.3389/fnhum.2014.00213

Macmillan, N. A., Creelman, C. D., & Macmillan, A. (1990). Response bias: Characteristics of detection theory, threshold theory, and "nonparametric" indexes. *Psychological Bulletin*, *107*(3), 401–413. https://doi.org/10.1037/0033-2909.107.3.401

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., Klunk, W. E., Koroshetz, W. J., Manly, J. J., Mayeux, R., Mohs, R. C., Morris, J. C., Rossor, M. N., Scheltens, P., Carrillo, M. C., Thies, B., Weintraub, S., & Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's Disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's Disease. *Alzheimer's and Dementia*, *7*(3), 263–269. https://doi.org/10.1016/j.jalz.2011.03.005

Mendoza, N., Del Valle, S., Rioja, N., Gomez-Pilar, J., & Hornero, R. (2018). Potential benefits of a cognitive training program in Mild Cognitive Impairment (MCI). *Restorative Neurology and Neuroscience*, *36*(2), 207–213. https://doi.org/10.3233/RNN-170754

Moussavi, Z., Kimura, K., Kehler, L., de Oliveira Francisco, C., & Lithgow, B. (2021). A novel program to improve cognitive function in individuals with dementia using transcranial alternating current stimulation (tACS) and tutored cognitive exercises. *Frontiers in Aging*, *2*, Article 632545. https://doi.org/10.3389/fragi.2021.632545

Osaka, M., Osaka, N., Kondo, H., Morishita, M., Fukuyama, H., Aso, T., & Shibasaki, H. (2003). The neural basis of individual differences in working memory capacity: An fMRI study. *NeuroImage*, *18*(3), 789–797. https://doi.org/10.1016/S1053-8119(02)00032-0

Reinhart, R. M. G., & Nguyen, J. A. (2019). Working memory revived in older adults by synchronizing rhythmic brain circuits. *Nature Neuroscience*, *22*(5), 820–827. https://doi.org/10.1038/s41593-019-0371-x

Riddle, J., Scimeca, J. M., Cellier, D., Dhanani, S., & D'Esposito, M. (2020). Causal evidence for a role of theta and alpha oscillations in the control of working memory. *Current Biology*, *30*(9), 1748–1754. https://doi.org/10.1016/j.cub.2020.02.065

Roux, F., & Uhlhaas, P. J. (2014). Working memory and neural oscillations: α-γ versus θ-γ codes for distinct WM information? *Trends in Cognitive Sciences*, *18*(1), 16–25. https://doi.org/10.1016/J.TICS.2013.10.010

Sanches, C., Stengel, C., Godard, J., Mertz, J., Teichmann, M., Migliaccio, R., & Valero-Cabré, A. (2021). Past, present, and future of non-invasive brain stimulation approaches to treat cognitive impairment in neurodegenerative diseases: Time for a comprehensive critical review. *Frontiers in Aging Neuroscience*, *12*, Article 578339. https://doi.org/10.3389/fnagi.2020.578339

Sauseng, P., Griesmayr, B., Freunberger, R., & Klimesch, W. (2010). Control mechanisms in working memory: A possible function of EEG theta oscillations. *Neuroscience and Biobehavioral Reviews*, *34*(7), 1015–1022. https://doi.org/10.1016/j.neubiorev.2009.12.006

Saykin, A. J., Wishart, H. A., Rabin, L. A., Santulli, R. B., Flashman, L. A., West, J. D., McHugh, T. L., & Mamourian, A. C. (2006). Older adults with cognitive complaints show brain atrophy similar to that of amnestic MCI. *Neurology*, *67*(5), 834–842. https://doi.org/10.1212/01.wnl.0000234032.77541.a2

Schutter, D. J. L. G., & Wischnewski, M. (2016). A meta-analytic study of exogenous oscillatory electric potentials in neuroenhancement. *Neuropsychologia*, *86*, 110–118. https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2016.04.011

Tavakoli, A. V., & Yun, K. (2017). Transcranial alternating current stimulation (tACS) mechanisms and protocols. *Frontiers in Cellular Neuroscience*, *11*, Article 214. https://doi.org/10.3389/fncel.2017.00214

Uhlhaas, P. J., Pipa, G., Lima, B., Melloni, L., Neuenschwander, S., Nikolić, D., & Singer, W. (2009). Neural synchrony in cortical networks: History, concept and current status. *Frontiers in Integrative Neuroscience*, *3*, Article 17. https://doi.org/10.3389/neuro.07.017.2009

Varela, F., Lachaux, J. P., Rodriguez, E., & Martinerie, J. (2001). The brainweb: Phase synchronization and large-scale integration. *Nature Reviews Neuroscience*, *2*(4), 229–239. https://doi.org/10.1038/35067550

Viviano, R. P., Hayes, J. M., Pruitt, P. J., Fernandez, Z. J., van Rooden, S., van der Grond, J., Rombouts, S. A. R. B., & Damoiseaux, J. S. (2019). Aberrant memory system connectivity and working memory performance in subjective cognitive decline. *NeuroImage*, *185*, 556–564. https://doi.org/10.1016/j.neuroimage.2018.10.015

Wang, X. J. (2010). Neurophysiological and computational principles of cortical rhythms in cognition. *Physiological Reviews*, *90*(3), 1195–1268. https://doi.org/10.1152/PHYSREV.00035.2008

Wang, X., Mao, Z., Ling, Z., & Yu, X. (2020). Repetitive transcranial magnetic stimulation for cognitive impairment in Alzheimer's Disease: a meta-analysis of randomized controlled trials. *Journal of Neurology*, *267*(3), 791–801. https://doi.org/10.1007/S00415-019-09644-Y

Wischnewski, M., Alekseichuk, I., & Opitz, A. (2023). Neurocognitive, physiological, and biophysical effects of transcranial alternating current stimulation. *Trends in Cognitive Sciences*, *27*(2), 189–205. https://doi.org/10.1016/j.tics.2022.11.013

Zanto, T. P., Jones, K. T., Ostrand, A. E., Hsu, W. Y., Campusano, R., & Gazzaley, A. (2021). Individual differences in neuroanatomy and neurophysiology predict effects of transcranial alternating current stimulation. *Brain Stimulation*, *14*(5), 1317–1329. https://doi.org/10.1016/J.BRS.2021.08.017

Zurrón, M., Lindín, M., Cespón, J., Cid-Fernández, S., Galdo-álvarez, S., Ramos-Goicoa, M., & Díaz, F. (2018). Effects of mild cognitive impairment on the event-related brain potential components elicited in executive control tasks. *Frontiers in Psychology*, *9*, Article 842. https://doi.org/10.3389/fpsyg.2018.00842