# After-effects of 10 Hz tACS over the prefrontal cortex on phonological word decisions

Vera Moliadze [a, *], Leon Sierau [a], Ekaterina Lyzhko [b, c], Tristan Stenner [a], Michael Werchowski [a], Michael Siniatchkin [a, d], Gesa Hartwigsen [e, **]

[a] Institute of Medical Psychology and Medical Sociology, University Medical Center Schleswig Holstein, Kiel University, Germany
[b] Department of Neuropediatrics, University Medical Center Schleswig Holstein, Kiel University, Germany
[c] Institute of Mathematical Problems of Biology RAS - the Branch of Keldysh Institute of Applied Mathematics of Russian Academy of Sciences, Pushchino, Moscow Region, Russia
[d] Clinic for Child and Adolescent Psychiatry and Psychotherapy, Medical Center Bethel, Bielefeld, Germany
[e] Lise Meitner Research Group Cognition and Plasticity, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

## ARTICLE INFO

## ABSTRACT

Introduction: Previous work in the language domain has shown that 10 Hz rTMS of the left or right posterior inferior frontal gyrus (pIFG) in the prefrontal cortex impaired phonological decision-making, arguing for a causal contribution of the bilateral pIFG to phonological processing. However, the neurophysiological correlates of these effects are unclear. The present study addressed the question whether neural activity in the prefrontal cortex could be modulated by 10 Hz tACS and how this would affect phonological decisions.
Methods: In three sessions, 24 healthy participants received tACS at 10 Hz or 16.18 Hz (control frequency) or sham stimulation over the bilateral prefrontal cortex before task processing. Resting state EEG was recorded before and after tACS. We also recorded EEG during task processing.
Results: Relative to sham stimulation, 10 Hz tACS significantly facilitated phonological response speed. This effect was task-specific as tACS did not affect a simple control task. Moreover, 10 Hz tACS significantly increased theta power during phonological decisions. The individual increase in theta power was positively correlated with the behavioral facilitation after 10 Hz tACS.
Conclusion: Our results show a facilitation of phonological decisions after 10 Hz tACS over the bilateral prefrontal cortex. This might indicate that 10 Hz tACS increased task-related activity in the stimulated area to a level that was optimal for phonological performance. The significant correlation with the individual increase in theta power suggests that the behavioral facilitation might be related to increased theta power during language processing.

## Introduction

Some of the most thoroughly investigated neural networks for cognitive functions are language networks. Functional neuro-imaging has provided a relatively sound understanding of the structures involved in certain language functions. This holds true especially for the processing of the sound of written and spoken words (i.e., phonological processing) [1,2]. One structure of exceptional importance for phonological processing is the left posterior inferior frontal gyrus (pIFG), located in the prefrontal cortex. The pIFG shows increased task-related activation during phonological decisions compared to decisions on the meaning of words (i.e., semantic decisions) [1–3]. The functional relevance of the left pIFG in phonological decisions was demonstrated by "virtual lesions" induced by online (repetitive) transcranial magnetic stimulation (TMS) applied during task-processing [4,5]. While most studies focused on the left-hemisphere, Hartwigsen et al. [6] showed that the left and the right pIFG essentially contribute to phonological decision-making.

At the neurophysiological level, phonological processing has been associated with modulations of several early and late components at the sublexical and lexical phonological level, including the N100, P200, P300 and N400 [7–10]. A growing body of

evidence further associates language processing with the underlying oscillatory neural dynamics. Correlative studies emphasize a decrease of alpha activity and an increase in gamma and theta activity in key language areas during different language tasks [11–14]. Other studies found a higher event-related desynchronization of alpha activity in the IFG after challenging relative to easy word listening conditions [15] and for low-frequent compared to high-frequent words [11]. These findings suggest an association between the magnitude of reduction in alpha activity and task-difficulty, speaking in favour of a functional role of alpha-oscillations in cognitive tasks.

A major limitation of most of the available studies is their purely correlative nature. While many studies observed a relationship between alpha activity and the (dis-)inhibition of brain areas, one can hardly draw causal conclusions on the relevance of these oscillatory changes for certain cognitive functions. Recently, rhythmic neuro-stimulation by means of rTMS or transcranial alternating current stimulation (tACS) has been shown to modulate the ongoing oscillatory activity [16–22]. Behavioral and neurophysiological effects of both techniques have been reported to outlast the stimulation period for several minutes [23–28]. For tACS, lasting after-effects on the oscillatory activity have been reported for up to 70 min after stimulation [24]. Such "offline" effects allow for a combination of tACS and EEG without having to deal with the strong artifacts caused by the electrical stimulation. Importantly, the after-effects of tACS likely differ from the immediate online effects observed during stimulation. Specifically, it was argued that offline effects reflect short-term synaptic plasticity in response to the stimulation rather than entrained activity as observed during online tACS [22,28,29]. The results by Vossen et al. [28] suggested that online tACS entrainment effects may not be strong enough to outlast the stimulation, while offline tACS plasticity effects may be present in the absence of entrainment echoes. Notably, only few studies considered both behavioral and oscillatory after-effects simultaneously [27], although a better understanding of the after-effects of tACS would be mandatory to validate the efficacy of this approach and its potential for therapeutic purposes.

The present study aimed at investigating offline effects of 10 Hz tACS on phonological language processing. Motivated by our previous study [6], we combined offline tACS to modulate alpha activity in the bilateral prefrontal cortex before subsequent phonological decision-making with simultaneous EEG measurements to map changes in oscillatory dynamics. Our study addressed the following questions. First, we aimed at determining whether offline 10 Hz tACS would affect behavior in a language task and how this might be reflected in the underlying neural dynamics. Specifically, we were interested in tACS-induced changes in the alpha power during phonological processing. Based on the above-discussed studies, we expected to find behavioral disruption with 10 Hz tACS. The disruptive after-effect of our tACS protocol should be reflected in a change in the oscillatory power during rest and task processing.

## Materials and methods

The study was in accordance with the latest revision of the *Declaration of Helsinki*. Experimental procedures were approved by the local ethics committee of the Medical Faculty at Kiel University. Prior to the experiment, subjects gave their written informed consent.

### Subjects

Twenty four healthy, native German-speaking students (12 female, 12 male participants) aged between 18 and 30 years

(M = 22.0, SD = 3.36) participated in the study. To calculate our sample size, we used g*Power [31] with the following settings: effect size f = 0.25, $\alpha$ level = 0.05, power = 0.9, correlation among repeated measures = 0.7. The minimum sample size was found to be 22, which we increased to 24 to fully counterbalance the order of stimulation conditions across participants. All participants were right-handed according to the Edinburgh Handedness Inventory [32]. None of them took any medication, or had a history of neurological diseases, or metallic head implants. Subjects were recruited via social media and flyers at Kiel University. They received either course credit or one cinema voucher for each session.

### Experimental design

Participants underwent three sessions with three different stimulation conditions. tACS was applied before task processing. To control for learning effects, the order of stimulation frequencies was counterbalanced across subjects. During tACS application, participants were asked to sit still with eyes open in a silent room. We included an inter-session interval of 2 weeks to prevent carry-over effects of tACS and minimize task-related learning effects.

Fig. 1 provides a schematic overview of our experimental session. At the beginning of each session, participants performed a short training of the phonological task. Thereafter, EEG and tACS electrodes were mounted. Five minutes of resting state EEG were recorded with open eyes, followed by 20 min of tACS and another 5 min of resting state EEG. Subjects were then placed in front of a 22″ screen (16:9 aspect ratio) at a distance of 60 cm. They performed 1 min of a non-linguistic control task and 15 min of the phonological task (Fig. 1A). At the end of each session, subjects completed a questionnaire on potential side-effects of the stimulation (adapted from Ref. [33]).

### Experimental tasks and stimuli

Both tasks were programmed in PsychoPy 1.8.5.1 [34,35]. Stimulus onset, responses and type of stimulus (left/right or 2/3 syllables, respectively) were registered via LabJack U3 LV in the EEG.

The phonological decision task was adapted from our previous studies [6,30]. A total of 300 words (150 two- and three-syllable words each) were presented in random order and subjects were asked to decide via button press whether the respective words consisted of two or three syllables. The original data set in the previous studies consisted of 120 high-frequent non-ambiguous German nouns from the CELEX lexical database [36]. An additional set of 180 German nouns were selected based on the same inclusion criteria (i.e., highly frequent, unambiguous nouns, 50% 2-syllable and 50% 3-syllable words, respectively, matched for the number of letters) to increase the power for the EEG analyses. An additional set of 50 words was selected for task practice before the main experiment. During each trial, stimuli were presented for 800 ms and responses were counted from stimulus onset. After stimulus offset, a fixation cross was shown for 1166 ± 166 ms, resulting in an average inter-trial interval of 3000 ms (Fig. 1B). We used a simple decision making task to test task specificity. For more details, see SI Methods.

