"Broadband Alpha Transcranial Alternating Current Stimulation": Exploring a new biologically calibrated brain stimulation protocol

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ABSTRACT

Transcranial alternating current stimulation (tACS) can be used to study causal contributions of oscillatory brain mechanisms to cognition and behavior. For instance, individual alpha frequency (IAF) tACS was reported to enhance alpha power and impact visuospatial attention performance. Unfortunately, such results have been inconsistent and difficult to replicate. In tACS, stimulation generally involves one frequency, sometimes individually calibrated to a peak value observed in an M/EEG power spectrum. Yet, the 'peak' actually observed in such power spectra often contains a broader range of frequencies, raising the question whether a biologically calibrated tACS protocol containing this fuller range of alpha-band frequencies might be more effective. Here, we introduce 'Broadband-alpha-tACS', a complex individually calibrated electrical stimulation protocol. We band-pass filtered left posterior resting-state EEG data around the IAF ($\pm$ 2 Hz), and converted that time series into an electrical waveform for tACS stimulation of that same left posterior parietal cortex location. In other words, we stimulated a brain region with a 'replay' of its own alpha-band frequency content, based on spontaneous activity. Within-subjects ($N = 24$), we compared to a sham tACS session the effects of broadband-alpha tACS, power-matched spectral inverse ('alpha-removed') control tACS, and individual alpha frequency (IAF) tACS, on EEG alpha power and performance in an endogenous attention task previously reported to be affected by alpha tACS. Broadband-alpha-tACS significantly modulated attention task performance (i.e., reduced the rightward visuospatial attention bias in trials without distractors, and reduced attention benefits). Alpha-removed tACS also reduced the rightward visuospatial attention bias. IAF-tACS did not significantly modulate attention task performance compared to sham tACS, but also did not statistically significantly differ from broadband-alpha-tACS. This new broadband-alpha-tACS approach seems promising, but should be further explored and validated in future studies.

1. Introduction

Non-invasive brain stimulation techniques such as transcranial alternating current stimulation (Antal and Paulus, 2013; Thut, Schyns, and Gross, 2011) have been used to enhance posterior alpha power (Helfrich et al., 2014; Kasten et al., 2016; Kasten and Herrmann, 2017; Neuling et al., 2013; Stecher et al., 2017; Vossen et al., 2015; Witkowski et al., 2016; Zaehle et al., 2010). Alpha tACS to left posterior parietal cortex (PPC), a brain area typically associated with visuospatial attention (Duecker et al., 2017), affected reaction times in an endogenous attention task (Kasten et al., 2020; Kemmerer et al., 2020; Schuhmann et al., 2019). Moreover, alpha activity seems to be causally involved in active distractor suppression, as evidenced by a reduced congruency effect in the Erikson flanker paradigm (Wiesman and Wilson, 2019) and improved performance in a visual conjunction search task (Müller et al., 2015) after alpha tACS. In line with this, inattentional blindness induced by alpha tACS has been explained by enhanced inhibition of irrelevant stimuli (Hutchinson et al., 2020). In sum, a number of studies successfully applied posterior alpha-frequency tACS to provide

causal evidence for the involvement of alpha oscillations in visuospatial attention.

