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6 Hz transcranial alternating current stimulation of mPFC improves sustained attention and modulates alpha phase synchronization and power in dorsal attention network

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ABSTRACT

Transcranial alternating current stimulation (tACS) is a noninvasive brain stimulation tool appropriate to modulate cortical oscillations and activity via the application of weak currents. The major goal of this study was to investigate the effects of medial Prefrontal Cortex (mPFC) stimulation on sustained attention task performance measured by Rapid Visual Information Processing (RVIP) task and the brain networks assumed to be critical to sustained attention. mPFC has been shown to be involved in sustained attention performance and as a main hub in default mode network (DMN). mPFC activity modulation via theta tACS was implemented in this study. This was a single blind study with 21 participants receiving active and sham stimulation with the electrodes on FPz and the Inion. tACS was able to impact different RVIP measures (total hits, A' (sensitivity to target), total correct rejection, etc.). Relative power spectrum density (PSD) analysis yielded significant increases in theta frequency mostly in the fronto-central regions after active tACS and current source density (CSD) analysis yielded significant power modulations in theta frequency band in post-central gyrus. Furthermore, phase locking value (PLV) analysis showed that there were significant changes in cortical connections in the Dorsal Attention Network (DAN) in alpha frequency band. This study showed that theta frequency tACS over mPFC, was able to produce significant modulations in an RVIP task and its associated brain networks in healthy participants.

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Sustained attention; tACS; medial prefrontal cortex; theta frequency; RVIP

1. Introduction

Human and animal studies have demonstrated the crucial role of the mPFC in sustained attention (Geday & Gjedde, 2009; Rossi et al., 2009; Sharpe & Killcross, 2018; Williams et al., 1999); (Gill et al., 2000; Kahn et al., 2012; Luchicchi et al., 2016; Miner et al., 1997). Damage to mPFC in mice, for instance, disrupts sustained attention (Kahn et al., 2012) and has been found to both disrupt sustained attention processing and impair response inhibition in rats (Broersen & Uylings, 1999).

Specific areas of the brain that affect, control, or modulate sustained attention have been investigated in human studies showing that activity of the DMN diminishes, under goal-directed activity and increases when one is wakeful and alert (i.e., in resting)(Raichle et al., 2001). Association between this network and mind wandering (Poerio et al., 2017), and also between mind wandering and sustained attention deficit (SAD) have been confirmed in other studies (Thomson et al., 2015). mPFC is a considered as a main functional hub in the DMN network and exhibits more activation during mind wandering (Christoff et al., 2009) and functional connectivity (FC) between mPFC and other brain regions, predicts sustained attention performance in patients with psychiatric disorders (Bonnelle et al., 2011; Christakou et al., 2013). For example, decreased resting state FC between mPFC and left Superior Frontal Gyrus (SFG) is significantly associated with SAD in obsessive compulsive disorder and decreased FC between left mPFC and bilateral Anterior Cingulate Cortex (ACC) is associated with sustained attention deficits in patients with schizophrenia (Fan et al., 2018). These findings may suggest that interaction of mPFC with other regions of the brain is necessary to achieve normal sustained attention performance.

In the context of FC analysis, phase synchronization is an appropriate index, which provides the opportunity to examine neuronal plasticity and cognitive functions, especially attention (Cavanagh et al., 2009; Engel et al., 2001). Phase synchronization is a concept based on the fact that in and out of phase oscillations are a means of connection between neurons of different brain regions.

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In phase oscillations facilitate connectivity between regions and thereby post-synaptic activity is promoted, but out of phase oscillations diminish connectivity (Clayton et al., 2015; Fell & Axmacher, 2011).

It is relatively established that theta frequency plays a crucial role in cognitive control (Buzzell et al., 2019; Cavanagh & Frank, 2014; Sauseng et al., 2019; Wang et al., 2016). It has been well documented that increased theta phase synchronization between mPFC and subthalamic nuclei, and also increased theta power in the prefrontal cortex are associated with response inhibition; while increased theta power in subthalamic nuclei is associated with response provision (Zavala et al., 2018). Control over attention networks is believed to be achieved through the connection between mPFC and lateral prefrontal cortex (LPFC), which is facilitated through theta phase synchronization (Duverne & Koechlin, 2017; Ridderinkhof et al., 2004; Taren et al., 2011) and theta oscillations in mPFC modulating gamma power in the LPFC (Clayton et al., 2015).

Numerous studies have investigated the role of theta phase synchronization in cognitive functions (Mizuhara & Yamaguchi, 2007; Nyhus & Curran, 2010; Schack et al., 2005), but so far few studies focused on its causal role in cognitive control and performance (Polanía et al., 2012). Noninvasive brain stimulation techniques have become very popular to investigate the causal relationships between cognitive functions and specific brain areas (Parkin et al., 2015). Among them, tES is the most widely used technique for examining brain regions involved in cognitive functions. Several studies have examined the impacts of transcranial direct current stimulation (tDCS) on sustained attention (Borducchi et al., 2016; Borragán et al., 2018; Miller et al., 2015; Naka et al., 2018; Nelson et al., 2014; Plewnia et al., 2013; Sakai et al., 2014; Sarasso et al., 2019). However, there is only one tDCS study on the role of frontal midline theta (FMθ) rhythm in sustained attention (Miller et al., 2015) in which tDCS was used for anodal stimulation of mPFC and the results showed no changes in the Go/No-go task, but there were changes in FMθ amplitude, as well as the delta and alpha frequency bands.

Due to its potential to modulate endogenous cortical oscillations in the brain, tACS has attracted much attention. Many studies show that tACS is capable of changing the power of specific frequency bands (Neuling et al., 2012; Ruhnau et al., 2016; Zaehle et al., 2010) and is also capable of affecting the phase of cortical oscillations, besides the amplitude and frequency (Fiene et al., 2019; Schwab et al., 2019). tACS is able to change phase synchronization and applying tACS in and out of phase can potentially lead to synchronization and desynchronization, respectively (Alekseichuk et al., 2016; Polanía et al., 2012; Violante et al., 2017). Inducing frontoparietal theta phase synchronization via tACS in synchronized conditions (0-degree phase) improved visual reaction time (VRT), compared to the placebo group(s); while frontoparietal theta phase desynchronization in desynchronized conditions (180-degree phase) worsened performance (Polanía et al., 2012).

Based on the above findings, we hypothesized that theta frequency tACS over mPFC has the potential to change theta phase synchronization and improve sustained attention performance measured by the RVIP task, which is widely used in the literature and has been shown to be a reliable measure of sustained attention.

2. Materials and methods

2.1. Participants

Twenty-one healthy volunteers participated in the study (11 females and 10 males, mean±SD age 32.48 ± 11.2). The tests were conducted at Atieh Clinical Neuroscience Center, Tehran, Iran. The inclusion criteria were being above 18 years old, no report of any psychiatric disorders, and average intelligence in Raven Progressive Matrices Test. None of the participants reported any history of head injury or trauma. Additional investigation was made by asking each participant whether they had been using specific drugs, and if they or their family members had been or were diagnosed with chronic clinical, psychological, or neurological disorders. Finally, all the participants were evaluated using the Symptom Checklist-90 (SCL-90) and no significant disorders were diagnosed in any of them. Due to technical errors in the recording procedure, 13 participants were considered in the behavioral data analysis. The participants were all offered 500,000 IRR as compensation.

This study was confirmed by University of Tehran's Ethics Committee and all the participants were informed about the duration and stages of the tests. All the participants signed informed consent forms before the experimental procedure began.

2.2. Experimental procedure

All the participants were instructed to rest well and not smoke or consume caffeine on the day of testing. Upon finishing the SCL-90 and the Raven Test, every participant went through eyes closed and eyes open EEG recordings in an acoustically and electromagnetically shielded EEG room. RVIP task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) was administered next and then tACS was applied. After tACS administration another resting state EEG recording and RVIP test was conducted. Previous studies have shown that tACS aftereffects could be traced after 70 minutes (Kasten et al., 2016) and 30 minutes (Neuling et al., 2013) so it was potentially feasible to trace the effects of stimulation in our experimental procedure. This experiment was single-blinded. Active and sham stimulation were delivered in exactly the same experimental steps in separate sessions 1 week apart. All the participants received the sham stimulation in the first session and active in the second. The overall design of the experiment is illustrated in Figure 1.

