tACS-mediated modulation of the auditory steady-state response as seen with MEG

Petteri Hyvärinen, Dawoon Choi, Gianpaolo Demarchi, Antti A. Aarnisalo, Nathan Weisz

PII: S0378-5955(17)30066-7
DOI: 10.1016/j.heares.2018.03.023
Reference: HEARES 7526

To appear in: *Hearing Research*

Received Date: 23 February 2017
Revised Date: 11 March 2018
Accepted Date: 23 March 2018

Please cite this article as: Hyvärinen, P., Choi, D., Demarchi, G., Aarnisalo, A.A., Weisz, N., tACS-mediated modulation of the auditory steady-state response as seen with MEG, *Hearing Research* (2018), doi: 10.1016/j.heares.2018.03.023.

tACS-mediated modulation of the auditory steady-state response as seen with MEG

Petteri Hyvärinen[a,b], Dawoon Choi[c], Gianpaolo Demarchi[d,e], Antti A. Aarnisalo[a],
Nathan Weisz[d,e]

a. Department of Otorhinolaryngology—Head and Neck Surgery
University of Helsinki and Helsinki University Hospital
Biomedicum Helsinki 1, P.O. Box 220, FI-00029 HUS, Finland

b. Department of Neuroscience and Biomedical Engineering, Aalto University School of Science, Finland

c. Department of Psychology, The University of British Columbia, Canada

d. Center for Mind/Brain Sciences, University of Trento, Italy

e. Centre for Cognitive Neuroscience, University of Salzburg, Austria

Corresponding author: Petteri Hyvärinen, petteri.hyvarinen@aalto.fi

Abstract

Background: Previous studies have shown that transcranial electrical stimulation can be successfully applied during simultaneous MEG measurements. In particular, using beamforming they have established that changes of stimulus induced as well as evoked activity can be inspected during transcranial alternating current stimulation (tACS).

Objective/Hypothesis: We studied tACS-mediated changes of the auditory steady-state response (ASSR), hypothesizing that—due to the putatively inhibitory role of alpha oscillations—these evoked responses would be diminished.

Methods: We compared ASSRs in conditions with and without 12-Hz and 6.5-Hz sinusoidal 1.5 mA tACS, applied bilaterally over temporal areas. Source-level activity was estimated using a linearly constrained minimum variance beamformer and compared across tACS conditions using paired t-tests following a condition-internal normalization procedure.

Conclusions: By separating the electrical and auditory stimulation to non-overlapping parts of the frequency spectrum, we were able to compare auditory-evoked steady-state activity across tACS conditions. We observed a significant decrease in normalized ASSR power in the 12-Hz tACS condition, illustrating that tACS could induce immediate changes in auditory evoked activity. This study sets a methodology to further interrogate the causal roles of oscillatory dynamics in auditory cortices, as well as suggests perspectives for employing tACS in clinical contexts.

Introduction

Growing interest in the impact of transcranial electrical stimulation (tES) techniques on human cognition and behaviour, as well as their therapeutic potential has motivated researchers to further develop approaches to better understand tES effects on brain activity [1,2]. In particular, transcranial alternating current stimulation (tACS) putatively taps into intrinsic oscillatory rhythms within the brain by inducing a weak sinusoidal electrical current between scalp electrodes. Already a number of behavioural studies have demonstrated frequency-tuned tACS effects in the visual and motor domains [3,4]. However, due to the enormous artifacts in the recordings created by the electrical stimulation, the electrophysiological correlates accompanying the behavioural effects of tACS have been mostly demonstrated *offline*. Only recently, *online* methods combining tES and magnetoencephalography (MEG) in a concurrent fashion have been implemented, allowing to monitor brain dynamics concurrent to the electrical stimulation [5–9]. tES-induced changes in neuronal oscillatory and evoked activity reflect altered levels of cortical excitability and can reveal important aspects of the mechanisms through which tES methods deliver their therapeutic effects. In order to diminish the influence of artifacts from the magnetic fields associated with the stimulating currents, spatial filtering approaches — the linearly constrained minimum variance (LCMV) [10] and the synthetic aperture magnetometry (SAM) [11] beamformers — have been employed in the source-level analysis of the measurement signals and they have been shown to perform well when facing the presence of highly correlated interference [5,7]. Sekihara *et al.* [12] examined the beamformer's performance in the presence of an additive low-rank interference and found the beamformer to be largely insensitive to the unwanted signals when MEG data is projected in the source space, thereby boosting signal-to-noise ratios (SNRs) significantly. Especially when combined with controlled experimental contrasts, the described property makes the beamformer a powerful tool for inspecting source-level activity in MEG during tACS as long as the technical limits of the instrumentation are taken into consideration [13,14].