Nevertheless, not all results have been positive and consistent (Veniero et al., 2015). For instance, 10 Hz tACS does not always affect attention task performance and does not always lead to significant aftereffects on EEG alpha power (Battaglini et al., 2020b; Coldea et al., 2021). Such null findings may in part be explained by variations in individual alpha frequency (IAF) (Haegens et al., 2014; Stecher and Herrmann, 2018), which points to the importance of individualizing stimulation protocols (Hamidi et al., 2009; Janssens et al., 2021; Kemmerer et al., 2020; Lin et al., 2021). But even when tACS is delivered at IAF instead of at a standard (e.g., 10 Hz) frequency, sometimes there are no detectable effects on alpha power (Fekete et al., 2018). Such inconsistencies have not only been found at the neuronal level, but also at the behavioral level. For example, while alpha tACS to right PPC led to a visuospatial attention bias in a line bisection task in a first experiment, this finding could then not be replicated by the same experimenters in a second attempt (Veniero et al., 2017). Another study showed decreased detection performance, but not discrimination performance, after alpha tACS – but this effect was neither retinotopically- nor frequency-specific (Brignani et al., 2013). Furthermore, while some reports provided evidence for the involvement of alpha oscillations in distractor processing (Schneider et al., 2021; Wöstmann et al., 2019), other studies did not find evidence for such a link (Noonan et al., 2016) or even directly contradicted the notion of a causal link (Antonov et al., 2020). Clearly, the role of alpha oscillations in distractor processing is not fully understood yet. Moreover, it is not entirely clear whether or under which constraints alpha tACS affects endogenous visuospatial attention. Even when effects are found, tACS effect sizes are generally small (Antal et al., 2008; Schutter and Wischnewski, 2016). It is therefore important to investigate whether previously found tACS effects can be enhanced by developing novel stimulation protocols. As tACS is increasingly being explored as a treatment strategy for a range of brain-based neurological and psychiatric disorders (Elyamany et al., 2020), any development in improving its efficacy is not only relevant for research, but also for clinical applications.

The standard tACS protocol, even when calibrated to an individual peak frequency, does not capture the complexity, or the idiosyncrasy, of the neuronal oscillatory response or intrinsic activity. For instance, IAF tACS stimulates at only one frequency, while the M/EEG power spectrum often shows enhanced power over a range of frequencies in the alpha-band (a 'broad peak'). Moreover, M/EEG power spectra show substantial variability between participants with sometimes multiple peaks (Chiang et al., 2011; Haegens et al., 2014). Parts of those more broadband signals might be attributable to the nature of the measurement, but others could reflect meaningful neuronal processes. There could be functionally relevant oscillators in posterior brain regions that operate at slightly slower or faster frequencies than the individual peak frequency (Benwell et al., 2019; Klimesch et al., 1997, 1999). While the precise mechanistic basis of tACS effects on behavior, as well as M/EEG measured oscillations, remains unknown, it might include processes of entrainment (Thut et al., 2011b) and spike-timing dependent plasticity (Vossen et al., 2015). Spike-timing dependent plasticity mechanisms could be engaged by tACS in circuits operating with time-constraints closely matching the tACS frequency (Zaehle et al., 2010). If different circuits (oscillators) in posterior brain regions respond optimally to slightly different frequencies, tACS targeting a band of frequencies, as opposed to just a single frequency, might impact a larger range of functionally relevant circuits, and thereby yield a stronger effect on behavior and/or oscillatory activity as measured with M/EEG.

Here, we therefore developed individually tailored 'broadband-alpha' tACS protocols directly based on resting-state EEG data from posterior parietal electrodes, essentially filtering out frequencies outside the alpha band and 'feeding back' the native alpha-filtered time course content through electrical stimulation during attention task performance. This approach also naturally allowed us to develop an 'alpha-removed'

control protocol, which was the spectral inverse of the broadband-alpha-tACS protocol. To create this protocol, we took the exact same individual EEG time series, but instead filtered out the alpha-band signals, keeping the content of all other frequencies between 1 and 49 Hz. This alpha-removed tACS protocol was matched to the broadband-alpha protocol in terms of overall power in the electrical waveform. We speculatively hypothesized that this alpha-removed protocol might effectively decrease, as opposed to increase, alpha-band activity in the brain. Thus, while the IAF and 'broadband-alpha' tACS protocols may result in alpha synchronization, the 'alpha-removed' tACS protocol could perhaps lead to alpha desynchronization (albeit in an indirect way, by promoting other frequencies). To our knowledge, this study is among the first to explicitly target enhancement of oscillatory power in a broader frequency band along these lines with cognitive effects. Encouragingly, a recent proof-of-principle study already showed that a replay of individual 'neurodynamics' based on EEG measurements of motor cortex activity could more successfully enhance motor excitability than conventional tACS protocols (Cottone et al., 2018).