2.3. Transcranial alternating current stimulation (tACS)

tACS was administered for twenty minutes through a battery-driven stimulator (NeuroConn, Ilmenau, Germany). Considering that mPFC was the target of stimulation, in reference to a previous study with similar conditions (Hämmerer et al., 2016), the stimulating electrode was placed on Fpz and the reference electrode was placed under the inion according to the International 10–20 System.

tACS was applied via two electrodes (5x7 cm^2) in saline-soaked sponges (0.9%-NaCl) which were attached to the scalp using rubber bands. Impedance was always kept below 10 kΩ. The stimulation protocol was set as the following: Frequency of 6 Hz, 20 minutes (7200 cycles), 10 seconds fade in/out, zero-degree phase, and 1 mA peak-to-peak amplitude. In the sham group, all parameters were similar except for the current amplitude, which was only applied for the first 30s of the session and was then cut off.

2.4. EEG recording

EEG was recorded by a 19-channel Mitsar amplifier (Mitsar, St. Petersburg, Russia) using a 19-channel Electro-Cap (ElectroCap, Inc, OH). Electrodes were placed on the cap in accordance with the International 10–20 System. A1 + A2 electrodes were used as reference. Impedances of all electrodes were kept below 5 kΩ. EEG signals were recorded with a high-pass filter of 0.3 Hz and a low-pass filter of 50 Hz and a sampling rate of 500 Hz. Prior to the analysis, artifacts were removed using independent component analysis (ICA) technique in EEGLAB toolbox in MATLAB (MathWorks, Inc., Natick, Massachusetts, United States). The criteria to select the continuous 60 second EEG epochs was to consider the interval between 30 s and 180 s of the whole EEG record. Making the selection of EEG epochs a process of finding 60 second clean data after the first 30 seconds. This was to allow the subjects to stabilize and get used to a relaxed state of sitting and not moving (the first 30 seconds) and to avoid subjects' lowering of consciousness and possible movements of head or body (after 180 seconds). In case no such continuous clean epoch was found in the interval between 30 and 180 seconds, we extended the interval up to the end of the recording.

2.5. Rapid visual information processing (RVIP) task

Modified and simplified from the CANTAB Battery (Cambridge Cognition Ltd., UK), RVIP is a visual task specifically designed to assess the capacity of sustained attention. Participants are asked to look fixedly at the monitor screen. Single digits from 2 to 9 appear in the center of the screen with a speed of 100 digits per minute. Among the train of numbers, certain pre-

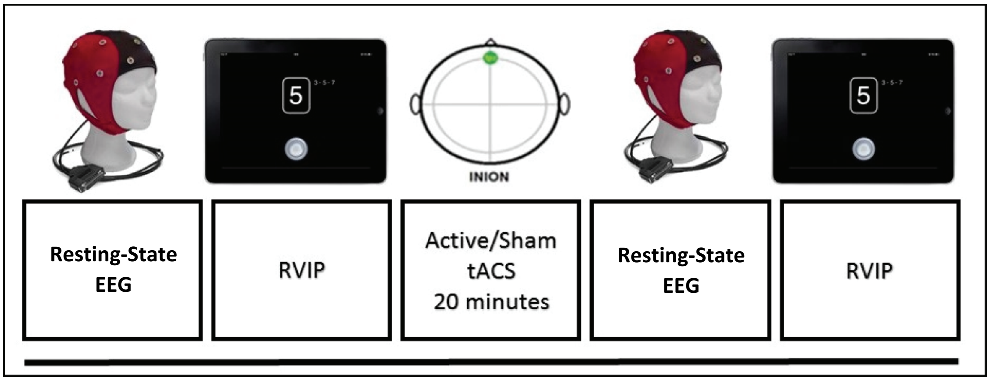

Figure 1. Experimental procedure for the study. The same steps were exactly repeated in active and sham sessions (separated by one week).

defined target sequence of numbers is shown, for example, “3-5-7,” “2-4-8,” or “4-6-8.” Participants are required to watch out for these sequences, and press a button as soon as they spot the last number in thesequence. Each number stimulus subtended a visual angle of 1.3 ○ . In this study, a 5-min practice run was administered, followed by the main task lasting about 7 minutes.

The goal was to measure and analyze the probability of signal detection by the participants using the decision theory; therefore, the following variables were extracted from the RVIP test results:

(1) **A′**: according to the Signal Detection Theory, this variable indicates sensitivity to target while controlling for the participant’s propensity to respond, calculated by the following formula (Sahgal, 1987), in which h represents correct and f represents incorrect responses,

Eq.1)

(1) **B′′**: This variable reflects the response tendency of the participant and is calculated by formula 2 (Sahgal, 1987):

Eq.2)

(1) **Mean latency**: how long it takes the participant to respond (Reaction Time) to a stimulus correctly
(2) **Probability of hits (h)**: ratio of total hits to total hits plus total misses.
(3) **Total correct rejections**: number of times when the participant is required not to respond, and does not.
(4) **Total hits**: number of correct responses given by the participant.
(5) **Total misses**: number of times when the participant does not respond when they are required to.
(6) **Total false alarms**: number of times when the participant responds to non-target stimuli

2.6. EEG analysis

2.6.1. EEG seeds

To select the electrodes for the sensor-level analysis of the DAN, a study by Rojas et al. (2018) was considered in which the seven networks in the brain determined by Thomas Yeo et al. (2011) by studying the brain scans of 1000 healthy individuals, were matched with the 10–20 international system (Rojas et al., 2018; Thomas Yeo et al., 2011). Results of their functional connectivity analysis revealed five EEG seeds including C3 (BA 3, Post-central Gyrus), C4 (BA 3, Post-central Gyrus), T5 (BA 19, Inferior Temporal Gyrus), T6 (BA 19, Inferior Temporal Gyrus), and Pz (BA 7, Precuneus). These seeds were the basis for the EEG analysis in this study (Table 1).

Table 1. MNI coordinates of the EEG seeds.

	MNI Coordinates					
Seed	X	Y	Z	Lobe (Hemisphere)	Region	BA
C3	−48	−18	52	Parietal Lobe (L)	Post-central Gyrus	3
C4	52	−14	48	Parietal Lobe (R)	Post-central Gyrus	3
T5	−52	−64	0	Temporal Lobe (L)	Inferior Temporal Gyrus	19
T6	54	−60	−2	Temporal Lobe (R)	Inferior Temporal Gyrus	19
Pz	4	−64	58	Parietal Lobe (R)	Precuneus	7

2.6.2. Power analysis

Five frequency bands were defined for frequency domain analysis, namely delta (2–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz) and gamma (30–45 Hz). Power spectral density (PSD) analysis was computed using EEGLAB toolbox (Delorme & Makeig, 2004) together with custom scripts in MATLAB. EEG time-series of every channel were windowed by a Hamming window of full time length followed by filtering of each frequency band and computation of PSD using Welch’s averaged and modified periodogram (Welch, 1967). Relative power was computed by dividing the averaged PSD of each frequency band over the averaged PSD of the full band (2–45 Hz) and is therefore unit-free. Statistical analysis was consequently applied on the relative power matrices in each frequency band and across the experimental conditions. In order to evaluate the tACS-induced cortical modulations, mean spectral amplitude within the frequency range of each individual band was calculated. Paired-samples t-test (two-tailed) was used to compare post- and pre-stimulation values of interest. P-values of <0.05 were considered statistically significant after FDR corrections for all the 19 channels.

2.6.3. EEG source localization

Artifact-free EEG segments were used to calculate the intracranial spectral density by eLORETA with a 1 Hz resolution from 2 to 45 Hz. eLORETA functional images of spectral density were calculated for the following 5 frequency bands: Delta (2 to 4 Hz), Theta (4–8 Hz), Alpha (8–13 Hz), Beta (13 – 30 Hz) and gamma (30 – 45 Hz).

eLORETA takes advantage of a non-parametric mapping method (SnPM) for current source density analysis (Holmes et al., 1996). Localization differences of cortical sources between groups were evaluated by voxel-by-voxel independent F-ratio based on eLORETA logtransformed current source density power, in each frequency band. As a result of the three dimensional mapping, cortical voxels with a significant difference were determined by a non-parametric randomization method (based on Fischer's method, with a 5% threshold). Source power means were compared in each voxel. eLORETA uses 5000 randomized data to determine the threshold for critical probability values for corrected log F-ratio values for multiple comparisons in all the voxels and frequency bands (Anderer et al., 1998; Pascual-Marqui et al., 1999).