### Transcranial alternating current stimulation

tACS was applied via two round rubber electrodes (9 cm$^2$), using a battery-operated stimulator system (neuroConn, Ilmenau, Germany). Electrodes were attached to the head underneath an EEG Recording Cap (EasyCap GmbH, Herrsching, Germany) using
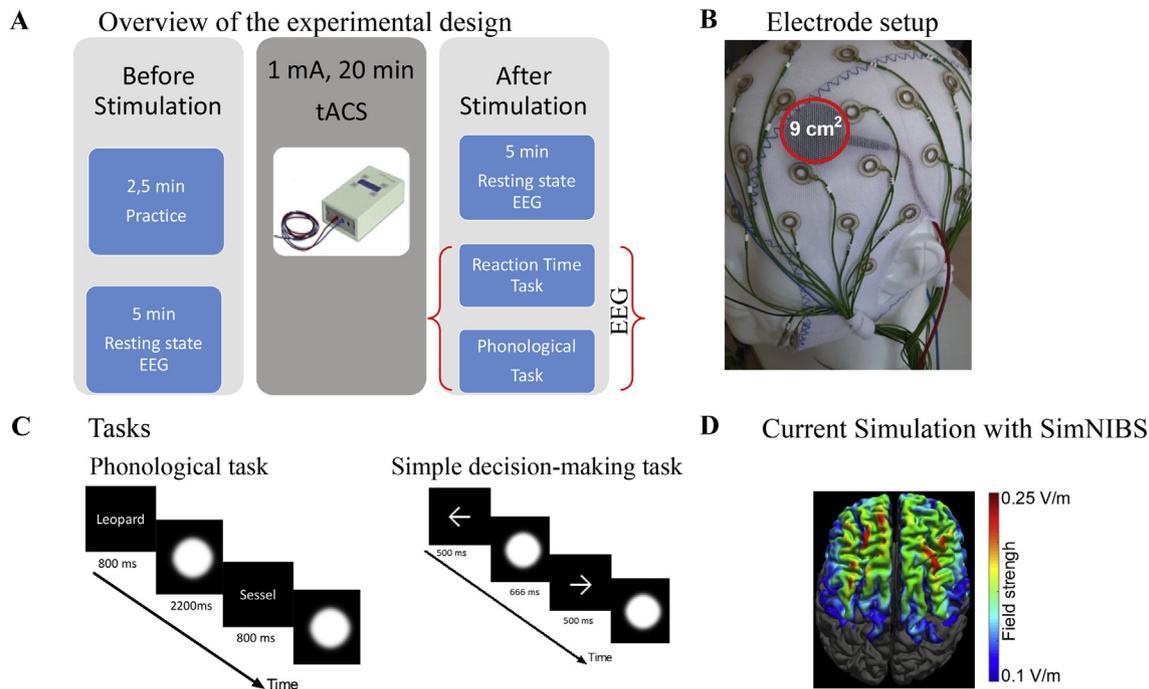
## A Overview of the experimental design



## B Electrode setup



## C Tasks



## D Current Simulation with SimNIBS



**Fig. 1. Experimental Design**. (A) Time-course of the experiment. At the beginning of each session, participants performed a short training of the phonological task. Five minutes of resting state EEG were recorded with open eyes, followed by 20 min of tACS and another 5 min of resting state EEG. Subjects performed 1 min of a non-linguistic control task and 15 min of the phonological task. (B) Tasks. Phonological decision task. Stimuli were presented visually for 800 ms and subjects had to decide via button press whether the respective word consisted of two or three syllables. Control task. Directional arrows were presented visually and subjects had to indicate their direction by pressing the corresponding button. (C) Electrode setup. tACS was applied via two round rubber electrodes (9 cm$^2$) that were placed bilaterally over the prefrontal cortex. The prefrontal cortex was located based on the crossing-point of T3-Fz x F7-Cz (right prefrontal cortex) and T4-Fz x F8-Cz (left prefrontal cortex). (D) Simulation of the electric field of the stimulation.

conductive Ten20 EEG paste (Ten20, Weaver and Company, Aurora, CO, USA). They were placed bilaterally over the prefrontal cortex (Fig. 1C). Stimulation sites were located based on the crossing-point of T3-Fz x F7-Cz (right prefrontal cortex) and T4-Fz x F8-Cz (left prefrontal cortex) [25,37,38]. To allow for placement of the tACS electrodes between the EEG electrodes, we slightly adapted the montage such that the final position was located between F1, F5 and FC3 (left hemisphere) and F2, F6 and FC4 (right hemisphere), respectively. The impedances were kept below 10 kΩ. We applied oscillating currents at 10 Hz (frequency of interest), 16.18 Hz (control frequency) or sham stimulation for 20 min with an intensity of 1 mA. The current was ramped up and down over the first and last 15 s of stimulation. During sham stimulation, the current was ramped up for 15 s, followed by 30 s of 1 mA stimulation (at either 10 Hz or 16.18 Hz) and then ramped down for 15 s.

We chose 16.18 Hz as control frequency since the ratio of 16.18 Hz and 10 Hz minimizes the probability of synchronization [39] and the sensations of tACS in the beta range are similar to those of tACS in the alpha range (compared to tACS in theta or gamma range) [40].

### Electroencephalography (EEG) recordings

The Experiment was conducted in a dimly lit room. EEG was measured from 64 sintered Ag—AgCl electrodes mounted in an elastic cap (FMS, Munich, Germany). The electrodes were arranged in an equidistant 64-channel montage with Cz, C3, and C4 corresponding to the international 10—20 system. Reference and ground electrode were positioned between Fp1 and Fp2. Additionally, a vertical Electrooculogram (EOG) was recorded underneath the right eye to monitor eye-movements during the experiment. All impedances were kept below 10 kΩ with some tolerance to avoid delaying the experiment. EEG was recorded using two 32-channel

BrainAmp (Brain Products GmbH, Gilching, Germany) amplifiers and the BrainVision Recorder Software (Brain Products GmbH, Gilching, Germany). The signal was registered at a rate of 1000 Hz and low-pass filtered at 250 Hz.

### Signal preprocessing

EEG signal pre-processing was performed in BrainVisionAnalyzer 2 (Brain Products GmbH, Gilching, Germany). First, resting state data before and after stimulation were preprocessed. All data were re-referenced to the common average reference (CAR). A fourth order IIR Butterworth filter was then applied. Data were low-pass filtered at 40 Hz and high-pass filtered at 1 Hz (filter borders indicate the half-power cutoff). The data were segmented into 1-s-intervals. The segmented data underwent a gross artifact removal, which automatically removed segments included voltage jumps greater than 125 μV in a period of 500 ms or less. On average, 266 (SD: 44) of originally 300 segments remained after this procedure. The remaining data were corrected for ocular artifacts, using the "fast ICA" algorithm implemented in Analyzer 2. On average, 88 (SD: 71) segments contained ocular artifacts. For task related EEG data, instead of using segmentation into 1-s intervals, trials were formed relative to the stimulus onset, 800 ms before and 1000 ms after stimulus.

After preprocessing, signal processing was continued using the Fieldtrip toolbox (http://fieldtrip.fcdonders.nl/). A fast Fourier transform (FFT) with a Hanning taper was applied and the frequency range was defined to be within the interval from 1 to 30 Hz with steps of 1 Hz. For resting state data, FFT transformations with estimation of power-spectra were performed across 1 s segments before and after stimulation. The power-spectra were averaged over the segments before and after stimulation in every subject.

For task related EEG data, the first interval was selected 800 ms before stimulus until stimulus onset (i.e. 0 ms); the second interval ranged from stimulus onset to 800 ms after stimulus.

### Statistical analyses

#### Behavioral data

Statistical analyses for behavioral data were performed in R 3.4 [41] (URL https://www.R-project.org/). The effects of the factors *tACS* (10 Hz, 16.18 Hz or sham) and *session order* (first, second or third) were analyzed separately for each task with linear mixed effects models (LME) including fixed slopes and random intercept. Degrees of freedom analogous to repeated measures ANOVAs were approximated using the Kenward-Rogers method [42]. Prior to analysis, response time data was inversely transformed to avoid potential problems associated with skewed data [43] and response times for invalid trials were removed. For the error analysis, hierarchical LME models with a Poisson distributed error were fitted to the data and compared with likelihood ratio tests. While task accuracy is easy to interpret, ANOVAs are not well suited to compare this data [43]. Using the absolute error count (which, due to the constant trial count is equivalent to the error rate) enabled us to adequately compare errors with common analysis models [44].