The auditory steady-state response (ASSR) represents the synchronized neural activity elicited by a continuous, rhythmically repeated or modulated sound. First described by Galambos *et al.* (1981) [15] the ASSR, as measured with electroencephalography (EEG) in response to repeated clicks and tone pips, was found to be strongest at stimulus repetition rates around 40 Hz. The corresponding neuromagnetic response follows the same dynamics as measured on the scalp potentials [16], localizing to the primary auditory cortices [17,18]. The high frequency-specificity of the ASSR can be obtained by using a pure tone as a carrier signal and modulating the tone's amplitude, frequency, or both. To elicit larger — albeit less frequency-specific — responses, broad-band clicks or modulated noise are used [19,20].

Rationale

Although online effects of tDCS on brain activity have previously been described with MEG [9,21,22], no studies exist on online tACS-induced changes in auditory evoked activity. Earlier MEG studies with tACS have focused on identifying evoked and induced activity in the presence of tACS [6,7], but have not compared the activity between multiple tACS conditions. In addition, the majority of simultaneous tDCS/tACS-EEG/MEG studies have targeted modulation in the motor [9,23] and visual [6–8,24] cortices. Notably, Neuling *et al.* (2015) [7] used the whole-brain tACS-MEG approach and appropriate controls to successfully recover increased alpha power during the eyes closed condition compared to the eyes opened condition during tACS. We aimed to simultaneously modulate the excitability levels of the auditory cortices with frequency-specific tACS while eliciting ASSR. To that end, we examined the magnetic ASSR to a 41-Hz continuous click train while participants were either stimulated at 12 Hz (alpha) frequency, 6.5 Hz control frequency (non-harmonic to 12 Hz), or received no tACS stimulation. Alpha frequency oscillatory rhythm is theorized to exert an inhibitory impact, in which corresponding power increase is observed to suppression of cortical excitability [25]. Thus, if alpha-frequency tACS were to entrain the intrinsic neural oscillations, we hypothesized that such an effect should be observable as a diminutive ASSR under alpha frequency stimulation compared to 6.5-Hz control stimulation.

Material and Methods

Subjects

Eighteen subjects (6 female, 12 male; average age 26.6 years, SD 4.1 years) participated in the study. Subjects did not report any hearing impairment. The study was approved by the ethical committee of University of Trento and was carried out in accordance with the Declaration of Helsinki. All subjects gave written informed consent prior to the experiment.

Experimental Setup

The experiment was conducted in a magnetically shielded room (AK3b, Vacuumschmelze, Germany) using a 306-sensor whole-head (102 magnetometers, 204 planar gradiometers) MEG device (Neuromag Vectorview, Elekta Oy, Helsinki, Finland), in a within-subject design that consisted of one block of resting state and five recording blocks with varying combinations of auditory and electrical stimulation (Table 1). Head shape was digitized with the Polhemus FasTrak® system. A minimum of 200 points was captured for each subject in addition to the fiducial points at left and right preauricular points and at the nasion. Five fiducial coils were used for determining the head position at the beginning of each recording block: two coils were placed over the mastoids behind each ear, and three coils were placed on the forehead. No correction for head movements during the recording was applied. Signals were recorded at a sampling rate of 1000 Hz and filtered with an analog bandpass-filter from 0.1 Hz to 300 Hz. The 6.5-Hz tACS blocks were restricted to 1 minute in order to keep the total time of applied electrical stimulation to a minimum. This difference in stimulation duration was taken into account in the analysis (see below). Resting state measurements were always conducted first, but for the following conditions the block order was shuffled across all participants to account for possible carry-over effects. Further, the 6.5-Hz tACS block and the ASSR combined with 6.5-Hz tACS block were always measured during a single block, in which the auditory stimulus was introduced halfway through the recording block. During the recordings, the dewar was set in an upright position, and the subjects watched a silent film and were not involved in any active task.