Global subject-wise scaling (normalization) was used in order to eliminate the non-physiological sources of variability in EEG. In this process, a normalization factor is defined as the mean spectral power in all the voxels (6239) and frequency bands for each participant and condition (Friston et al., 1991; Petersson et al., 1999). The significance level in all the comparisons in this study was considered at 0.05.

2.6.4. Phase analysis

In order to measure EEG phase changes, Neurophysiological Biomarker Toolbox (NBT) (http://www.nbtwiki.net) was utilized to compute the phase-locking value (PLV). Each channel was FIR-filtered in each frequency band, followed by computation of instantaneous phase using the analytic representation (equation 1). In equation (1), $x(t)$ represents the filtered data for each channel in time t and $H(x)(t)$ its Hilbert transform.

Eq.3)

$$x_a(t) = x(t) + iH(x)(t)$$

The instantaneous phase was subsequently obtained by equation (2).

Eq.4)

$$\phi_x(t) = \arctan\left(\frac{H(x)(t)}{x(t)}\right)$$

Finally, PLV was obtained by the following equation, where $x(t)$ and $y(t)$ contain every two channel time series, $\phi_{x(t)}$ and $\phi_{y(t)}$ being their corresponding instantaneous phase and T the full-time length.

Eq.5)

$$PLV_{x(t),y(t)} = \left| \sum_{t=1}^{T} e^{i.(\phi_{x(t)} - \phi_{y(t)})} \right|$$

The PLV matrix of every subject in each band was obtained as a square matrix, which was then statistically analyzed by paired-samples t-test (two-tailed) to determine significance for every channel across the conditions. P-values of <0.05 were considered to be statistically significant, after the FDR correction for the 5 channels. It is worth noting that PLV is an independent measure from PSD values, although both methods initially compute a representation of a new space (frequency in periodogram or analytic representation), PSD only considers the amplitude, while PLV is a result of using signal phase changes in its respective equation. Consequently, since amplitude and phase of a signal in frequency space are independent, results of PSD and PLV analysis can be interpreted in light of the independence and thus there will be no concern regarding the potential effects of one on another.

2.7. Statistical analysis

Baseline characteristics were reported using descriptive statistics. For describing the data, mean± standard deviations were reported for RVIP scores (Table 2). Marginal models with generalized estimating equations (GEE), with identity link function for RVIP scores were used to assess the effect of tACS on sustained attention scores and compare the differences between active and sham tACS conditions.

Generalized Estimating Equation model (GEE) is a relatively robust statistical tool compared to the standard general linear model (GLM) due to the availability of more types of distributions and covariance structures of the repeated-measures data (Fitzmaurice et al., 2012). In addition, normal distribution is not an absolute necessity for a GEE analysis, and it provides acceptable outcome with lower sample sizes relative to many other statistical methods.

In our model, post-stimulation active or sham scores were compared with pre-stimulation scores in each condition separately. SPSS software version 19.0 (SPSS Inc. Chicago, IL, USA) was utilized for data analysis, and p< 0.05 were considered statistically significant.

3. Result

Results of the behavioral (RVIP) and electrophysiological data analysis are presented below. It should be noted that none of the participants reported any side effects other than a mild sensation of tingling because of the stimulation.

3.1. Behavioral data (RVIP)

The study started with 21 participants (age; Mean ± Standard Deviation: 32.48 ± 11.2). Eight participants were then excluded from the final analysis of the behavioral data, due to technical issues. The mean ± SD age of

Table 2. Results of Generalized Estimating Equations (GEE) analysis regarding the effects of tACS on RVIP scores.

	Mean	SD	Median	β_1(Adj. coefficient)	OR	SE	Wald Chi-Square	P-value		
A′	Active	Post	0.97	0.03	0.97	0.01	1.01	0.01	7.05	**0.008**
		Pre	0.95	0.02	0.95					
	Sham	Post	0.95	0.03	0.95	0.01	1.01	0.01	2.03	0.154
		Pre	0.94	0.03	0.94					
B″	Active	Post	0.93	0.11	1	−0.01	0.99	0.04	0.08	0.771
		Pre	0.95	0.06	0.96					
	Sham	Post	0.92	0.06	0.92	−0.04	0.96	0.02	4.86	**0.027**
		Pre	0.96	0.05	0.97					
Mean Latency	Active	Post	366.49	59.94	337.96	−40.07	0.00	14.54	7.59	**0.006**
		Pre	406.56	63.44	402.25					
	Sham	Post	391.76	90.84	367.66	−21.47	0.00	22.1	0.94	0.331
		Pre	413.23	75.97	391.54					
Probability of hits (h)	Active	Post	0.87	0.1	0.89	0.05	1.05	0.02	5.08	**0.024**
		Pre	0.82	0.07	0.81					
	Sham	Post	0.81	0.12	0.81	0.11	1.12	0.07	2.47	0.116
		Pre	0.7	0.24	0.7					
Total Correct Rejections	Active	Post	265.38	5.75	266	4.46	86.49	1.4	10.16	**0.001**
		Pre	260.92	4.75	260					
	Sham	Post	260	7.55	261	1.92	6.82	1.52	1.6	0.206
		Pre	258.08	6.92	256					
Total False Alarms	Active	Post	0.54	0.78	0	−0.31	0.73	0.27	1.25	0.263
		Pre	0.85	0.9	1					
	Sham	Post	1.54	1.27	1	−0.69	0.50	1.26	0.9	0.582
		Pre	2.23	5.39	1					
Total Hits	Active	Post	23.62	2.81	24	1.38	3.97	0.6	5.3	**0.021**
		Pre	22.23	1.96	22					
	Sham	Post	22	3.29	22	1.15	3.16	0.7	2.69	0.101
		Pre	20.85	3.29	20					
Total Misses	Active	Post	3.38	2.81	3	−1.38	0.25	0.6	5.3	**0.021**
		Pre	4.77	1.96	5					
	Sham	Post	5	3.29	5	−1.15	0.32	0.7	2.69	0.101
		Pre	6.15	3.29	7					

participants was 25.37 ± 2.9, among them 6 females (23.9 ± 2.19) and 7 males (24.89 ± 3.89).

In our statistical model, the aim was to find out if there were any significant differences between pre and post-stimulation in RVIP scores, in active and sham conditions so post-stimulation scores were compared with pre-stimulation scores in each condition. The model can be represented by the following equation: Eq.6)

$$RVIP_{scores} = \beta_0 + \beta_1 Time + \varepsilon$$

Where Time is 0 for pre and 1 for post.

There were significant differences between pre and post-active stimulation with an increasing trend in **A′**(OR = 1.01, P = 0.008), **Total correct rejections** (OR = 86.49, P = 0.001), **Probability of hits** (OR = 1.05, P = 0.024), **and Total hits** (OR = 3.97, P = 0.021), and a decreasing trend in **Mean Latency** (OR<0.0001, P = 0.006) and **Total misses** (OR = 0.25, P = 0.021), after active stimulation (Table 2).

3.2 Electrophysiological data

3.2.1. Sensor-level analysis

3.2.1.1. Power spectrum density (PSD). Relative PSD showed significant changes after active tACS in theta frequency band in right frontal (F4, t ≈ 3.35), left frontal (F3, t ≈ 2.24), right central (C4, t ≈ 2.39), and midline (Fz, t ≈ 2.79) of the brain (Figure 2.b2).

There were no such significant relations in the sham condition in theta frequency band and in any of the other four frequency bands in the sham or active conditions

3.2.1.2. Phase locking value (PLV). In order to investigate the interregional connections in the brain, PLV analysis was used. After active tACS there were significant changes in cortical connections among the majority of brain regions in alpha frequency band (Figure 3). A significant increase in PLV was observed between T5-C3 (t ≈ 3.4), T5-C4 (t ≈ 2.7), T5-Pz (t ≈ 3.1), and C4-T6 (t ≈ 2.9), in the alpha frequency band in the active condition. There was no significant difference between pre-stimulation average PLVs in any of the five channels. Also, there were no significant post-versus pre relations in the sham group in alpha frequency and in sham or active conditions in any of the other 4 frequency bands. The abovementioned changes were all incremental. There were no significant changes after sham stimulation in all theta and alpha frequency bands.