#### EEG data

Statistical analysis was performed on FFT-transformed data using 2-way within-subject cluster-based permutation ANOVA [45–47] based on non-parametric statistics in the FieldTrip toolbox (http://fieldtrip.fcdonders.nl/). The significance probability was estimated based on a Monte-Carlo Permutation test with a cluster-based approach. The Permutation test avoids assumptions on normal distribution of data and solves the problem of multiple comparisons by cluster correction. First, for observed data, the method calculates statistics (t-values) for each sample point and thresholds them by critical t-values corresponding to a probability level of 0.05. In a second step, a cluster-based correction method [48] was used. With this approach, a sample point is included in the cluster, if it has at least one neighboring point with a t-value greater than the critical value. The sum of t-values is then assigned to its respectively built cluster. This procedure was repeated for 1000 permuted data. After that, for permuted data, significance probability was estimated as a proportion between the number of cases with a larger test statistic than the observed one to the number of permutations. A *p*-value below 0.05 (i.e. > 95% of the permuted datasets did not show clusters with larger sums of t-values) was considered significant.

#### Frequency analyses of resting state and task related EEG

Using the magnitude of the FFT-transformed resting state data, a 2-way cluster-based permutation ANOVA with the within-subjects factors *tACS* (10 Hz, 16.18 Hz, sham) and *time* (before or after tACS) was performed separately for different frequency bands (theta: 4–7 Hz, alpha: 8–12 Hz and beta: 13–30 Hz). Analyses of potential tACS-induced changes in the beta and theta band were exploratory. These analyses were motivated by the fact that we chose a control condition (16.18 Hz) in the beta band and, for the theta band, that previous work associated modulation in the theta band with working memory processes. Since our phonological task (syllable counting) relies on (phonological) working memory processes [49], potential behavioural tACS effects might be related to the modulation of working memory processes.

The same procedure was performed for task related EEG, with the cluster-based permutation ANOVA including the within-subject factors *tACS* (10 Hz, 16.18 Hz, sham) and *time window* (pre- or post-stimulus presentation). Time windows were defined on averaged

power spectra in the time intervals before and after the stimulus. For FFT of resting state and task related EEG, time intervals were defined as described above.

#### ROI analyses

To further explore tACS induced changes under the stimulation electrodes and directly contrast the effects in both hemispheres, region of interest (ROI) analyses were computed for the EEG electrodes located in the left (F1; F5; FC3) and right (F2; F6; FC4) prefrontal cortex separately for resting state and task related EEG. We used cluster-based permutation ANOVAs including the within-subjects factors *tACS* (10 Hz, 16.18 Hz, sham) and *region* (left prefrontal cortex: F1; F5; FC3 and right prefrontal cortex: F2; F6; FC4) for each frequency band (theta: 4–7 Hz, alpha: 8–12 Hz and beta: 13–30 Hz). Conditional on significant F-values, post-hoc paired t-tests were used to further characterize differences among conditions.

Task related EEG analyses for the control task are reported in the SI Methods section.

### Results

None of the subjects requested to terminate stimulation or asked for any medical intervention during or after the end of tACS (For more details about side effects, see SI Results).

#### Behavioral data

#### Effects of tACS on phonological response speed

Statistical analysis of response speed showed significant main effects of *tACS* (F(2, 40) = 3.69, *p* = 0.034) and *session order* (F(2, 40) = 17.2, *p* < 0.001), but no significant interaction (F(4, 42) = 0.327, *p* = 0.858). Post-hoc tests revealed significantly faster decisions reflected in higher response speed values (inverse response time: responses per second [1/s]) after 10 Hz compared to sham stimulation, independent of the session order (t = −2.66, *p* = 0.029; Fig. 2A) and a significant learning effect between sessions (Table 1).

For the error analysis, hierarchical linear mixed effect models with a Poisson distributed error were fitted to the data and compared with likelihood ratio tests. Both *session order* ($\chi^2$ (2) = 23, *p* < 0.001) and the interaction of *tACS* and *session order* ($\chi^2$ (4) = 12.2, *p* = 0.016) were significant, but there was no main effect of *tACS* ($\chi^2$ (2) = 1.83, *p* = 0.4; Table 1). The interaction was driven by an increase in the mean error rates for 10 Hz relative to sham tACS in the first session (z = −2.40; *p* = 0.044), which was not significant for 16.18 Hz relative to sham tACS (z = −2.3; *p* = 0.055) or 10 Hz relative to 16.18 Hz (z = 0.20; *p* = 0.98). There were no significant effects in the following sessions (all *p*-values > 0.1).

There was no significant correlation between errors and mean inverse response time (10 Hz tACS: Spearman's r = −0.1, *p* = 0.63; 16.18 Hz tACS: r = 0.03, *p* = 0.90; sham tACS: r = − 0.1, *p* = 0.63; see Fig. 2B–D), precluding a strong influence of a speed-accuracy tradeoff.

For behavioral effects of tACS on the control task, see SI Results.

#### Neurophysiological data

#### Resting state EEG

A 2 × 3 cluster-based permutation ANOVA revealed no main effect of *tACS*, but a significant main effect of *time* in all frequency bands (Fig. 3A and Table 2). The interaction between *tACS* and *time* was not significant in either frequency band. Analysis of power spectra of segments after active or sham stimulation revealed an
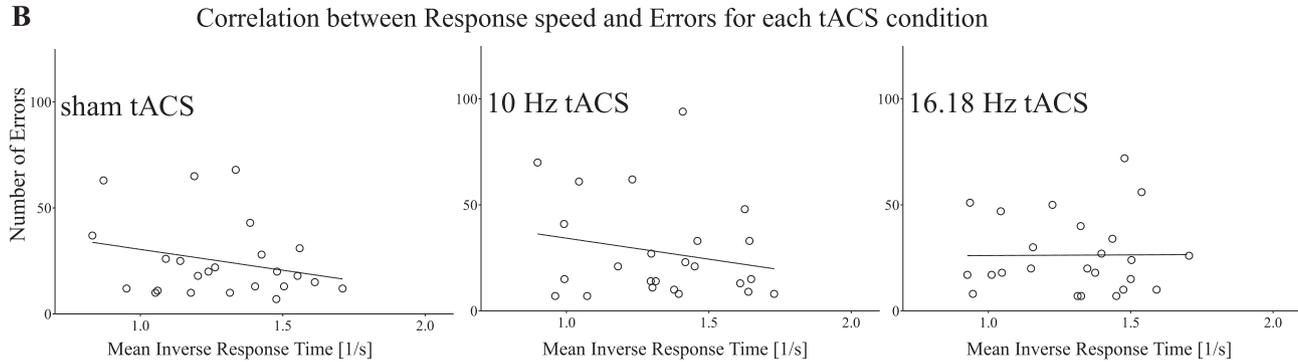
**A**
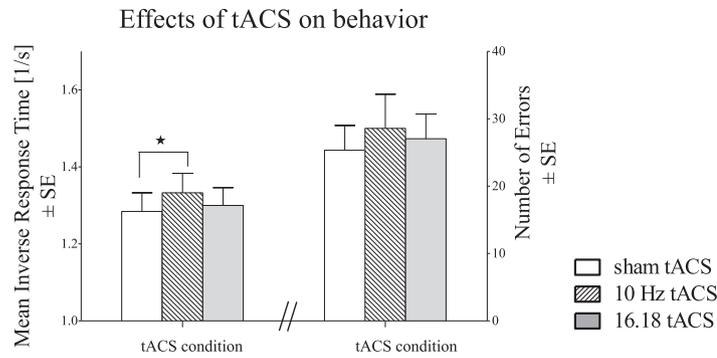


**B**



**Fig. 2. Behavioral Data.** **(A)** Effects of tACS on response speed (left) and error rates (right). The left panel illustrates the significant facilitation in phonological response speed after 10 Hz tACS relative to sham tACS. **(B–D)** There was no significant correlation between errors and response speed. Note that since response times were inversely transformed [1/s], higher values indicate faster responses.

**Table 1**
Behavioral results.

| Phonological Task (mean ± SEM) | | | |
|---|---|---|---|
| | sham tACS | 10 Hz tACS | 16.18 tACS |
| *Inverse response time [1/s]* | 1.28 ± 0.05 | 1.33 ± 0.05 | 1.30 ± 0.05 |
| *Errors* | 25.33 ± 3.68 | 28.58 ± 5.06 | 27.04 ± 3.67 |

**Post-hoc comparisons of conditions**
***Inverse response time***

| Post-hoc test | estimate | SE | df | t | *p* |
|---|---|---|---|---|---|
| sham tACS - 16.18 Hz tACS | −0.0156 | 0.0182 | 40 | −0.857 | 0.67 |
| sham tACS - 10 Hz tACS | −0.0484 | 0.0182 | 40 | −2.66 | ***0.029*** |
| 16.18 Hz tACS - 10 Hz tACS | −0.0328 | 0.0182 | 40 | −1.8 | 0.181 |
| S1 - S2 | −0.0621 | 0.0182 | 40 | −3.41 | ***0.004*** |
| S1 - S3 | −0.106 | 0.0182 | 40 | −5.84 | ***< .001*** |
| S2 - S3 | −0.0441 | 0.0182 | 40 | −2.43 | 0.051 |