Block	Auditory stimulation	Electrical stimulation	Block length
'resting'	no	no	5 min
'ASSR'	41-Hz click train	no	5 min
'tACS12'	no	Sinusoidal tACS at 12 Hz	5 min
'ASSR-tACS12'	41-Hz click train	Sinusoidal tACS at 12 Hz	5 min
'tACS6.5'	no	Sinusoidal tACS at 6.5 Hz	1 min
'ASSR-tACS6.5'	41-Hz click train	Sinusoidal tACS at 6.5 Hz	1 min

Table 1 — Stimulation parameters used in the MEG recording blocks

Electrical Stimulation

The battery-operated stimulator device (DC-Stimulation Plus, NeuroConn GmbH, Ilmenau, Germany) was placed outside the magnetically shielded room. The stimulator was connected to a magnetic resonance imaging (MRI) module (NeuroConn GmbH, Ilmenau, Germany), and also to two electrodes administered to the subjects. Each of the electrodes was covered with 35-cm^2 saline-soaked sponges (0.9%-NaCl), which were held in position by a latex swimming cap covering the head. This approach allowed an evenly distributed pressure on the electrodes and additionally prevented drying of the electrode sponges during the experiment. We placed the electrodes bilaterally at EEG positions T3 and T4, according to the international 10/20 system, chosen to target the auditory cortices. The impedance value of each subject was kept below 20kΩ.

Stimulation waveform was sinusoidal, with a peak-to-peak current amplitude of 1.5 mA, and without a DC offset.

Auditory stimulation

Auditory steady-state responses (ASSRs) were evoked by a continuous train of 100-µs clicks repeated at 41 Hz presented from a MEG-compatible loudspeaker. Before the first recording block, individual hearing thresholds to 1-second bursts of the auditory stimulus were determined with a standard manual audiometric procedure: a simple up/down staircase was used with fixed 5-dB and 10-dB step sizes for up and down respectively. Threshold was defined as the level where there were at least two correct responses within three consecutive ascending trials [26]. The intensity level of the auditory stimulus was set to 30 dB above this hearing threshold.

Data analysis

Noisy and flat channels were identified using a semi-automated procedure and excluded from further analysis. In the recording blocks including tACS, detection of bad channels was based on the pre-stimulation period at the beginning of each block. Further preprocessing, such as eyeblink detection or removal of noisy epochs, was prevented by the tACS artifacts. The same preprocessing steps were taken for both the tACS and non-tACS recording blocks to avoid artificially introducing any bias between conditions.

Sensor-level signals were digitally bandpass filtered from 1 Hz to 100 Hz and divided into 4.88-s epochs (200 cycles of the 41-Hz auditory stimulus). Long epochs were used for maximizing the FFT frequency resolution, to ensure that possible tACS artifacts could be identified and differentiated from the auditory activity.

For source analysis, source volumes were constructed either based on individual structural MRI scans (n = 10), or by fitting a template MRI to the individual headshape of each subject (n = 8). Co-registration of the MEG and MRI coordinates was obtained by alignment of the fiducial points. Individual source dipole grids were constructed by warping an 889-point template grid with 1.5 cm spacing to each subject's source volumes. The MEG forward model was based on a single-shell model. Determination of LCMV beamformer [10] spatial filter weights was based on an average covariance matrix estimated across all epochs. No regularization was applied to the covariance matrix, i.e. the lambda-value was set to zero [13]. Source-level virtual sensor time courses were estimated by applying the beamformer to each epoch individually. Virtual sensor power spectra for the Hanning-windowed epochs were then calculated using a Fast Fourier Transform (FFT). Finally, for each tACS variant (no tACS, 12-Hz tACS, or 6.5-Hz tACS), a normalized spectrum between two recording blocks of the same tACS variant—A (with auditory stimuli) and B (without auditory stimuli)—was calculated as: $\overline{PSD}(A,B) = \frac{(A-B)}{B}$ for each virtual sensor and frequency bin individually. In other words, block 'ASSR' was normalized with respect to block 'resting', 'ASSR-tACS12' to 'tACS12', and 'ASSR-tACS6.5' to 'tACS6.5' to obtain three normalized spectra. Via this approach, we assured that no potential residual artifact of the tACS in source space could explain our findings. The effect of beamforming can be seen in Fig. 1, showing sensor- and source-level activation patterns and spectra for no tACS and 12-Hz tACS conditions.

Figure 1 —Sensor- and source-level activation patterns and spectra. On the left panel, conditions without tACS, and on the right panel conditions with 12-Hz tACS. Sensor-level data is shown only for gradiometer sensors. Sensor topography and source-level activation patterns are plotted for the 41-Hz ASSR.

Statistical testing of source-level activity included first identifying the location of the maximum average ASSR activity in a data-driven manner by running a whole-head non-parametric, cluster-based permutation test comparing the non-normalized ‘resting’ and ‘ASSR’ spectral values at 41 Hz. Second, to evaluate the effect of tACS on auditory evoked activity, another whole-head permutation test compared normalized spectral values at 41 Hz between 12-Hz tACS conditions and no tACS conditions. Lastly, to determine whether the observed effect might be tACS-frequency-dependent, the effects of 12-Hz tACS and 6.5-Hz tACS on normalized ASSR power were compared for voxels in the right auditory cortex, identified in the first step. Reported statistical values for each contrast are based on values from the right AC region of interest and calculated using the Fisher-Pitman permutation test. For our actual contrast of interest, i.e. 12-Hz tACS blocks versus blocks without tACS, the full five minutes of the recording were used, but when comparing both 12-Hz tACS and 6.5-Hz tACS to no tACS, only the first minute of the 12-Hz tACS and no tACS recordings were used in order to keep (SNRs) comparable across conditions.