3.2.2. Source-level analysis

3.2.2.1. Current density analysis. Current source density (CSD) analysis conducted in eLORETA yielded

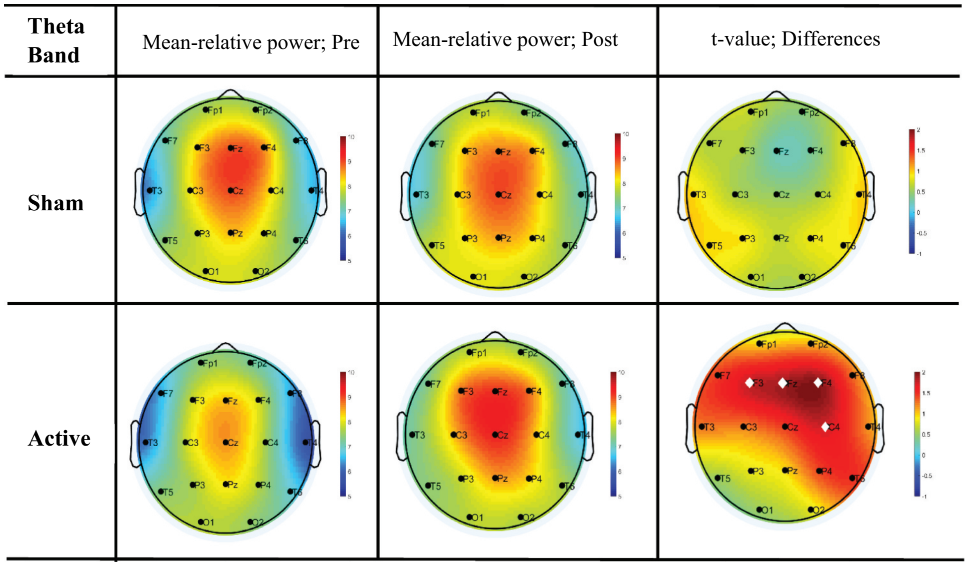

Figure 2. The first two columns represent relative power in theta frequency band before and after active and sham stimulation. There is no significant difference between active and sham conditions before stimulation. In the third column, z-values of the differences between pre and post-stimulation in active and sham conditions are presented. Significance was calculated after FDR corrections for all the 19 channels. C4($t \approx 2.39$), Fz($t \approx 2.79$), F4($t \approx 3.35$), and F3($t \approx 2.24$) channels (shown in white) showed significant differences between pre and post-stimulation, in active condition. There were no such relations in the sham condition in theta frequency band and in any of the other four frequency bands in the sham or active conditions. Significance level is considered at 0.05.

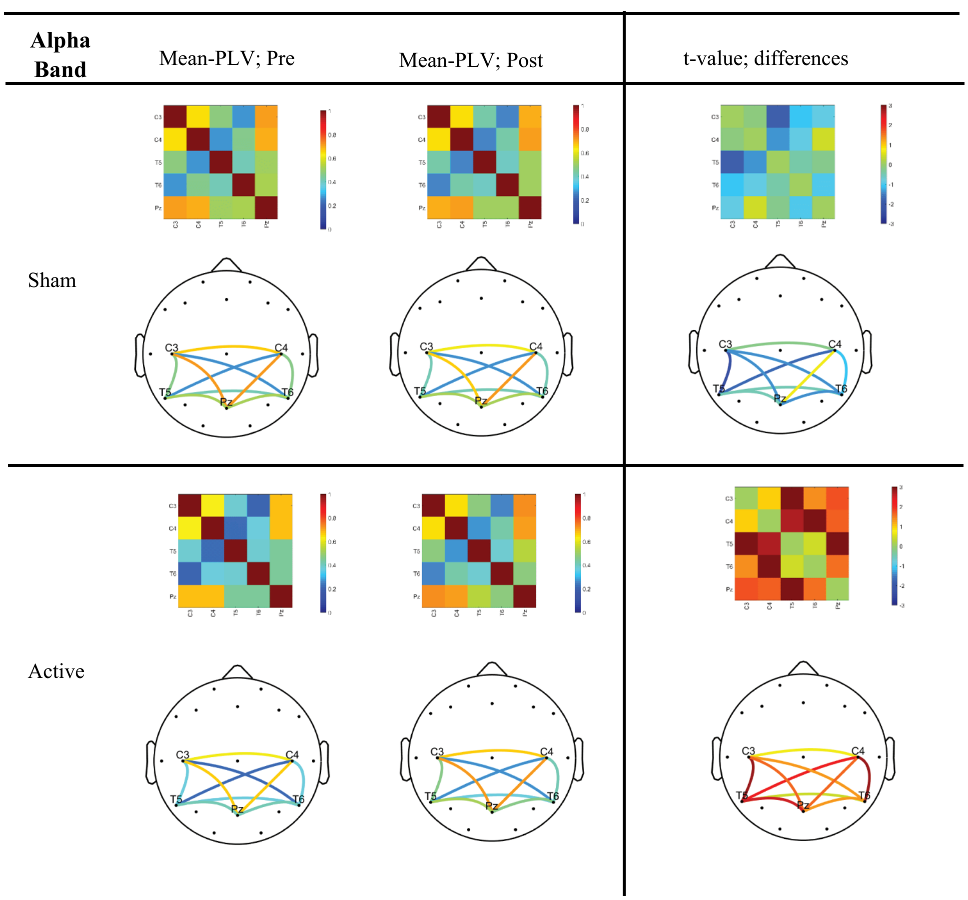

Figure 3. The first two columns represent average PLV values before and after stimulation in the sham and active conditions. z-values of pre- and post-differences are presented in the third column. Average adjacency matrices for PLV before and after active and sham tACS in alpha frequency band after FDR correction for all the 5 electrodes are presented. A significant increase in PLV was observed between T5-C3 ($t \approx 3.4$), T5-C4 ($t \approx 2.7$), T5-Pz ($t \approx 3.1$), and C4-T6 ($t \approx 2.9$), in the alpha frequency band in the active condition. There was no significant difference between pre-stimulation average PLVs in any of the five channels. Also, there were no significant post- versus pre-relations in the sham group in alpha frequency and in sham or active conditions in any of the other 4 frequency bands. The blue and red spectrum represent decreasing and increasing trends between electrode pairs, respectively, and significance level is considered at 0.05.

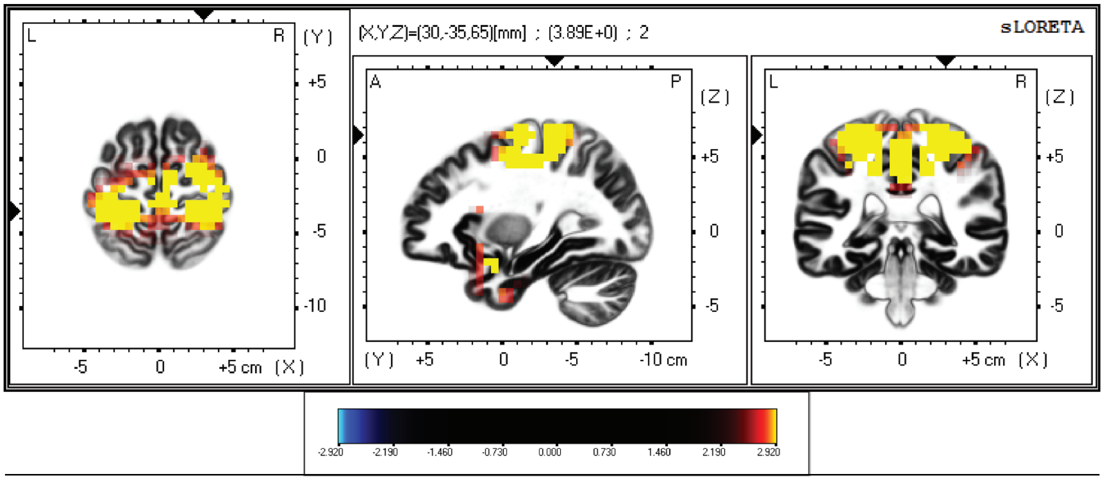

Figure 4. eLORETA current source density analysis yielded significantly increased activity in Post-central Gyrus (Maximally in BA 3, MNI coordinates: x = 30, y = −35, z = 65), (threshold: t ≈ 3.89, $p < 0.05$) in theta frequency band, in a post- vs. pre-comparison in the active condition. *The colorful parts represent the voxels with significant differences in current source density in the theta tACS.