***Errors***
***S1***

| Post-hoc test | estimate | SE | df | t | *p* |
|---|---|---|---|---|---|
| sham tACS - 16.18 Hz tACS | −0.3028 | 0.1315 | Inf | −2.304 | 0.055 |
| sham tACS - 10 Hz tACS | −0.2785 | 0.1163 | Inf | −2.395 | ***0.044*** |
| 16.18 Hz tACS - 10 Hz tACS | 0.0243 | 0.1236 | Inf | 0.197 | 0.978 |

***S2***

| | | | | | |
|---|---|---|---|---|---|
| sham tACS - 16.18 Hz tACS | 0.0803 | 0.1293 | Inf | 0.621 | 0.809 |
| sham tACS -10 Hz tACS | −0.1746 | 0.1244 | Inf | −1.403 | 0.339 |
| 16.18 Hz tACS - 10 Hz tACS | −0.2549 | 0.1289 | Inf | −1.977 | 0.118 |

***S3***

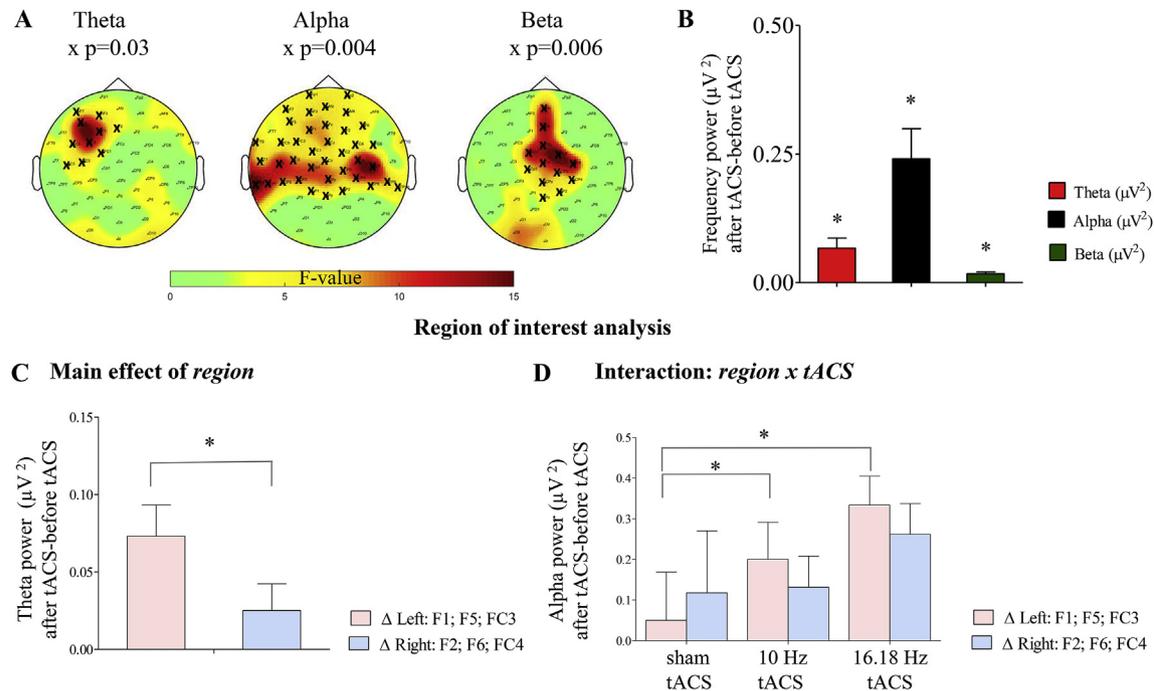| | | | | | |
|---|---|---|---|---|---|
| sham tACS - 16.18 Hz tACS | 0.0094 | 0.1168 | Inf | 0.080 | 0.997 |
| sham tACS - 10 Hz tACS | 0.2606 | 0.1391 | Inf | 1.873 | 0.147 |
| 16.18 Hz tACS - 10 Hz tACS | 0.2512 | 0.1325 | Inf | 1.896 | 0.140 |

S1−S3= Session 1−3.

**Fig. 3. Resting State EEG results.** (A) Main effect of time (after tACS - before tACS) for the power value of each frequency band. (B) Significant increase in the power values in the theta, alpha and beta frequency bands. *indicates a significant difference in the post-hoc comparison. (C) Main effect of region. The difference in theta power (after tACS - before tACS) was significantly lower in the right prefrontal cortex. (D) Significant interaction between *tACS* and *region* in the alpha band. Post-hoc analyses of power values show that compared to sham stimulation, both active tACS conditions led to a significant increase in alpha power differences in the left prefrontal cortex. All p < 0.05.

increase in the theta ($p = 0.03$), alpha ($p = 0.04$) and beta power ($p = 0.006$) (for significant channel topography see SI Fig. 1).

In the ROI analyses, cluster-based permutation ANOVAs revealed no main effect of *tACS* in either frequency band, but a significant main effect of *region* in the theta band ($p = 0.01$), indicating that theta power differences were significantly lower in the right prefrontal cortex (Fig. 3C). The interaction between *tACS* and *region* was significant in the alpha band only ($p = 0.02$). Post-hoc analyses of power values showed that compared to sham stimulation, both active tACS conditions led to a significant increase in alpha power in the left prefrontal cortex (Fig. 3D, Tables 2 and 3 for all comparisons).

*Task related EEG*

A $2 \times 3$ cluster-based permutation ANOVA revealed no main effect of *tACS*, however, the main effect of *time window* was significant for all frequency bands (Fig. 4A and Tables 2 and 3). Most importantly, we found a significant interaction between *tACS* and *time window* for theta power ($p = 0.04$). Analysis of power spectra from pre- and post-stimulus intervals after active or sham stimulation revealed an overall increase in the theta and decrease in the alpha and beta power after the stimulus (Fig. 4B, for significant channel topography, see SI Fig. 2).

The significant interaction between *tACS* and *time window* in the theta band was driven by the difference between 10 Hz tACS and sham tACS (Fig. 5A). Post-hoc tests showed a significant increase in theta power after the stimulus for 10 Hz tACS compared to sham tACS ($p = 0.02$) that was not significant for 16.18 Hz relative to sham tACS ($p = 0.1$) or 10 Hz relative to 16.18 Hz ($p = 0.1$) (Fig. 5B). Moreover, the individual increase in theta power after 10 Hz tACS was positively correlated with the phonological response speed (Spearman's $r = 0.55$; $p = 0.005$; Fig. 5C), indicating faster response speed with increased theta power. This correlation was specific for 10 Hz and not significant for 16.18 Hz (Spearman's $r = 0.33$,

$p = 0.12$) or sham tACS (Spearman's $r = 0.35$, $p = 0.2$). Additionally, we compared the correlations between response speed and theta power between all three tACS conditions (using Pearson & Filon's z [50]) and found a significantly stronger correlation for 10 Hz tACS relative to 16.18 Hz tACS ($z = 1.82$, $p = 0.034$) and a trend towards a stronger correlation for 10 Hz relative to sham tACS ($z = 1.57$, $p = 0.05$). The difference between 16.18 Hz and sham tACS was not significant ($z = 0.372$, $p = 0.355$).

In the ROI analyses, cluster-based permutation ANOVAs revealed no main effect of *tACS*, but a significant main effect of *region* ($p = 0.02$). There was a significant decrease in theta power after the stimulus compared to before the stimulus in the right prefrontal cortex. The interaction between *tACS* and *region* was also significant in the theta band only ($p = 0.01$). Post-hoc analysis of power values showed that compared to sham stimulation, both active tACS conditions led to a significant increase in theta power differences in the right prefrontal cortex (Fig. 4C and D, Tables 2 and 3 for all comparisons). For neurophysiological effects of tACS on the control task, see SI Results.

**Discussion**

Here, we combined 10 Hz offline tACS over the bilateral prefrontal cortex with a phonological decision task and simultaneous EEG measurements to investigate the after-effects of rhythmic non-invasive brain stimulation on language processing. As a main finding, phonological response speed was significantly facilitated after 10 Hz tACS relative to sham stimulation. This effect was task-specific, as tACS did not modulate response speed in an easy control task (decision making). However, we cannot draw conclusions on the frequency specificity of the observed behavioural facilitation since phonological response speed was not significantly different between 10 Hz tACS and the control frequency (16.18 Hz).

**Table 2**
Neurophysiological effects.

| Measurement | Factor | p |
|---|---|---|
| *Resting state EEG* | | |
| Theta | tACS | 0.2 |
| | time | **0.03** |
| | tACS x time | no clusters |
| Alpha | tACS | 0.2 |
| | time | **0.004** |
| | tACS x time | 0.2 |
| Beta | tACS | 0.2 |
| | time | **0.006** |
| | tACS x time | no clusters |
| *Task related EEG* | | |
| Theta | tACS | no clusters |
| | time window | **0.02** |
| | tACS x time window | **0.04** |
| Alpha | tACS | no clusters |
| | time window | **0.001** |
| | tACS x time window | no clusters |
| Beta | tACS | no clusters |
| | time window | **0.001** |
| | tACS x time window | no clusters |
| *ROI analyses resting state EEG* | | |
| Theta | tACS | 0.2 |
| | region | **0.01** |
| | tACS x region | 0.7 |
| Alpha | tACS | 0.1 |
| | region | 0.6 |
| | tACS x region | **0.02** |
| Beta | tACS | 0.8 |
| | region | 0.7 |
| | tACS x region | 0.2 |
| *ROI analyses task related EEG* | | |
| Theta | tACS | 0.4 |
| | region | **0.02** |
| | tACS x region | **0.02** |
| Alpha | tACS | 0.1 |
| | region | 1 |
| | tACS x region | 0.2 |
| Beta | tACS | 0.8 |
| | region | 0.5 |
| | tACS x region | 0.8 |

All p-values are derived from cluster-based permutation tests.