Results and Discussion

ASSRs at 41 Hz could be detected in conditions both with and without tACS. Responses were located predominantly in the right auditory cortex (AC) (Fig. 2A) as could be expected for binaural auditory stimuli [27]. Within the right AC region of interest, a comparison of the no tACS conditions to 12-Hz tACS conditions revealed a significant decrease in normalized ASSR power under 12-Hz tACS stimulation (tACS vs. no tACS: −81.3; $Z = -2.51, p < 0.01$, *Cohen’s* $d = 0.72$) (Fig. 2B).

Figure 2 — A) Normalized source-level auditory activity at 41 Hz in the no tACS condition. B) Modulation of ASSR power by 12-Hz tACS. C) Normalized source-level spectra

around the ASSR frequency 41 Hz in the no tACS condition (red line) and in the tACS conditions (blue line).

To compare the normalized power between no tACS, 6.5-HZ tACS, and 12 HZ tACS, we examined only the first 1-min time window across all three conditions, thus excluding total duration as confound for potential differences. Restricting the analysis to the first minute of the 12-Hz tACS condition, the same tACS-induced ASSR suppression was observed (tACS vs. no tACS: −35.4; $Z = -1.96, p < 0.05, d = 0.51$), in contrast to the 6.5-Hz tACS condition whereby a smaller, non-significant change in ASSR power was observed (tACS vs. no tACS: −24.7; $Z = -1.50, p > 0.05, d = 0.37$) (Fig 3.). This suggests that tACS of the AC could have a frequency-specific effect on the ASSR, which would be in line with previous studies reporting frequency-dependent after-effects of tACS when stimulation has been targeted to motor areas [23,28] and visual areas [29]. However, the difference between 12-Hz tACS and 6.5-Hz tACS was nonsignificant (tACS 12 Hz vs. tACS 6.5 Hz: −10.7; $Z = -1.0, p > 0.05, d = 0.24$). Thus, no definitive conclusions can be drawn regarding the possible frequency-specificity of tACS on the ASSR.

Figure 3 — Normalized source-level spectra around the ASSR frequency for the 1-minute blocks comparing no tACS condition (red line) to 6.5-Hz tACS (dark green line).

From a technical point of view, it is important to assure that the observed modulation in ASSR power is not caused by stimulation artifacts. However, electrical artifacts would be expected to appear as increases in spectral power, such as peaks at harmonic multiples of the stimulation frequency, or as spreading of the spectral peaks due to windowing in the temporal domain, neither of which are present in the normalized spectra (Fig. 1, Fig. 2C). The main result indicated a decrease in auditory activity, and any effects due to artifacts may be ruled out since the ASSR and tACS stimulation frequencies were selected so that the ASSR frequency does not coincide with the tACS stimulation frequencies and their harmonics. In addition, the relatively large spectral separation between the stimulation frequencies (12 Hz and 6.5 Hz) and the frequency of the steady-state response (41 Hz) may mean that the effects are relatively immune from the non-linear artifacts caused by the interaction between the stimulation and movement during respiration and heartbeat, which have been shown to affect signals during tACS at and beyond the side peaks around stimulation frequency [14]. Although, as has been recently demonstrated, steady-state responses can be recovered even at the same frequency as the tACS stimulation frequency using the same beamformer approach as in this study [24]. Considering the strengths of the current paradigm against artifact contaminations, the observed change in ASSR power is better situated to reflect a stimulation induced reduction in auditory evoked response.

A putative mechanism for the observed tACS-induced effect is the entrainment of auditory alpha activity through 12-Hz tACS. Alpha oscillations have been recognized as a marker for increased inhibition in multiple sensory domains including the auditory modality [30,31]. An inverse relationship was identified between the ASSR amplitude and the amplitude of alpha oscillations by Plourde et al. [32] although an earlier study by Tesche and Hari found no such linear relationship [33]. Limited evidence was also found by Simpson et al. [34], who reported non-linear interactions between intrinsic alpha oscillations and the ASSR as measured by mutual information. Entrainment by tACS has been demonstrated in multiple studies, both as an after-effect [35–38] and during tACS [6], and online effects of tACS have been described by changes in behavioral measures [39]. Despite the attractiveness of interpreting the current finding in light of the reported finding in which we observed an increased tACS-induced suppression of ASSR, the proposed model remains speculative, since no behavioral measures were collected in this proof-of-concept study. Linking the ASSR effect to auditory task performance would be necessary to demonstrate an inhibitory effect.