Table 3. Number and names of voxels, Brodmann areas and anatomical regions with significant differences. Results of the comparisons with the baseline values via eLORETA.

All	L	C	R	BA	Lobe	Structure	Maximum t-statistic (x, y, z)
265	75	23	167	4	Frontal Lobe	Inferior Frontal Gyrus, Medial Frontal Gyrus, Middle Frontal Gyrus, Paracentral Lobule, Postcentral Gyrus, Precentral Gyrus, Rectal Gyrus, Subcallosal Gyrus, Sub-Gyral, Superior Frontal Gyrus	3.83 (25, −30,60)
195	62	26	107	24	Limbic Lobe	Anterior Cingulate, Cingulate Gyrus, Paracentral Lobule, Parahippocampal Gyrus, Uncus	3.76 (10, −15,45)
115	56	1	58	3	Parietal Lobe	Postcentral Gyrus, Precentral Gyrus, Precuneus, Sub-Gyral, Superior Parietal Lobule	3.89 (30, −35,65)
6	0	0	6	13	Sub-lobar	Insula	3.09 (35,5,15)
6	0	0	6	38	Temporal Lobe	Superior Temporal Gyrus	3.21 (25,10, −25)

Positive t-values indicate increased activity in post vs. pre in active theta tACS. Number of all significant voxels (separately for the left and right hemispheres and central regions) are presented for every affected Brodmann area. L, left; R, right; C, Canter; x, y, z = MNI coordinates.

significant power modulations in theta frequency band in post-central gyrus (Figure 4). There were 587 significant voxels overlapping with medial frontal gyrus, precentral gyrus, post-central gyrus and cingulate gyrus in a descending order (Table 3).

4. Discussion

Results of the current study showed that 6 Hz tACS could increase frontal-midline theta, modulate activity in DAN, and lead to significant changes in RVIP scores. EEG power analysis showed that 6 Hz tACS resulted in changes in theta relative PSD in frontal, central, and temporal regions mostly in the right hemisphere. Furthermore, Phase synchronization analysis showed extensive modulations in alpha frequency band in DAN as a result of active tACS administration.

Fast reaction time (RT) for correct responses can be considered a performance index in RVIP (Lawrence et al., 2003). RT significantly decreased in the active tACS group in our study which accords with other studies recruiting tDCS (Ball et al., 2013; Roe et al., 2016) and tACS (Hopfinger et al., 2017) to enhance attention, although there are reports of no significant change in RT too (Li et al., 2015). Considering the fact that different montages and stimulation parameters were used in these studies, reaching a conclusion about RT modulations is still not completely viable.

Our results showed that maximum power modulations were in F4, F3, and Fz regions. Studies about frontal-midline theta have shown that it tends to increase in F4 (Griesmayr et al., 2010) and especially Fz (Inouye et al., 1994; Shinomiya et al., 1994) while performing cognitive tasks. Other studies report increased theta power in frontal areas (F3, F4) (Gärtner et al., 2015) and central regions (Enriquez-Geppert et al., 2014), in addition to Fz.

CSD analysis was conducted in order to find out if mPFC activity is affected by the 6 Hz tACS and the results yielded 587 significant voxels in theta frequency band, mostly involving cingulate gyrus, post-central gyrus, precentral gyrus and medial frontal gyrus. Previous M/EEG source localization studies showed that ACC and mPFC are possible sources of frontal-midline theta (Asada et al., 1999; Ishii et al., 2014; Onton et al., 2005). Therefore, according to the results of the source and sensor analysis, it is possible to conclude that 6 Hz tACS resulted in an increase in frontal-midline theta and that the modulation in phase synchronization in DAN is a result of the increased frontal-midline theta.

Phase synchronization increased in our seeds of choice and in all the regions of the brain in alpha frequency band. Due to the low number of EEG channels (19) in this study, source-level functional connectivity analysis has not been conducted and the electrodes that best represent the DAN were chosen based on a study by Rojas et al., (2018) for a sensor-level analysis. Significant changes were observed in DAN. There were no significant changes in phase synchronization after sham tACS.

Results of the PLV analysis yielded an increase in alpha phase synchronization between temporal (T5/T6, inferior temporal lobe) and parietal (C3/C4, post-central lobe) regions of the brain. Alpha oscillations have been shown to be related to inhibitions of regions of the brain associated with task-irrelevant sensory processing. For instance, alpha power in visual and auditory cortex has been reported to be negatively correlated with performance in visual oddball task performance (Bollimunta et al., 2008) and positively correlated with initiation of auditory attention (Mazaheri et al., 2014), respectively. Studies on functional connectivity have shown that alpha phase synchronization between inter-areal regions correlate with attention task performance (Palva & Palva, 2011). Furthermore, alpha activity in inferior temporal regions are negatively related to performance in attention-related tasks (Bollimunta et al., 2008) and is more pronounced in visual rather than auditory tasks (Mo et al., 2011). Altogether, considering the fact that alpha phase synchronization has increased in task-irrelevant regions after tACS administrations, it can be concluded that the observed improvement in attention scores may be a result of the modulations of the activity in the aforementioned regions of the brain.

Chander et al. (2016) studied the role of frontal midline theta activity in working memory, using tACS with electrodes on FPz and Pz and stimulation frequency adjusted based on each individual's theta frequency. tACS phase-locked FMT mapping showed that tACS phase locking increased in FMT generating regions, mPFC, and ACC (Chander et al., 2016). The study by Miller et al. (2015) being the only study using tDCS to stimulate mPFC, investigated the role of frontal-midline theta activity in sustained attention. Here, anode was placed on AFz and cathode on the chin and a total stimulation duration of 15 minutes and an intensity of 1 mA was selected. The results showed that resting state frontal midline theta; ACC, and RDLPFC activation increased after stimulation. No significant changes were observed in EEG while performing the tasks so the authors concluded that the go/no-go paradigm had a weak task demand or the stimulation intensity (1 mA) was low because the cathode was not placed on the scalp (Miller et al., 2015).

To the best our knowledge, there are two relatively comparable studies on the effects of tACS on attention to date (Cui et al., 2018; Van Schouwenburg et al., 2019) and in both studies stimulation frequency and montage of choice may have contributed in the disparity of the results. There was a recent study with a large sample size about the effects of tDCS and tACS over mPFC on vigilant attention and the results show no significant difference in anodal and cathodal stimulation between active and sham stimulation. One of the explanations provided by the authors is their failure to modulate mPFC activity due to an inefficient montage. In the same study, 4 Hz tACS resulted in diminished performance in the attention task in the experimental group and 10 Hz tACS in the control group enhanced the participants' performance. The authors concluded that worsening of performance in vigilant attention was due to a mismatch between the stimulation frequency and individual theta frequency. In a simulation study, Hämmerer et al. (2016) proposed FPz and inion as proper sites for effective stimulation of mPFC and our study showed that this montage results in current density increase mainly in MFG. This may be considered as one reason for the failure of the aforementioned study to observe significant results when comparing active and sham stimulations (Hämmerer et al., 2016), but a lack of imaging methods, makes it difficult to explain the exact mechanisms through which the effects were produced. However, the main explanations could be based on the inefficient choice of montage and region of stimulation putting electrodes on FCz, Cz, and the cheek (Van Schouwenburg et al., 2019).

In another study about the effects of tACS on vigilant attention (Cui et al., 2018), 6 Hz stimulation was applied over Fz and F3 and yielded a significant reduction in psychomotor vigilant task in addition to theta phase synchronization after stimulation. The montage and stimulation frequencies in the two studies by Cui et al., and Van Schouwenburg et al. (2019) were different and both of these parameters may be potentially influencing the outcomes. The majority of studies that investigated the effects of tACS on cognitive performance have used 6 Hz stimulation frequency (Antonenko et al., 2016; Jaušovec & Jaušovec, 2014). In van Schouwenburg's study, the choice of 4 Hz could be the reason for not observing the expected outcome because it has been shown that if individual alpha peak is not considered for an accurate selection of stimulation frequency, 6 Hz is relatively a more efficient choice (Jaušovec & Jaušovec, 2014).

Taking advantage of the state of the art imaging methods and possibly combining it with on/offline stimulation in future research could add invaluable insights into the mechanism through which the stimulation is influencing the behavioral and electrophysiological outcomes, and provide the opportunity for more reliable interpretation.