The aims of the current experiment were threefold. First of all, to develop and test the methodology for broadband-alpha-tACS and power-matched spectral control ('alpha-removed') stimulation protocols. Secondly, to assess whether broadband-alpha-tACS can enhance posterior EEG alpha power and/or modulate visuospatial attention, not (or in opposite direction) shown for the alpha-removed protocol. Thirdly, to assess whether we could replicate previous IAF-tACS effects on alpha power and/or attention task performance, or whether broadband-alpha-tACS might have more reliable effects in light of the inconsistency of IAF-tACS reports.

We stimulated left PPC (10–20 electrode position P3) with a high-density ('ring electrode') tACS montage, using four different tACS protocols (IAF tACS, broadband-alpha-tACS, alpha-removed tACS, sham tACS) on separate days in 24 participants, in a counterbalanced fully within-subjects paradigm. The left hemisphere was chosen to replicate previous designs with positive results (Kemmerer et al., 2020; Schuhmann et al., 2019, though see Coldea et al., 2021), and because effects have typically been stronger for or even restricted to the left hemisphere (Bagherzadeh et al., 2020; Kasten et al., 2020; Okazaki et al., 2014). In all four experimental sessions, participants performed a modified endogenous visuospatial attention task (Posner, 1980; Posner et al., 1980). Half of the attention task trials were traditional Posner trials with a central valid, neutral or invalid cue, followed by target gratings requiring an orientation judgment. The other half of the trials included bilateral, whole-field distractors during target presentation. Given the unclear role of neuronal alpha oscillations in distractor processing (as outlined above), alpha-tACS effects might differ between trials with and without distractors (because of alpha power increases following rhythmic stimulation, as hypothesized in de Graaf and Duecker, 2021). To investigate the effects of tACS on neuronal alpha power, EEG data were recorded during eyes closed resting state and during task performance, immediately after each 5-min tACS/task block.