The limitations in the experimental design of the current study should be considered in the interpretation of the reported results. The normalization method employed in the current study is sensitive to changes in the SNR, and thus spurious effects could arise from changes in the background noise level. Despite large spectral artifacts at multiple harmonics of the tACS frequency, because the frequency region of interest (i.e. 41Hz ASSR) was distanced far from the electrical stimulation, the SNR can be assumed to be preserved across conditions. Contributions from other sensory modalities—such as the somatosensory system [40]—cannot be ruled out, although no somatic sensations were reported by the subjects in the current study. Novel approaches involving sham electrodes that produce similar tactile sensations through closely-placed anode and cathode electrodes could provide a more constraint control condition [41]. Spread of stimulation current on the scalp and in the brain volume could also lead to activation of brain areas not intentionally targeted by tACS. The specificity of the ASSR effect could be explored by repeating the experiment with different electrode placements. However, safety considerations regarding the use of transcranial electrical stimulation place a practical upper limit on the number of stimulation varieties that can be explored within a single experimental session.

Conclusions

Selecting the tACS and ASSR frequencies in such a way that their harmonic multiples do not coincide, it was possible to inspect ASSR in the unaffected part of the spectrum during electrical stimulation. The effect had a frequency-specific tendency, showing a reduction in ASSR for 12-Hz tACS but not for 6.5-Hz tACS. Unfortunately, since the difference between the 12-Hz and 6.5-Hz tACS conditions was not significant, no conclusions can be drawn regarding the hypothesized oscillatory mechanisms behind the observed decrease in ASSR. Nevertheless, the current study demonstrates a viable methodological approach for future studies investigating the online effects of tACS in MEG.

The possibility of inspecting the specific targeting of tACS is highly relevant in studies involving transcranial electrical stimulation (tES, i.e. tACS or tDCS) as therapeutic tools. Relating treatment outcomes to acute stimulation-induced changes in brain activity could allow predicting suitable treatment options for individual subjects and for subtyping patients in conditions such as tinnitus where there might be multiple overlapping brain networks involved in maintaining the symptoms. Furthermore, techniques that allow concurrent monitoring of brain dynamics during tES could aid in individualizing electrical stimulation properties. Using tES methods in combination with MEG opens exciting and unique possibilities for probing the dynamics of these networks.

Acknowledgements

This work was financially supported by an ERC Starting Grant (#283404) and by a STSM grant from the TINNET EU COST Action BM1306. Work of PH was also supported by personal grants from Jenny and Antti Wihuri Foundation and the Paulo Foundation.

References

[1] Thut G, Miniussi C, Gross J. The functional importance of rhythmic activity in the brain. Curr Biol 2012;22:R658–63. doi:10.1016/j.cub.2012.06.061.

[2] Kuo MF, Paulus W, Nitsche MA. Therapeutic effects of non-invasive brain stimulation with direct currents (tDCS) in neuropsychiatric diseases. Neuroimage 2014;85:948–60. doi:10.1016/j.neuroimage.2013.05.117.

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

[4] Paulus W. Transcranial electrical stimulation (tES – tDCS; tRNS, tACS) methods. Neuropsychol Rehabil 2011;21:602–17. doi:10.1080/09602011.2011.557292.

[5] Soekadar SR, Witkowski M, Cossio EG, Birbaumer N, Robinson SE, Cohen LG. In vivo assessment of human brain oscillations during application of transcranial electric currents. Nat Commun 2013;4:2032. doi:10.1038/ncomms3032.

[6] Witkowski M, Garcia-Cossio E, Chander BS, Braun C, Birbaumer N, Robinson SE, et al. Mapping entrained brain oscillations during transcranial alternating current stimulation (tACS). Neuroimage 2016;140:89–98. doi:10.1016/j.neuroimage.2015.10.024.

[7] Neuling T, Ruhnau P, Fuscà M, Demarchi G, Herrmann CS, Weisz N. Friends, not foes: magnetoencephalography as a tool to uncover brain dynamics during transcranial alternating current stimulation. Neuroimage 2015;118:406–13. doi:10.1016/j.neuroimage.2015.06.026.