5. Limitations

Considering the fact that EEG is prone to temporal variations across sessions, one of the main limitations of the current study is the fact that the authors did not take advantage of a counterbalanced design in order to minimize the potential effects of the order of sham/active tACS administrations, thus the results should be interpreted cautiously and conclusion drawn carefully with that in mind.

Furthermore, although tES is relatively more potent in blinding the subjects regarding the type of stimulation (active or sham) they receive, another limitation in our study is the lack of a systematic investigation of the sensations of tACS administration on subjects and how the sensations across active and sham sessions would or would not potentially affect the behavioral and electrophysiological outcomes. This consideration could add valuable results on the relationship between sensations of stimulation and actual modulations of brain activity.

6. Conclusion

This study showed that theta tACS over mPFC as a main hub in DMN results in significant performance enhancement in an attention task in healthy participants and this shows its potential as an intervention to enhance sustained attention in various psychiatric disorders.

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Disclosure statement

The authors declare no conflict of interest.

References

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

Anderer, P., Pascual-Marqui, R. D., Semlitsch, H. V., & Saletu, B. (1998). Electrical sources of P300 event-related brain potentials revealed by low resolution electromagnetic tomography. *Neuropsychobiology*, *37*(1), 20–27. https://doi.org/10.1159/000026472

Antonenko, D., Faxel, M., Grittner, U., Lavidor, M., & Flöel, A. (2016). Effects of transcranial alternating current stimulation on cognitive functions in healthy young and older adults. *Neural Plasticity*, *2016*, 1–13. https://doi.org/10.1155/2016/4274127

Asada, H., Fukuda, Y., Tsunoda, S., Yamaguchi, M., & Tonoike, M. (1999). Frontal midline theta rhythms reflect alternative activation of prefrontal cortex and anterior cingulate cortex in humans. *Neuroscience Letters*, *274*(1), 29–32. https://doi.org/10.1016/S0304-3940(99)00679-5

Ball, K., Lane, A. R., Smith, D. T., & Ellison, A. (2013). Site-dependent effects of tDCS uncover dissociations in the communication network underlying the processing of visual search. *Brain Stimulation*, *6*(6), 959–965. https://doi.org/10.1016/j.brs.2013.06.001

Bollimunta, A., Chen, Y., Schroeder, C. E., & Ding, M. (2008). Neuronal mechanisms of cortical alpha oscillations in awake-behaving macaques. *Journal of Neuroscience*, *28*(40), 9976–9988. https://doi.org/10.1523/JNEUROSCI.2699-08.2008

Bonnelle, V., Leech, R., Kinnunen, K. M., Ham, T. E., Beckmann, C. F., De Boissezon, X., Greenwood, R. J., & Sharp, D. J. (2011). Default mode network connectivity predicts sustained attention deficits after traumatic brain injury. *Journal of Neuroscience*, *31*(38), 13442–13451. https://doi.org/10.1523/JNEUROSCI.1163-11.2011

Borducchi, D. M., Gomes, J. S., Akiba, H., Cordeiro, Q., Borducchi, J. H. M., Valentin, L. S. S., Borducchi, G. M., & Dias, Á. M. (2016). Transcranial direct current stimulation effects on athletes' cognitive performance: An exploratory proof of concept trial. *Frontiers in Psychiatry*, *7*, 183. https://doi.org/10.3389/fpsyt.2016.00183

Borragán, G., Gilson, M., Guerrero-Mosquera, C., Di Ricci, E., Slama, H., & Peigneux, P. (2018). Transcranial direct current stimulation does not counteract cognitive fatigue, but induces sleepiness and an inter-hemispheric shift in brain oxygenation. *Frontiers in Psychology*, *9, 2351*. https://doi.org/10.3389/fpsyg.2018.02351

Broersen, L., & Uylings, H. (1999). Visual attention task performance in Wistar and Lister hooded rats: Response inhibition deficits after medial prefrontal cortex lesions. *Neuroscience*, *94*(1), 47–57. https://doi.org/10.1016/S0306-4522(99)00312-7

Buzzell, G. A., Barker, T. V., Troller-Renfree, S. V., Bernat, E. M., Bowers, M. E., Morales, S., … & Fox, N. A. (2019). Adolescent cognitive control, theta oscillations, and social observation. NeuroImage, 198, 13–30.https://doi.org/10.1016/j.neuroimage.2019.04.077

Cavanagh, J. F., Cohen, M. X., & Allen, J. J. (2009). Prelude to and resolution of an error: EEG phase synchrony reveals cognitive control dynamics during action monitoring. *Journal of Neuroscience*, *29*(1), 98–105. https://doi.org/10.1523/JNEUROSCI.4137-08.2009

Cavanagh, J. F., & Frank, M. J. (2014). Frontal theta as a mechanism for cognitive control. *Trends in Cognitive Sciences*, *18*(8), 414–421. https://doi.org/10.1016/j.tics.2014.04.012

Chander, B. S., Witkowski, M., Braun, C., Robinson, S. E., Born, J., Cohen, L. G., Birbaumer, N., & Soekadar, S. R. (2016). tACS phase locking of frontal midline theta oscillations disrupts working memory performance. *Frontiers in Cellular Neuroscience*, *10*, 120. https://doi.org/10.3389/fncel.2016.00120

Christakou, A., Murphy, C., Chantiluke, K., Cubillo, A., Smith, A., Giampietro, V., Ecker, C., Robertson, D., Murphy, D. G., Rubia, K., & Daly, D. (2013). Disorder-specific functional abnormalities during sustained attention in youth with attention deficit hyperactivity disorder (ADHD) and with autism. *Molecular Psychiatry*, *18*(2), 236. https://doi.org/10.1038/mp.2011.185

Christoff, K., Gordon, A. M., Smallwood, J., Smith, R., & Schooler, J. W. (2009). Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proceedings of the National Academy of Sciences*, *106*(21), 8719–8724. https://doi.org/10.1073/pnas.0900234106

Clayton, M. S., Yeung, N., & Kadosh, R. C. (2015). The roles of cortical oscillations in sustained attention. *Trends in Cognitive Sciences*, *19*(4), 188–195. https://doi.org/10.1016/j.tics.2015.02.004

Cui, H., Wei, J., Ke, Y., An, X., Sun, C., Xu, M., ... & Zhou, P. (2018, July). Research of the Regulation Effect of Transcranial Alternating Current Stimulation on Vigilant Attention. In 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (pp. 3481-3484). IEEE, Honolulu, Hawaii.

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

Duverne, S., & Koechlin, E. (2017). Rewards and cognitive control in the human prefrontal cortex. *Cerebral Cortex*, *27*(10), 5024–5039. https://doi.org/10.1093/cercor/bhx210

Engel, A. K., Fries, P., & Singer, W. (2001). Dynamic predictions: Oscillations and synchrony in top–down processing. *Nature Reviews Neuroscience*, *2*(10), 704. https://doi.org/10.1038/35094565

Enriquez-Geppert, S., Huster, R. J., Figge, C., & Herrmann, C. S. (2014). Self-regulation of frontal-midline theta facilitates memory updating and mental set shifting. *Frontiers in Behavioral Neuroscience*, *8*, 420. https://doi.org/10.3389/fnbeh.2014.00420

Fan, J., Gan, J., Liu, W., Zhong, M., Liao, H., Zhang, H., Yi, J., Chan, R. C. K., Tan, C., & Zhu, X. (2018). Resting-state default mode network related functional connectivity is associated with sustained attention deficits in schizophrenia and obsessive-compulsive disorder. *Frontiers in Behavioral Neuroscience*, *12*, 319. https://doi.org/10.3389/fnbeh.2018.00319

Fell, J., & Axmacher, N. (2011). The role of phase synchronization in memory processes. *Nature Reviews Neuroscience*, *12*(2), 105. https://doi.org/10.1038/nrn2979

Fiene, M., Schwab, B., Misselhorn, J., Herrmann, C., Schneider, T., & Engel, A. (2019). Phase-specific aftereffects of transcranial alternating current stimulation on visual processing. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *12*(2), 421. https://doi.org/10.1016/j.brs.2018.12.366

Fitzmaurice, G. M., Laird, N. M., & Ware, J. H. (2012). *Applied longitudinal analysis* (Vol. 998). John Wiley & Sons.