2. Materials and methods

2.1. Participants

Twenty-four healthy individuals participated in this experiment (11 males, age range 19 – 34). Participants were right-handed, had (corrected-to-normal) vision, and did not have any transcranial alternating current stimulation (tACS) contraindications (Antal et al., 2017). Participants were compensated with either research participation credits or vouchers. Ethical approval was obtained from the Ethical Review Committee Psychology and Neuroscience at Maastricht University, the Netherlands.
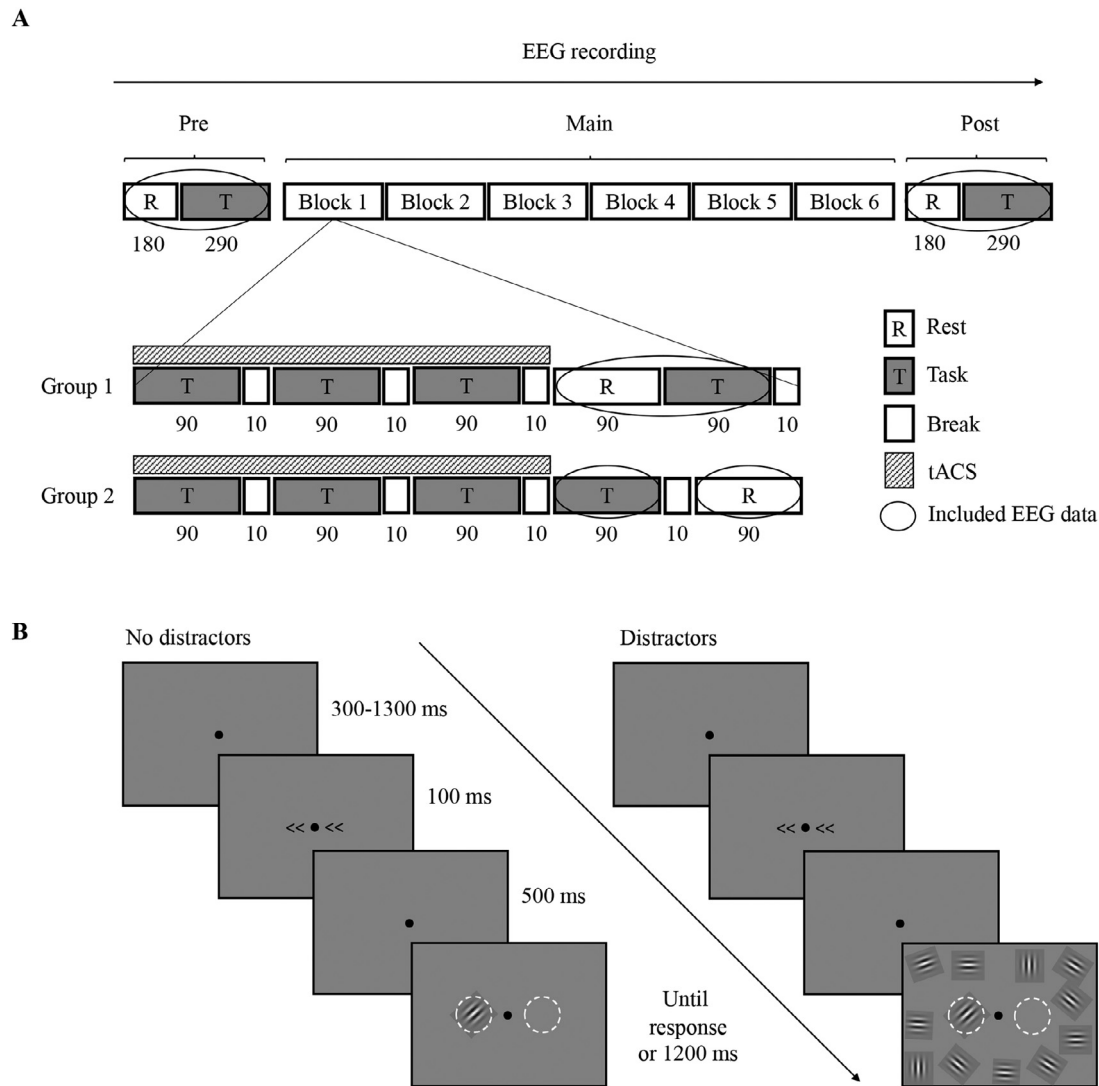
Fig. 1. Experimental design. A) Overview of procedures during a single experimental session. In the "pre-measurement", baseline EEG activity was measured during 3-min eyes closed resting state and ~5-min attention task performance. The "main-measurement" consisted of six identical blocks during which EEG was continuously recorded. Each block started with 5 min of attention task performance during which tACS was delivered (striped segments). Note that the same tACS protocol was delivered in all six blocks of an experimental session (and four tACS protocols were tested in four different sessions on different days). In the "post-measurement", EEG data were recorded during 90 s of eyes closed resting state and 90 s of attention task performance without tACS, the order being counterbalanced across two participant groups. Note that only tACS-artifact-free EEG data could be included (circled segments). B) Endogenous attention task example trials. After a randomly jittered fixation interval, a symbolic cue was presented for 100 ms. This cue either pointed towards the upcoming target (valid), towards the opposite hemifield (invalid), or towards both hemifields (neutral). A target grating was presented in the left or right hemifield after a cue-target interval of 500 ms. Participants reported as quickly and as accurately as possible the orientation of the target (clockwise or counterclockwise). In half of the trials, distractors with random orientation, phase and spatial frequency were presented bilaterally from target onset until target offset.