[8] Neuling T, Ruhnau P, Fuscà M, Demarchi G, Herrmann CS, Weisz N. Shed light on the black box: Using MEG to recover brain activity during tACS. Brain Stimul 2015;8:381–2. doi:10.1016/j.brs.2015.01.221.

[9] Garcia-Cossio E, Witkowski M, Robinson SE, Cohen LG, Birbaumer N, Soekadar SR. Simultaneous transcranial direct current stimulation (tDCS) and whole-head magnetoencephalography (MEG): assessing the impact of tDCS on slow cortical magnetic fields. Neuroimage 2015. doi:10.1016/j.neuroimage.2015.09.068.

[10] Van Veen B, van Drongelen W, Yuchtman M, Suzuki A. Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. IEEE Trans Biomed Eng 1997;44:867–80. doi:10.1109/10.623056.

[11] Robinson SE, Vrba J. Functional neuroimaging by synthetic aperture magnetometry (SAM). In: Yuoshimoto T, Kotani M, Kuriki S, Karibe H, Nakasato N, editors. Recent Adv. Biomagn., Tohoku University Press; 1998, p. 302–305.

[12] Sekihara K, Nagarajan SS, Poeppel D, Marantz A. Performance of an MEG adaptive-beamformer source reconstruction technique in the presence of additive low-rank interference. IEEE Trans Biomed Eng 2004;51:90–9. doi:10.1109/TBME.2003.820329.

[13] Neuling T, Ruhnau P, Weisz N, Herrmann CS, Demarchi G. Faith and oscillations recovered: On Analyzing EEG/MEG signals during tACS. Neuroimage 2016:0–1. doi:10.1016/j.neuroimage.2016.11.022.

[14] Noury N, Hipp JF, Siegel M. Physiological processes non-linearly affect electrophysiological recordings during transcranial electric stimulation. Neuroimage 2016;140:99–109. doi:10.1016/j.neuroimage.2016.03.065.

[15] Galambos R, Makeig S, Talmachoff PJ. A 40-Hz auditory potential recorded from the human scalp. Proc Natl Acad Sci U S A 1981;78:2643–7. doi:10.1073/pnas.78.4.2643.

[16] Hari R, Hamalainen M, Joutsiniemi SL. Neuromagnetic steady-state responses to auditory stimuli. J Acoust Soc Am 1989;86:1033–9. doi:10.1097/00001756-199509000-00001.

[17] Pantev C, Roberts LE, Elbert T, Ross B, Wienbruch C. Tonotopic organization of the sources of human auditory steady-state responses. Hear Res 1996;101:62–74.

doi:10.1016/S0378-5955(96)00133-5.

[18] Herdman AT, Lins O, Van Roon P, Stapells DR, Scherg M, Picton TW. Intracerebral Sources of Human Auditory Steady-State Responses. Brain Topogr 2002;15:69–86. doi:10.1023/A:1021470822922.

[19] Picton TW, John MS, Dimitrijevic A, Purcell D. Human auditory steady-state responses. Int J Audiol 2003;42:177–219.

[20] John MS, Dimitrijevic a, Picton TW. Efficient stimuli for evoking auditory steady-state responses. Ear Hear 2003;24:406–23. doi:10.1097/01.AUD.0000090442.37624.BE.

[21] Hanley CJ, Singh KD, McGonigle DJ. Transcranial modulation of brain oscillatory responses: A concurrent tDCS–MEG investigation. Neuroimage 2016;140:20–32. doi:10.1016/j.neuroimage.2015.12.021.

[22] Marshall TR, Esterer S, Herring JD, Bergmann TO, Jensen O. On the relationship between cortical excitability and visual oscillatory responses — A concurrent tDCS–MEG study. Neuroimage 2016;140:41–9. doi:10.1016/j.neuroimage.2015.09.069.

[23] Wach C, Krause V, Moliadze V, Paulus W, Schnitzler A, Pollok B. Effects of 10 Hz and 20 Hz transcranial alternating current stimulation (tACS) on motor functions and motor cortical excitability. Behav Brain Res 2013;241:1–6. doi:10.1016/j.bbr.2012.11.038.

[24] Ruhnau P, Keitel C, Lithari C, Weisz N, Neuling T. Flicker-Driven Responses in Visual Cortex Change during Matched-Frequency Transcranial Alternating Current Stimulation. Front Hum Neurosci 2016;10:1–13. doi:10.3389/fnhum.2016.00184.

[25] Jensen O, Mazaheri A. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. Front Hum Neurosci 2010;4:186. doi:10.3389/fnhum.2010.00186.

[26] British Society of Audiology. Recommended procedure. Pure-tone air-conduction and bone-conduction threshold audiometry with and without masking. 2012. doi:10.1017/CBO9781107415324.004.