**Table 3**
Post-hoc comparisons for neurophysiological effects.

| Resting state EEG: Effect of *time* (after vs. before tACS) | Theta | Alpha | Beta |
|---|---|---|---|
| after vs. before tACS | 0.03 | 0.004 | 0.006 |
| **Task related EEG: Effect of *time window* (post- vs. pre-stimulus presentation)** | Theta | Alpha | Beta |
| post- vs. pre-stimulus presentation | 0.02 | 0.001 | 0.001 |
| **Task related EEG: Interaction: *tACS x time window* (post- vs. pre-stimulus presentation)** | Theta | Alpha | Beta |
| sham tACS vs. 10 Hz tACS | 0.02 | – | – |
| sham tACS vs. 16.18 Hz tACS | 0.1 | – | – |
| 10 Hz tACS vs. 16.18 Hz tACS | 0.1 | – | – |
| **ROI analyses: Effect of *region*: Comparison between left and right prefrontal regions** *Resting state EEG* | Theta | Alpha | Beta |
| left vs. right prefrontal region | 0.01 | – | – |
| *Task related EEG* | Theta | Alpha | Beta |
| left vs. right prefrontal region | 0.02 | – | – |
| ROI analyses: Interaction: *region x tACS* *Resting state EEG* | Theta | Alpha | Beta |
| sham tACS vs. 10 Hz tACS | – | 0.02 | – |
| sham tACS vs. 16.18 Hz tACS | – | 0.007 | – |
| 10 Hz tACS vs. 16.18 tACS | – | 0.5 | – |
| *Task related EEG* | Theta | Alpha | Beta |
| sham tACS vs. 10 Hz tACS | 0.02 | – | – |
| sham tACS vs. 16.18 Hz tACS | 0.02 | – | – |
| 10 Hz tACS vs. 16.18 tACS | 0.5 | – | – |

Paired t-tests were used in case of significant p-values (cluster-based permutation tests). Region: left prefrontal region comprised electrodes F1; F5; FC3; right prefrontal cortex comprised electrodes F2; F6; FC4.

We further observed a significant interaction between tACS and session on phonological error rates that was driven by increased errors after 10 Hz relative to sham tACS in the first session only. However, we did not find a significant correlation between the individual increase in errors and the facilitation in response speed. Consequently, there is no evidence for a speed-accuracy tradeoff in our data. While the effect of 10 Hz tACS on errors was only significant in the first session, the observed facilitation in response speed was significant across all sessions. The divergent effects of 10 Hz tACS on speed and error rates are difficult to explain. These findings might indicate an early disinhibition of behavior induced by 10 Hz tACS over the prefrontal cortex that might have been disguised by a learning effect in the following sessions.

As another finding of our study, we observed a significant increase in task-related theta power after the word stimulus following 10 Hz tACS relative to sham tACS. A significant (but moderate) positive correlation between individual increase in theta power and the individual behavioral facilitation that was specific for 10 Hz tACS suggests that increased theta power might represent the neurophysiological correlate of the observed behavioral facilitation. As an alternative explanation, one may assume that the observed increase in theta power could reflect the tACS-induced modulation of an underlying task-evoked electrophysiological response that might have disguised as an oscillation [51]. Indeed, several event-related potentials, some of which are also observed during phonological processing and working memory processes, have been associated with an increase in the alpha or theta power [51–54]. Even if we cannot dissociate the two explanations with our data, our findings suggest that the significant improvement in task performance was related to an increase in the underlying task-related neurophysiological signal.

Since task-related alpha power was not affected by 10 Hz tACS in our study, the observed after-effects seem to be unrelated to online entrainment in the stimulation frequency and may rather occur due to plastic alterations within the stimulated area or network [55]. While the absence of a tACS effect in the alpha band was unexpected, several previous studies have shown that after-effects of tACS are not restricted to the stimulation frequency, but can also occur in other frequency bands ([56,57] see Ref. [27] for review). Pahor and Jaušovec [57] showed that behavioral after-effects of theta-tACS on fluid intelligence correlated with changes in the theta and alpha band, suggesting that there might be functional cross-frequency modulation of those bands. In line with our findings, some previous studies found no after-effects in the stimulation frequency, but selectively in different frequency bands after
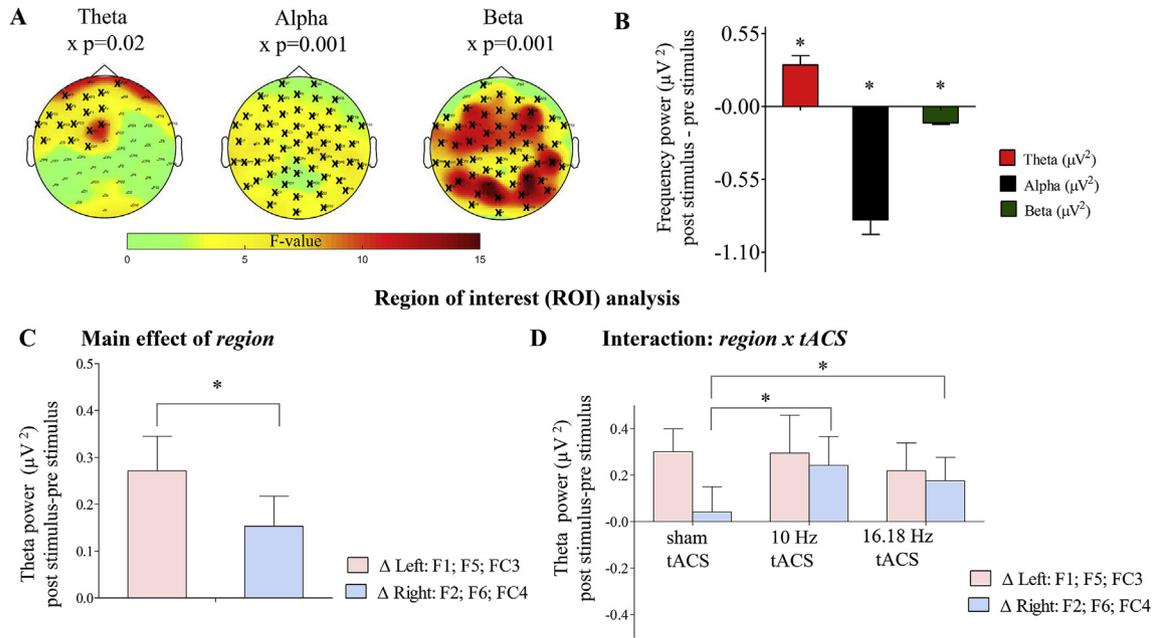
**Fig. 4. Task Related EEG results.** (A) Main effect of time window (post-vs. pre-stimulus presentation) for the power of each frequency band. (B) Significant increase in theta power after the stimulus [0 − 800 ms] compared to power before the stimulus [-800 − 0 ms] and decrease in the alpha and beta power. *indicates a significant difference in the post-hoc comparison. (C) Main effect of region: significant decrease in theta power after the stimulus [0 − 800 ms] compared to power before the stimulus [-800 − 0 ms] in the right prefrontal cortex. (D) Post-hoc analyses of power values showed that compared to sham stimulation, both active tACS conditions led to a significant increase in theta power differences in the right prefrontal cortex. All p < 0.05.
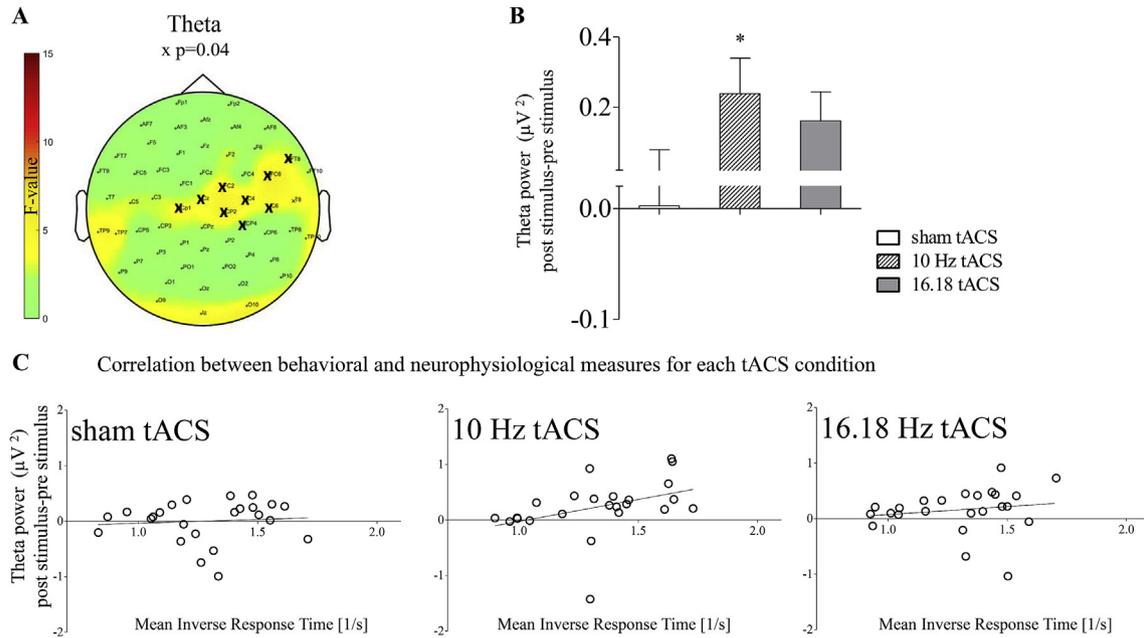