Friston, K. J., Frith, C., Liddle, P., & Frackowiak, R. (1991). Comparing functional (PET) images: The assessment of significant change. *Journal of Cerebral Blood Flow & Metabolism*, *11*(4), 690–699. https://doi.org/10.1038/jcbfm.1991.122

Gärtner, M., Grimm, S., & Bajbouj, M. (2015). Frontal midline theta oscillations during mental arithmetic: Effects of stress. *Frontiers in Behavioral Neuroscience*, *9*, 96. https://doi.org/10.3389/fnbeh.2015.00096

Geday, J., & Gjedde, A. (2009). Attention, emotion, and deactivation of default activity in inferior medial prefrontal cortex. *Brain and Cognition*, *69*(2), 344–352. https://doi.org/10.1016/j.bandc.2008.08.009

Gill, T. M., Sarter, M., & Givens, B. (2000). Sustained visual attention performance-associated prefrontal neuronal activity: Evidence for cholinergic modulation. *Journal of Neuroscience*, *20*(12), 4745–4757. https://doi.org/10.1523/JNEUROSCI.20-12-04745.2000

Griesmayr, B., Gruber, W. R., Klimesch, W., & Sauseng, P. (2010). Human frontal midline theta and its synchronization to gamma during a verbal delayed match to sample task. *Neurobiology of Learning and Memory*, *93*(2), 208–215. https://doi.org/10.1016/j.nlm.2009.09.013

Hämmerer, D., Bonaiuto, J., Klein-Flügge, M., Bikson, M., & Bestmann, S. (2016). Selective alteration of human value decisions with medial frontal tDCS is predicted by changes in attractor dynamics. *Scientific Reports*, *6*(1), 25160. https://doi.org/10.1038/srep25160

Holmes, A. P., Blair, R., Watson, J., & Ford, I. (1996). Nonparametric analysis of statistic images from functional mapping experiments. *Journal of Cerebral Blood Flow & Metabolism*, *16*(1), 7–22. https://doi.org/10.1097/00004647-199601000-00002

Hopfinger, J. B., Parsons, J., & Fröhlich, F. (2017). Differential effects of 10-Hz and 40-Hz transcranial alternating current stimulation (tACS) on endogenous versus exogenous attention. *Cognitive Neuroscience*, *8*(2), 102–111. https://doi.org/10.1080/17588928.2016.1194261

Inouye, T., Shinosaki, K., Iyama, A., Matsumoto, Y., Toi, S., & Ishihara, T. (1994). Potential flow of frontal midline theta activity during a mental task in the human electroencephalogram. *Neuroscience Letters*, *169*(1–2), 145–148. https://doi.org/10.1016/0304-3940(94)90377-8

Ishii, R., Canuet, L., Ishihara, T., Aoki, Y., Ikeda, S., Hata, M., Gunji, A., Takahashi, H., Nakahachi, T., Iwase, M., Takeda, M., & Katsimichas, T. (2014). Frontal midline theta rhythm and gamma power changes during focused attention on mental calculation: An MEG beamformer analysis. *Frontiers in Human Neuroscience*, *8*, 406. https://doi.org/10.3389/fnhum.2014.00406

Jaušovec, N., & Jaušovec, K. (2014). Increasing working memory capacity with theta transcranial alternating current stimulation (tACS). *Biological Psychology*, *96*, 42–47. https://doi.org/10.1016/j.biopsycho.2013.11.006

Kahn, J. B., Ward, R. D., Kahn, L. W., Rudy, N. M., Kandel, E. R., Balsam, P. D., & Simpson, E. H. (2012). Medial prefrontal lesions in mice impair sustained attention but spare maintenance of information in working memory. *Learning & Memory*, *19*(11), 513–517. https://doi.org/10.1101/lm.026302.112

Kasten, F. H., Dowsett, J., & Herrmann, C. S. (2016). Sustained aftereffect of α-tACS lasts up to 70 min after stimulation. *Frontiers in Human Neuroscience*, *10*, 245. https://doi.org/10.3389/fnhum.2016.00245

Lawrence, N. S., Ross, T. J., Hoffmann, R., Garavan, H., & Stein, E. A. (2003). Multiple neuronal networks mediate sustained attention. *J Cogn Neurosci*, *15*(7), 1028–1038. https://doi.org/doi:10.1162/089892903770007416

Li, L. M., Leech, R., Scott, G., Malhotra, P., Seemungal, B., Sharp, D. J., & Thut, G. (2015). The effect of oppositional parietal transcranial direct current stimulation on lateralized brain functions. *European Journal of Neuroscience*, *42*(11), 2904–2914. https://doi.org/10.1111/ejn.13086

Luchicchi, A., Mnie-Filali, O., Terra, H., Bruinsma, B., de Kloet, S. F., Obermayer, J., de Haan, R., de Kock, C. P. J., Deisseroth, K., Pattij, T., Mansvelder, H. D., & Heistek, T. S. (2016). Sustained attentional states require distinct temporal involvement of the dorsal and ventral medial prefrontal cortex. *Frontiers in Neural Circuits*, *10*, 70. https://doi.org/10.3389/fncir.2016.00070

Mazaheri, A., van Schouwenburg, M. R., Dimitrijevic, A., Denys, D., Cools, R., & Jensen, O. (2014). Region-specific modulations in oscillatory alpha activity serve to facilitate processing in the visual and auditory modalities. *Neuroimage*, *87*, 356–362. https://doi.org/10.1016/j.neuroimage.2013.10.052

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

Miner, L. A. H., Ostrander, M., & Sarter, M. (1997). Effects of ibotenic acid-induced loss of neurons in the medial prefrontal cortex of rats on behavioral vigilance: Evidence for executive dysfunction. *Journal of Psychopharmacology*, *11*(2), 169–178. https://doi.org/10.1177/026988119701100210

Mizuhara, H., & Yamaguchi, Y. (2007). Human cortical circuits for central executive function emerge by theta phase synchronization. *Neuroimage*, *36*(1), 232–244. https://doi.org/10.1016/j.neuroimage.2007.02.026

Mo, J., Schroeder, C. E., & Ding, M. (2011). Attentional modulation of alpha oscillations in macaque inferotemporal cortex. *Journal of Neuroscience*, *31*(3), 878–882. https://doi.org/10.1523/JNEUROSCI.5295-10.2011

Naka, M., Matsuzawa, D., Ishii, D., Hamada, H., Uchida, T., Sugita, K., Sutoh, C., & Shimizu, E. (2018). Differential effects of high-definition transcranial direct current stimulation on verbal working memory performance according to sensory modality. *Neuroscience Letters*, *687*, 131–136. https://doi.org/10.1016/j.neulet.2018.09.047

Nelson, J. T., McKinley, R. A., Golob, E. J., Warm, J. S., & Parasuraman, R. (2014). Enhancing vigilance in operators with prefrontal cortex transcranial direct current stimulation (tDCS). *Neuroimage*, *85*, 909–917. https://doi.org/10.1016/j.neuroimage.2012.11.061

Neuling, T., Rach, S., & Herrmann, C. S. (2013). Orchestrating neuronal networks: Sustained after-effects of transcranial alternating current stimulation depend upon brain states. *Frontiers in Human Neuroscience*, *7*, 161. https://doi.org/10.3389/fnhum.2013.00161

Neuling, T., Rach, S., Wagner, S., Wolters, C. H., & Herrmann, C. S. (2012). Good vibrations: Oscillatory phase shapes perception. *Neuroimage*, *63*(2), 771–778. https://doi.org/10.1016/j.neuroimage.2012.07.024

Nyhus, E., & Curran, T. (2010). Functional role of gamma and theta oscillations in episodic memory. *Neuroscience & Biobehavioral Reviews*, *34*(7), 1023–1035. https://doi.org/10.1016/j.neubiorev.2009.12.014

Onton, J., Delorme, A., & Makeig, S. (2005). Frontal midline EEG dynamics during working memory. *Neuroimage*, *27*(2), 341–356. https://doi.org/10.1016/j.neuroimage.2005.04.014

Palva, S., & Palva, J. M. (2011). Functional roles of alpha-band phase synchronization in local and large-scale cortical networks. *Frontiers in Psychology*, *2*, 204. https://doi.org/10.3389/fpsyg.2011.00204

Parkin, B. L., Ekhtiari, H., & Walsh, V. F. (2015). Non-invasive human brain stimulation in cognitive neuroscience: A primer. *Neuron*, *87*(5), 932–945. https://doi.org/10.1016/j.neuron.2015.07.032