[27] Ross B, Herdman AT, Pantev C. Right hemispheric laterality of human 40 Hz auditory steady-state responses. Cereb Cortex 2005;15:2029–39. doi:10.1093/cercor/bhi078.

[28] 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;1:97–105. doi:10.1016/j.brs.2007.10.001.

[29] Kanai R, Chaieb L, Antal A, Walsh V, Paulus W. Frequency-dependent electrical stimulation of the visual cortex. Curr Biol 2008;18:1839–43. doi:10.1016/j.cub.2008.10.027.

[30] Weisz N, Hartmann T, Müller N, Lorenz I, Obleser J. Alpha rhythms in audition: Cognitive and clinical perspectives. Front Psychol 2011;2:73. doi:10.3389/fpsyg.2011.00073.

[31] Frey JN, Mainy N, Lachaux J-P, Müller N, Bertrand O, Weisz N. Selective modulation of auditory cortical alpha activity in an audiovisual spatial attention task. J Neurosci 2014;34:6634–9. doi:10.1523/JNEUROSCI.4813-13.2014.

[32] Plourde G, Baribeau J, Bonhomme V. Ketamine increases the amplitude of the 40-Hz auditory steady-state response in humans. Br J Anaesth 1997;78:524–9.

[33] Tesche C, Hari R. Independence of steady-state 40-Hz response and spontaneous 10-Hz activity in the human auditory cortex. Brain Res 1993;629:19–22.

[34] Simpson MIG, Hadjipapas A, Barnes GR, Furlong PL, Witton C. Imaging the dynamics of the auditory steady-state evoked response. Neurosci Lett 2005;385:195–7. doi:10.1016/j.neulet.2005.05.043.

[35] 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. doi:10.3389/fnhum.2013.00161.

[36] Helfrich RF, Schneider TR, Rach S, Trautmann-Lengsfeld S a., Engel AK, Herrmann CS. Entrainment of brain oscillations by transcranial alternating current stimulation. Curr Biol 2014;24:333–9. doi:10.1016/j.cub.2013.12.041.

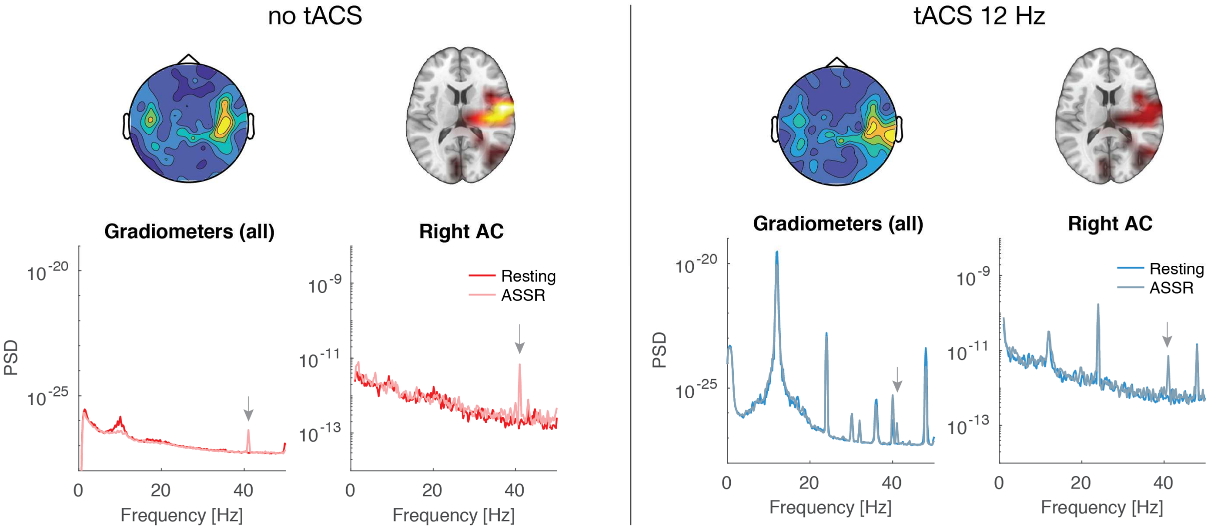
[37] Herrmann CS, Rach S, Neuling T, Strüber D. Transcranial alternating current stimulation: a review of the underlying mechanisms and modulation of cognitive processes. Front Hum Neurosci 2013;7:279. doi:10.3389/fnhum.2013.00279.