**Fig. 5. Task Related EEG results. (A)** Interaction between *tACS* and *time window* (pre-vs. post-stimulus presentation) for theta power. Significant channels: 'Cz' 'Cp1' 'FC2' 'CP2' 'C4' 'FC6' 'C6' 'FT8' 'T8' **(B)** Theta power was significantly increased after the stimulus for 10 Hz tACS compared to sham tACS. **(C)** The individual increase in theta power after 10 Hz tACS was positively correlated with the phonological response speed.

tACS [55,58] or oscillatory tDCS [59]. The absence of any modulatory effect during rest might indicate that the modulatory effects on short-term plasticity depended on the current brain state and interacted with the task (see below for discussion).

Notably, the observed tACS-induced facilitation of phonological response speed was unexpected as we initially hypothesized to find a significant disruption of phonological task performance. This assumption was based on previous studies that reported behavioral impairment when 10 Hz rTMS was applied over key language areas during different language tasks, including phonological processing [4,5,30,49,60,62]. As a main difference to the present study, the previous studies used online rTMS to interfere with task performance directly during processing. We refrained from online application here since the side effects induced by tACS (i.e.,

flickering sensations) and the tACS induced artifacts in the EEG signal might have interfered with the processes of interest. Consequently, our study design differs from the previous studies, which might explain the unexpected direction of the behavioral effect. It should be noted that the direction of the effects of many non-invasive brain stimulation protocols on performance in cognitive tasks is rather unclear. For instance, several studies reported faster response times with different online or offline rTMS protocols over temporal or frontal language areas [63—65], while other studies found delays in response speed during language tasks with these protocols [66,67]. However, only very few studies used 10 Hz protocols in an offline fashion in previous studies of cognition [64,68] and the expected effects on performance therefore remain unclear.

We believe that a likely explanation of the observed facilitation effects is related to the concept of state dependency [69]. Within this framework, it is argued that the direction of the behavioural outcome of TMS (i.e. facilitation or disruption) depends on the interaction of the current brain state and the stimulation intensity [70,71]. Crucially, changes in the brain state may result in a shift of the observed behavioral TMS pattern such that intensities, which normally impair perception, can have a facilitatory effect if the initial brain state has changed [71]. While these previous studies relied on TMS applied during task processing, effects of state dependency have also been suggested for transcranial electrical stimulation techniques [72]. It is plausible to assume that such effects might not only affect task processing directly during stimulation but might also prime the neural activity pattern in the stimulated area when given before the task by inducing neuroplasticity [29]. Hence, one might argue that offline tACS at 10 Hz could have primed neural activity in the stimulated area such that it was optimal for task performance in previous offline TMS studies [64,68] and in the present study.

The topographic changes after tACS should also be considered when interpreting the present results. Interestingly, task related theta-increase was confined to the left prefrontal cortex (Fig. 4A), while the modulatory effect of 10 Hz tACS on language performance increase was located in the right prefrontal cortex (Fig. 5A). This may point to a network effect, that is, a release of contralateral, right frontal activity from suppression of left frontal task-related theta activity. Indeed, ROI analyses revealed an increase in the theta frequency difference in the right prefrontal cortex after active stimulation at both frequencies. However, these changes were found for both active tACS conditions and were not correlated with the observed behavioural tACS effects. Consequently, it remains unclear whether this finding is behaviourally relevant.

Notably, the observed facilitatory effect of our 10 Hz tACS protocol is well in line with previous (online) tACS studies in the motor [23,73] and auditory spatial attentional system [74] as well as during working memory and inhibition tasks in the elderly [75]. These studies reported significant improvements in performance when 10 Hz tACS was given directly during task processing. To date, only a few studies used tACS to modulate language functions. Beneficial effects were reported for higher frequencies (35—40 Hz) during phonetic categorization in older subjects [76] or pitch memory in patients with congenital amusia [77] and for theta-tACS when applied during implicit language learning in the young and aging brain [78]. With respect to beneficial after-effects of tACS in the study of cognition, a few studies found increased working memory performance after tACS in the gamma or theta frequency [57,79—82]. To the best of our knowledge, the after-effects of (alpha-) tACS have not been explored in the language domain so far.

At the neurophysiological level, we found that 10 Hz tACS significantly modulated the task-induced event-related desynchronization in the theta band during phonological decisions. The observed increase in the post-stimulus theta power might indicate increased working memory efficiency that facilitated phonological decisions. Indeed, increased theta power was previously associated with successful performance in visual working memory tasks [83] and during phonological processing [84,85]. Initially, we expected a strong tACS-induced modulation in the alpha band. However, we only found an unspecific, general decrease in the alpha and beta band after the stimulus and an interaction with tACS for the theta band only. This indicates that rather than inducing a plastic aftereffect in the range of the stimulation frequency, tACS interacted with a different frequency that was related to a facilitation in task performance. This effect was task-specific and not reflected in the resting state EEG. A potential explanation for the absence of a strong tACS-induced effect in the alpha band during the task might be related to the fact that we did not stimulate with frequencies in the individual alpha band. It is possible that tACS may not increase alpha activity in participants who show a high level of alpha activity, but might rather induce improvement and alpha increase in subjects with a specific deficit in alpha activity, as suggested previously [86]. In that study, alpha activity was selectively increased by tACS with the individual subject's alpha frequency, when the individual alpha power had been low before stimulation. However, no increases in alpha activity were found if the individual alpha power had been high before stimulation. These findings speak in favour of an individual adjustment of the stimulation frequency to modulate alpha power. Consequently, stimulating with the individual alpha frequency might be used in future studies to induce changes also in alpha band and not only cross-frequencies effects. However, it is still unclear whether stimulation is more effective when it matches the "eigenfrequency" of the brain [87—90] or is slightly different [28,91].

Our findings might be also influenced by the fact that, with our electrode montage, stimulation of the two prefrontal sites was antiphasic (i.e., 180° phase difference between the two stimulated sites [92,93]. Consequently, different patterns were induced by tACS over the left and right prefrontal cortex, which might explain the observed differences between both sites after active tACS in our ROI analyses.

One limitation of our behavioral findings is the absence of specificity with respect to the stimulation frequency. The effects of 10 Hz tACS were significantly different from sham stimulation but not from the control frequency. While the control frequency was not significantly different from sham, the absence of a significant difference between both frequencies precludes strong conclusions on the frequency specificity of the observed effect. Results of the resting-state EEG recordings showed that theta, alpha and beta power was increased after tACS. However, this effect did not differ significantly between active and sham tACS conditions and likely reflects changes in general arousal [94—96].

As another limitation of our data, the control task was not matched to the phonological task in terms of task difficulty. Consequently, the observed task specificity has to be interpreted with caution. We wish to emphasize that we refrained from including a linguistic control task that might have been easier to match for difficulty to avoid potential interference with prefrontal language activity due to the low focality of our stimulation electrodes.

In summary, our results show that offline tACS over the bilateral prefrontal cortex significantly facilitated phonological decisions at the word level. This facilitatory effect was underpinned by an increase in the theta power during task processing. These results implicate that offline tACS provides a powerful tool to modulate task-related activity and behaviour beyond the time of stimulation. Our results further point to the importance of the inclusion of a control frequency to test for the frequency specificity of the observed modulatory tACS effects.

## Conflicts of interest

The authors declare that there is no financial or personal conflict of interests regarding the publication of this paper. All authors agree with the submission of the manuscript and approved the final version.

## Acknowledgment

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2019.06.021.

## References

[1] Poldrack RA, Wagner AD, Prull MW, Desmond JE, Glover GH, Gabrieli JD. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. Neuroimage 1999;10(1):15–35.