Pascual-Marqui, R. D., Lehmann, D., Koenig, T., Kochi, K., Merlo, M. C., Hell, D., & Koukkou, M. (1999). Low resolution brain electromagnetic tomography (LORETA) functional imaging in acute, neuroleptic-naive, first-episode, productive schizophrenia. *Psychiatry Research: Neuroimaging*, *90*(3), 169–179. https://doi.org/10.1016/S0925-4927(99)00013-X

Petersson, K. M., Nichols, T. E., Poline, J.-B., Holmes, A. P., Howseman, A., & Zeki, S. (1999). Statistical limitations in functional neuroimaging II. Signal detection and statistical inference. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *354*(1387), 1261–1281. https://doi.org/10.1098/rstb.1999.0478

Plewnia, C., Zwissler, B., Längst, I., Maurer, B., Giel, K., & Krüger, R. (2013). Effects of transcranial direct current stimulation (tDCS) on executive functions: Influence of COMT Val/Met polymorphism. *Cortex*, *49*(7), 1801–1807. https://doi.org/10.1016/j.cortex.2012.11.002

Poerio, G. L., Sormaz, M., Wang, H.-T., Margulies, D., Jefferies, E., & Smallwood, J. (2017). The role of the default mode network in component processes underlying the wandering mind. *Social Cognitive and Affective Neuroscience*, *12*(7), 1047–1062. https://doi.org/10.1093/scan/nsx041

Polanía, R., Nitsche, M. A., Korman, C., Batsikadze, G., & Paulus, W. (2012). The importance of timing in segregated theta phase-coupling for cognitive performance. *Current Biology*, *22*(14), 1314–1318. https://doi.org/10.1016/j.cub.2012.05.021

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences*, *98*(2), 676–682. https://doi.org/10.1073/pnas.98.2.676

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science*, *306*(5695), 443–447. https://doi.org/10.1126/science.1100301

Roe, J. M., Nesheim, M., Mathiesen, N. C., Moberget, T., Alnæs, D., & Sneve, M. H. (2016). The effects of tDCS upon sustained visual attention are dependent on cognitive load. *Neuropsychologia*, *80*, 1–8. https://doi.org/10.1016/j.neuropsychologia.2015.11.005

Rojas, G. M., Alvarez, C., Montoya, C. E., de la Iglesia-Vayá, M., Cisternas, J. E., & Gálvez, M. (2018). Study of Resting-State Functional Connectivity Networks Using EEG Electrodes Position As Seed. Frontiers in neuroscience, 12, 235. https://doi.org/10.3389/fnins.2018.00235

Rojas, G. M., Alvarez, C., Montoya, C. E., de la Iglesia-vayá, M., Cisternas, J. E., & Gálvez, M. (2018). Study of resting-state functional connectivity networks using EEG electrodes position as seed. *Frontiers in Neuroscience*, *12*, 235. https://doi.org/10.3389/fnins.2018.00235

Rossi, A. F., Pessoa, L., Desimone, R., & Ungerleider, L. G. (2009). The prefrontal cortex and the executive control of attention. *Experimental Brain Research*, *192*(3), 489. https://doi.org/10.1007/s00221-008-1642-z

Ruhnau, P., Neuling, T., Fuscá, M., Herrmann, C. S., Demarchi, G., & Weisz, N. (2016). Eyes wide shut: Transcranial alternating current stimulation drives alpha rhythm in a state dependent manner. *Scientific Reports*, *6*, 27138. https://doi.org/10.1038/srep27138

Sahgal, A. (1987). Some limitations of indices derived from signal detection theory: evaluation of an alternative index for measuring bias in memory tasks. Psychopharmacology, 91(4), 517–520. https://doi.org/10.1007/BF00216022 4 doi:10.1007/BF00216022

Sakai, H., Uchiyama, Y., Tanaka, S., Sugawara, S. K., & Sadato, N. (2014). Prefrontal transcranial direct current stimulation improves fundamental vehicle control abilities. *Behavioural Brain Research*, *273*, 57–62. https://doi.org/10.1016/j.bbr.2014.07.036

Sarasso, P., Ninghetto, M., Salatino, A., Ronga, I., Bongiardina, A., Iarrobino, I., Neppi-Modona, M., & Ricci, R. (2019). Everything is (still) illuminated: Dual right cathodal-left anodal tDCS of PPC prevents fatigue on a visual detection task. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *12* (1), 187–189. https://doi.org/10.1016/j.brs.2018.09.017

Sauseng, P., Tschentscher, N., & Biel, A. L. (2019). Be Prepared: Tune to FM-Theta for Cognitive Control. *Trends in Neurosciences*, *42*(5), 307–309. https://doi.org/10.1016/j.tins.2019.02.006

Schack, B., Klimesch, W., & Sauseng, P. (2005). Phase synchronization between theta and upper alpha oscillations in a working memory task. *International Journal of Psychophysiology*, *57*(2), 105–114. https://doi.org/10.1016/j.ijpsycho.2005.03.016

Schwab, B. C., Misselhorn, J., & Engel, A. K. (2019). Modulation of large-scale cortical coupling by transcranial alternating current stimulation. Brain stimulation, 12(5), 1187-1196.

Sharpe, M. J., & Killcross, S. (2018). Modulation of attention and action in the medial prefrontal cortex of rats. *Psychological Review*, *125*(5), 822. https://doi.org/10.1037/rev0000118

Shinomiya, S., Urakami, Y., Nagata, K., Takahashi, N., & Inoue, R. (1994). Frontal midline theta rhythm: Differentiating the physiological theta rhythm from the abnormal discharge. *Clinical Electroencephalography*, *25*(1), 30–35. https://doi.org/10.1177/155005949402500109

Taren, A. A., Venkatraman, V., & Huettel, S. A. (2011). A parallel functional topography between medial and lateral prefrontal cortex: Evidence and implications for cognitive control. *Journal of Neuroscience*, *31*(13), 5026–5031. https://doi.org/10.1523/JNEUROSCI.5762-10.2011

Thomas Yeo, B., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., Smoller, J. W., Zöllei, L., Polimeni, J. R., Fischl, B., Liu, H., Buckner, R. L., & Roffman, J. L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *106*(3), 1125–1165. https://doi.org/10.1152/jn.00338.2011

Thomson, D. R., Besner, D., & Smilek, D. (2015). A resource-control account of sustained attention: Evidence from mind-wandering and vigilance paradigms. *Perspectives on Psychological Science*, *10*(1), 82–96. https://doi.org/10.1177/1745691614556681

van Schouwenburg, M. R., Sligte, I. G., Giffin, M. R., Gunther, F., Koster, D., Spronkers, F. S., … Slagter, H. A. (2019). Effects of mid-frontal brain stimulation on sustained attention. *bioRxiv*, 641498.https://doi.org/10.1101/641498

Violante, I. R., Li, L. M., Carmichael, D. W., Lorenz, R., Leech, R., Hampshire, A., Rothwell, J. C., & Sharp, D. J. (2017). Externally induced frontoparietal synchronization modulates network dynamics and enhances working memory performance. *Elife*, *6*, e22001. https://doi.org/10.7554/eLife.22001

Wang, W., Viswanathan, S., Lee, T., Grafton, S. T., & Ben Hamed, S. (2016). Coupling between theta oscillations and cognitive control network during cross-modal visual and auditory attention: Supramodal vs modality-specific mechanisms. *PloS One*, *11*(7), e0158465. https://doi.org/10.1371/journal.pone.0158465

Welch, P. (1967). The use of fast Fourier transform for the estimation of power spectra: A method based on time averaging over short, modified periodograms. *IEEE Transactions on Audio and Electroacoustics*, *15*(2), 70–73. https://doi.org/10.1109/TAU.1967.1161901

Williams, J., Mohler, E., & Givens, B. (1999). The role of the medial prefrontal cortex in attention: Altering predictability of task difficulty. *Psychobiology*, *27*(4), 462–469. https://doi.org/10.3758/BF03332141

Zaehle, T., Rach, S., Herrmann, C. S., & Aleman, A. (2010). Transcranial alternating current stimulation enhances individual alpha activity in human EEG. *PloS One*, *5* (11), e13766. https://doi.org/10.1371/journal.pone.0013766

Zavala, B., Jang, A., Trotta, M., Lungu, C. I., Brown, P., & Zaghloul, K. A. (2018). Cognitive control involves theta power within trials and beta power across trials in the prefrontal-subthalamic network. *Brain*, *141*(12), 3361–3376. https://doi.org/10.1093/brain/awy266