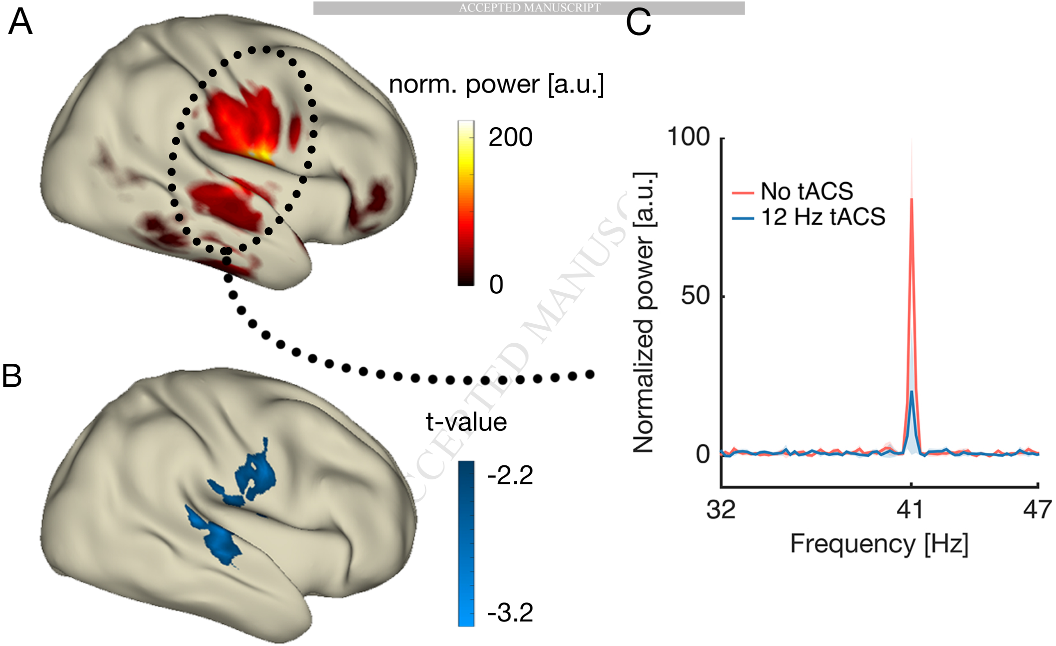
[38] Zaehle T, Rach S, Herrmann CS. Transcranial Alternating Current Stimulation Enhances Individual Alpha Activity in Human EEG. PLoS One 2010;5:1–7. doi:10.1371/journal.pone.0013766.

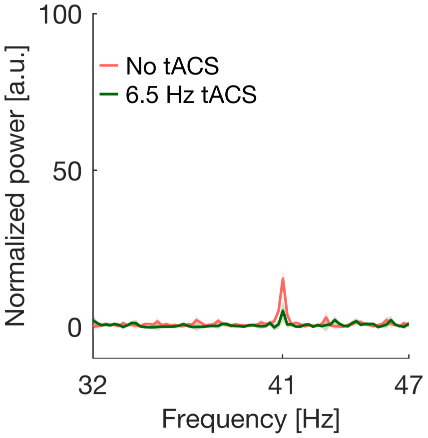
[39] Vosskuhl J, Huster RJ, Herrmann CS. Increase in short-term memory capacity induced by down-regulating individual theta frequency via transcranial alternating current stimulation. Front Hum Neurosci 2015;9:257. doi:10.3389/fnhum.2015.00257.

[40] Wu C, Stefanescu RA, Martel DT, Shore SE. Listening to another sense: somatosensory integration in the auditory system. Cell Tissue Res 2015;361:233–50. doi:10.1007/s00441-014-2074-7.

[41] Pal N, Maire R, Stephan M, Herrmann FR, Benninger DH. Transcranial direct current stimulation for the treatment of chronic tinnitus: a randomized controlled study. Brain Stimul 2015;8:1101–7. doi:10.1016/j.brs.2015.06.014.


no tACS
tACS 12 Hz
Gradiometers (all)
Right AC
Gradiometers (all)
Right AC
PSD
10^{-20}
10^{-25}
10^{-9}
10^{-11}
10^{-13}
Resting
ASSR
0
20
40
Frequency [Hz]


A
norm. power [a.u.]
200
0
B
t-value
-2.2
-3.2
C
Normalized power [a.u.]
100
50
0
No tACS
12 Hz tACS
32
41
47
Frequency [Hz]


100
50
0
Normalized power [a.u.]
No tACS
6.5 Hz tACS
32
41
47
Frequency [Hz]

- The tACS-related changes in auditory activity were studied online with MEG
- Alpha-range tACS significantly decreased ASSR power
- Source-level activity was investigated using an LCMV beamformer