[2] Vigneau M, Beaucousin V, Herve PY, Duffau H, Crivello F, Houde O, et al. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage 2006;30(4):1414–32.

[3] Burton H, Diamond J, McDermott K. Dissociating cortical regions activated by semantic and phonological tasks: a fMRI study in blind and sighted people. J Neurophysiol 2003;90(3):1965–82.

[4] Gough PM, Nobre AC, Devlin JT. Dissociating linguistic processes in the left inferior frontal cortex with transcranial magnetic stimulation. J Neurosci 2005;25(35):8010–6.

[5] Nixon P, Lazarova J, Hodinott-Hill I, Gough P, Passingham R. The inferior frontal gyrus and phonological processing: an investigation using rTMS. J Cogn Neurosci 2004;16(2):289–300.

[6] Hartwigsen G, Price CJ, Baumgaertner A, Geiss G, Koehnke M, Ulmer S, et al. The right posterior inferior frontal gyrus contributes to phonological word decisions in the healthy brain: evidence from dual-site TMS. Neuropsychologia 2010;48(10):3155–63.

[7] Ashby J. Phonology is fundamental in skilled reading: evidence from ERPs. Psychonomic Bull Rev 2010;17(1):95–100.

[8] Bann SA, Herdman AT. Event related potentials reveal early phonological and orthographic processing of single letters in letter-detection and letter-rhyme paradigms. Front Hum Neurosci 2016;10:176.

[9] Drakesmith M, El-Deredy W, Welbourne S. Differential phonological and semantic modulation of neurophysiological responses to visual word recognition. Neuropsychobiology 2015;72(1):46–56.

[10] Mazzotta G, Gallai V. Study of the P300 event-related potential through brain mapping in phonological dyslexics. Acta Neurol 1992;14(3):173–86.

[11] Grabner RH, Brunner C, Leeb R, Neuper C, Pfurtscheller G. Event-related EEG theta and alpha band oscillatory responses during language translation. Brain Res Bull 2007;72(1):57–65.

[12] Mainy N, Jung J, Baciu M, Kahane P, Schoendorff B, Minotti L, et al. Cortical dynamics of word recognition. Hum Brain Mapp 2008;29(11):1215–30.

[13] Rohm D, Klimesch W, Haider H, Doppelmayr M. The role of theta and alpha oscillations for language comprehension in the human electroencephalogram. Neurosci Lett 2001;310(2–3):137–40.

[14] Strauss A, Kotz SA, Scharinger M, Obleser J. Alpha and theta brain oscillations index dissociable processes in spoken word recognition. Neuroimage 2014;97:387–95.

[15] Obleser J, Weisz N. Suppressed alpha oscillations predict intelligibility of speech and its acoustic details. Cerebr Cortex 2012;22(11):2466–77.

[16] Deans JK, Powell AD, Jefferys JG. Sensitivity of coherent oscillations in rat hippocampus to AC electric fields. J Physiol 2007;583(2):555–65.

[17] Fröhlich F, McCormick DA. Endogenous electric fields may guide neocortical network activity. Neuron 2010;67(1):129–43.

[18] Reato D, Rahman A, Bikson M, Parra LC. Low-intensity electrical stimulation affects network dynamics by modulating population rate and spike timing. J Neurosci 2010;30(45):15067–79.

[19] Reato D, Rahman A, Bikson M, Parra LC. Effects of weak transcranial alternating current stimulation on brain activity—a review of known mechanisms from animal studies. Front Hum Neurosci 2013;7:687.

[20] Thut G, Schyns P, Gross J. Entrainment of perceptually relevant brain oscillations by non-invasive rhythmic stimulation of the human brain. Front Psychol 2011;2:170.

[21] Thut G, Veniero D, Romei V, Miniussi C, Schyns P, Gross J. Rhythmic TMS causes local entrainment of natural oscillatory signatures. Curr Biol 2011;21(14):1176–85.

[22] Zaehle T, Rach S, Herrmann CS. Transcranial alternating current stimulation enhances individual alpha activity in human EEG. PLoS One 2010;5(11): e13766.

[23] Antal A, Boros K, Poreisz C, Chaieb L, Terney D, Paulus W. Comparatively weak after-effects of transcranial alternating current stimulation (tACS) on cortical excitability in humans. Brain Stimul 2008;1(2):97–105.

[24] Kasten FH, Dowsett J, Herrmann CS. Sustained aftereffect of α-tACS lasts up to 70 min after stimulation. Front Hum Neurosci 2016;10:245.

[25] Monti A, Cogiamanian F, Marceglia S, Ferrucci R, Mameli F, Mrakic-Sposta S, et al. Improved naming after transcranial direct current stimulation in aphasia. J Neurol Neurosurg Psychiatry 2008;79(4):451–3.

[26] Thut G, Pascual-Leone A. A review of combined TMS-EEG studies to characterize lasting effects of repetitive TMS and assess their usefulness in cognitive and clinical neuroscience. Brain Topogr 2010;22(4):219.

[27] Veniero D, Vossen A, Gross J, Thut G. Lasting EEG/MEG aftereffects of rhythmic transcranial brain stimulation: level of control over oscillatory network activity. Front Cell Neurosci 2015;9:477.

[28] Vossen A, Gross J, Thut G. Alpha power increase after transcranial alternating current stimulation at alpha frequency (α-tACS) reflects plastic changes rather than entrainment. Brain Stimul 2015;8(3):499–508.

[29] Vosskuhl J, Strüber D, Herrmann CS. Non-Invasive Brain Stimulation: a paradigm shift in understanding brain oscillations. Front Hum Neurosci 2018;12.

[30] Hartwigsen G, Baumgaertner A, Price CJ, Koehnke M, Ulmer S, Siebner HR. Phonological decisions require both the left and right supramarginal gyri. Proc Natl Acad Sci U S A 2010;107(38):16494–9.

[31] Faul F, Erdfelder E, Lang A-G, Buchner AG. * Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39(2):175–91.

[32] Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971;9(1):97–113.

[33] Poreisz C, Boros K, Antal A, Paulus W. Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. Brain Res Bull 2007;72(4–6):208–14.

[34] Peirce JW. PsychoPy–Psychophysics software in Python. J Neurosci Methods 2007;162(1–2):8–13.

[35] Peirce JW. Generating stimuli for neuroscience using PsychoPy. Front Neuroinf 2008;2:10.

[36] Baayen R, Piepenbrock R, Gulikers L. CELEX2 LDC96L14. Web download philadelphia: linguistic data consortium, vol. 1; 1995. p. 3 (2).

[37] Jacobson L, Javitt DC, Lavidor M. Activation of inhibition: diminishing impulsive behavior by direct current stimulation over the inferior frontal gyrus. J Cogn Neurosci 2011;23(11):3380–7.

[38] Stramaccia DF, Penolazzi B, Sartori G, Braga M, Mondini S, Galfano G. Assessing the effects of tDCS over a delayed response inhibition task by targeting the right inferior frontal gyrus and right dorsolateral prefrontal cortex. Exp Brain Res 2015;233(8):2283–90.

[39] Pletzer B, Kerschbaum H, Klimesch W. When frequencies never synchronize: the golden mean and the resting EEG. Brain Res 2010;1335:91–102.

[40] Kanai R, Chaieb L, Antal A, Walsh V, Paulus W. Frequency-dependent electrical stimulation of the visual cortex. Curr Biol : CB 2008;18(23):1839–43.

[41] Team RC. R: a language and environment for statistical computing, vol. 2014. Vienna, Austria: R Foundation for Statistical Computing; 2016.

[42] Kenward MG, Roger JH. Small sample inference for fixed effects from restricted maximum likelihood. Biometrics 1997;53(3):983–97.

[43] Dixon P. Models of accuracy in repeated-measures designs. J Mem Lang 2008;59(4):447–56.

[44] Coxe S, West SG, Aiken LS. The analysis of count data: a gentle introduction to Poisson regression and its alternatives. J Personal Assess 2009;91(2):121–36.

[45] Anderson M, Braak CT. Permutation tests for multi-factorial analysis of variance. J Stat Comput Simul 2003;73(2):85–113.

[46] Brodski A, Paasch G-F, Helbling S, Wibral M. The faces of predictive coding. J Neurosci 2015;35(24):8997–9006.

[47] Suckling J, Bullmore E. Permutation tests for factorially designed neuroimaging experiments. Hum Brain Mapp 2004;22(3):193–205.

[48] Maris E, Oostenveld R. Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods 2007;164:177–90.

[49] Hartwigsen G, Weigel A, Schuschan P, Siebner HR, Weise D, Classen J, et al. Dissociating parieto-frontal networks for phonological and semantic word decisions: a condition-and-perturb TMS study. Cerebr Cortex 2016;26(6): 2590–601.

[50] Diedenhofen B, cocor Musch J. A comprehensive solution for the statistical comparison of correlations. PLoS One 2015;10(4):e0121945.

[51] Klimesch W, Sauseng P, Hanslmayr S. EEG alpha oscillations: the inhibition-timing hypothesis. Brain Res Rev 2007;53(1):63–88.

[52] Bridwell DA, Henderson S, Sorge M, Plis S, Calhoun VD. Relationships between alpha oscillations during speech preparation and the listener N400 ERP to the produced speech. Sci Rep 2018;8(1):12838.

[53] Klimesch W, Doppelmayr M, Schwaiger J, Winkler T, Gruber W. Theta oscillations and the ERP old/new effect: independent phenomena? Clin Neurophysiol 2000;111(5):781–93.

[54] Sauseng P, Klimesch W, Gruber WR, Hanslmayr S, Freunberger R, Doppelmayr M. Are event-related potential components generated by phase resetting of brain oscillations? A critical discussion. Neuroscience 2007;146(4):1435–44.

[55] Wach C, Krause V, Moliadze V, Paulus W, Schnitzler A, Pollok B. The effect of 10 Hz transcranial alternating current stimulation (tACS) on corticomuscular coherence. Front Hum Neurosci 2013;7:511.

[56] Neuling T, Wagner S, Wolters CH, Zaehle T, Herrmann CS. Finite-element model predicts current density distribution for clinical applications of tDCS and tACS. Front Psychiatry 2012;3:83.

[57] Pahor A, Jausovec N. The effects of theta transcranial alternating current stimulation (tACS) on fluid intelligence. Int J Psychophysiol 2014;93(3): 322–31.

[58] Chaieb L, Antal A, Pisoni A, Saiote C, Opitz A, Ambrus GG, et al. Safety of 5 kHz tACS. Brain Stimul 2014;7(1):92–6.

[59] Marshall L, Kirov R, Brade J, Molle M, Born J. Transcranial electrical currents to probe EEG brain rhythms and memory consolidation during sleep in humans. PLoS One 2011;6(2):e16905.

[60] Devlin JT, Matthews PM, Rushworth MF. Semantic processing in the left inferior prefrontal cortex: a combined functional magnetic resonance imaging and transcranial magnetic stimulation study. J Cogn Neurosci 2003;15(1): 71–84.

[62] Sliwinska MW, James A, Devlin JT. Inferior parietal lobule contributions to visual word recognition. J Cogn Neurosci 2015;27(3):593–604.

[63] Andoh J, Artiges E, Pallier C, Riviere D, Mangin J-F, Cachia A, et al. Modulation of language areas with functional MR image-guided magnetic stimulation. Neuroimage 2006;29(2):619–27.

[64] Andoh J, Zatorre RJ. Interhemispheric connectivity influences the degree of modulation of TMS-induced effects during auditory processing. Front Psychol 2011;2:161.

[65] Sparing R, Mottaghy FM, Hungs M, Brügmann M, Foltys H, Huber W, et al. Repetitive transcranial magnetic stimulation effects on language function depend on the stimulation parameters. J Clin Neurophysiol 2001;18(4): 326–30.

[66] Hartwigsen G. The neurophysiology of language: insights from non-invasive brain stimulation in the healthy human brain. Brain Lang 2015;148:81–94.

[67] Devlin JT, Watkins KE. Stimulating language: insights from TMS. Brain 2007;130(Pt 3):610–22.

[68] Andoh J, Paus T. Combining functional neuroimaging with off-line brain stimulation: modulation of task-related activity in language areas. J Cogn Neurosci 2011;23(2):349–61.

[69] Silvanto J, Muggleton N, Walsh V. State-dependency in brain stimulation studies of perception and cognition. Trends Cognit Sci 2008;12(12):447–54.

[70] Silvanto J, Bona S, Marelli M, Cattaneo Z. On the mechanisms of Transcranial Magnetic Stimulation (TMS): how brain state and baseline performance level determine behavioral effects of TMS. Front Psychol 2018;9.

[71] Silvanto J, Cattaneo Z. Common framework for "virtual lesion" and state-dependent TMS: the facilitatory/suppressive range model of online TMS effects on behavior. Brain Cogn 2017;119:32–8.

[72] Nguyen J, Deng Y, Reinhart RMG. Brain-state determines learning improvements after transcranial alternating-current stimulation to frontal cortex. Brain Stimul 2018;11(4):723–6.

[73] Joundi RA, Jenkinson N, Brittain J-S, Aziz TZ, Brown P. Driving oscillatory activity in the human cortex enhances motor performance. Curr Biol 2012;22(5):403–7.

[74] Wostmann M, Vosskuhl J, Obleser J, Herrmann CS. Opposite effects of lateralised transcranial alpha versus gamma stimulation on auditory spatial attention. Brain Stimul 2018;11(4):752–8.

[75] Borghini G, Candini M, Filannino C, Hussain M, Walsh V, Romei V, et al. Alpha oscillations are causally linked to inhibitory abilities in ageing. J Neurosci 2018;38(18):4418–29.

[76] Rufener KS, Oechslin MS, Zaehle T, Meyer M. Transcranial Alternating Current Stimulation (tACS) differentially modulates speech perception in young and older adults. Brain Stimul 2016;9(4):560–5.

[77] Schaal NK, Pfeifer J, Krause V, Pollok B. From amusic to musical?–Improving pitch memory in congenital amusia with transcranial alternating current stimulation. Behav Brain Res 2015;294:141–8.

[78] Antonenko D, Faxel M, Grittner U, Lavidor M, Flöel A. Effects of transcranial alternating current stimulation on cognitive functions in healthy young and older adults. Neural Plast 2016;2016.

[79] Hoy KE, Bailey N, Arnold S, Windsor K, John J, Daskalakis ZJ, et al. The effect of gamma-tACS on working memory performance in healthy controls. Brain Cogn 2015;101:51–6.

[80] Jausovec N, Jausovec K. Increasing working memory capacity with theta transcranial alternating current stimulation (tACS). Biol Psychol 2014;96: 42–7.

[81] Jausovec N, Jausovec K, Pahor A. The influence of theta transcranial alternating current stimulation (tACS) on working memory storage and processing functions. Acta Psychol 2014;146:1–6.

[82] Pahor A, Jausovec N. The effects of theta and gamma tACS on working memory and electrophysiology. Front Hum Neurosci 2017;11:651.

[83] Liang T, Hu Z, Liu Q. Frontal theta activity supports detecting mismatched information in visual working memory. Front Psychol 2017;8:1821.

[84] Mai G, Minett JW, Wang WSY. Delta, theta, beta, and gamma brain oscillations index levels of auditory sentence processing. Neuroimage 2016;133:516–28.

[85] Monsalve IF, Bourguignon M, Molinaro N. Theta oscillations mediate pre-activation of highly expected word initial phonemes. Sci Rep 2018;8(1):9503.

[86] Neuling T, Rach S, Herrmann CS. Orchestrating neuronal networks: sustained after-effects of transcranial alternating current stimulation depend upon brain states. Front Hum Neurosci 2013;7:161.

[87] Ali MM, Sellers KK, Fröhlich F. Transcranial alternating current stimulation modulates large-scale cortical network activity by network resonance. J Neurosci 2013;33(27):11262–75.

[88] Reato D, Rahman A, Bikson M, Parra LC. Effects of weak transcranial alternating current stimulation on brain activity-a review of known mechanisms from animal studies. Front Hum Neurosci 2013;7:687.

[89] Romei V, Thut G, Mok RM, Schyns PG, Driver J. Causal implication by rhythmic transcranial magnetic stimulation of alpha frequency in feature-based local vs. global attention. Eur J Neurosci 2012;35(6):968–74.

[90] Schmidt S, Mante A, Rönnefarth M, Fleischmann R, Gall C, Brandt SA. Progressive enhancement of alpha activity and visual function in patients with optic neuropathy: a two-week repeated session alternating current stimulation study. Brain Stimul 2013;6(1):87–93.

[91] Helfrich RF, Knepper H, Nolte G, Strüber D, Rach S, Herrmann CS, et al. Selective modulation of interhemispheric functional connectivity by HD-tACS shapes perception. PLoS Biol 2014;12(12):e1002031.

[92] Polania R, Nitsche MA, Korman C, Batsikadze G, Paulus W. The importance of timing in segregated theta phase-coupling for cognitive performance. Curr Biol : CB 2012;22(14):1314–8.

[93] Struber D, Rach S, Trautmann-Lengsfeld SA, Engel AK, Herrmann CS. Antiphasic 40 Hz oscillatory current stimulation affects bistable motion perception. Brain Topogr 2014;27(1):158–71.

[94] Jung TP, Makeig S, Stensmo M, Sejnowski TJ. Estimating alertness from the EEG power spectrum. IEEE Trans Biomed Eng 1997;44(1):60–9.

[95] Makeig S, Inlow M. Lapse in alertness: coherence of fluctuations in performance and EEG spectrum. Electroencephalogr Clin Neurophysiol 1993;86(1): 23–35.

[96] Makeig S, Jung TP. Changes in alertness are a principal component of variance in the EEG spectrum. Neuroreport 1995;7(1):213–6.