2.2. Procedures

The experiment consisted of four sessions of 2.5 – 3 h each, taking place on separate days. Sessions were identical except for the brain stimulation protocol being administered. Session order was counterbalanced across participants, and brain stimulation was delivered single-blinded (the experimenter was aware of the conditions). Participants were informed about the (order of the) stimulation conditions only after study completion. Sessions were separated by at least two days. When entering the lab, participants were first screened for tACS contraindications and provided written informed consent. TACS and electroencephalography (EEG) electrodes were then prepared (for details see section 2.4). The eyetracker was set-up using a 5-dot calibration pattern and 1000 Hz sampling frequency (EyeLink1000, SR Research, Ottawa, Ontario, Canada). Preparations took approximately 1 h altogether.

The experimental procedure consisted of three parts (see Fig. 1a). The "*pre-measurement*" served to measure baseline EEG activity and task performance. It consisted of a 3-min eyes closed resting state EEG measurement, followed by a ~5-min EEG measurement during which participants performed an endogenous attention task (see section 2.3 for task specifics). The "*main-measurement*" consisted of six identical blocks in which tACS was delivered and EEG was measured continuously. Note that all six blocks of one experimental session/day administered the same tACS protocol (and four different sessions/days were used to test the four different tACS protocols). Each of the main blocks consisted of three components: 1) a 5-min attention task with concurrent tACS, 2) 90 s of attention task without tACS and thus a tACS-artifact-free EEG signal, and 3) a 90-s eyes closed resting state EEG measurement without tACS. The order of the last two components was counterbalanced across two participant groups to prevent order effects. Four breaks of 10 s were

included during the attention task. Every main block took 520 s and the entire main measurement lasted 52 min. The "*post-measurement*" was identical to the pre-measurement and was included to assess potential after-effects of tACS on EEG signal and/or task performance. At the end of the experiment, participants were debriefed about experiment aims and tACS conditions.

2.3. Stimuli and task

Participants performed an endogenous Posner task in all four sessions (see Fig. 1b) (Posner, 1980; Posner et al., 1980). Stimuli were presented using MATLAB (The MathWorks, Inc., Natick, Massachusetts, United States) and Psychophysics Toolbox (Brainard, 1997) on a gamma-corrected 24 inch monitor with a 60 Hz refresh rate and a resolution of 1920 × 1080 pixels. Participants continuously fixated on a black dot of 0.2 degrees visual angle (DVA) presented in the center of a gray screen with a background luminance of 125 cd/m². Their heads were stabilized using a chin rest that was positioned 60 cm away from the computer screen. Eyetracking was performed to assess fixation stability. After a randomly jittered fixation period (300 – 1300 ms), an endogenous cue was presented for 100 ms. The cue was either valid (arrows pointing in the direction of the upcoming target), neutral (one arrow pointing to the left and the other to the right), or invalid (pointing away from the upcoming target) at a ratio of 3:1:1. After a cue-to-target interval of 600 ms, a target stimulus with a diameter of 3.5 DVA was presented at 7 DVA eccentricity on either the left or the right side of the screen. Target stimuli were sinusoidal gratings of 0.8 Michelson contrast (MC), rotated either 45° clockwise or counter-clockwise, with random spatial frequency and phase. Participants performed a two-alternative forced choice (2AFC) task for each target grating. More specifically, they indicated as quickly and as accurately as possible the orientation of the target, pressing with their right hand either the left arrow button or the right arrow button for counter-clockwise and clockwise oriented gratings, respectively. The target grating disappeared once the participant responded or when 1200 ms had passed without a response. In half of the trials, only the target grating was presented. In the other half of the trials, distractors were displayed bilaterally at target onset until target offset. Distractors were displayed around the target locations and had a random orientation, phase and spatial frequency. Distractor contrast was 0.8 MC and a drift speed of 4 Hz was used to make the distractors appear to move in space, thereby make them more salient. Average trial duration was 2100 ms (with pseudo-randomized jitter 1900 – 2300 ms), which was fixed such that the end of tACS always coincided with the end of the task. The pre- and post-measurement each contained 120 attention task trials, while the main measurement contained 960 trials divided equally over the six blocks.

2.4. Electroencephalography (EEG)

EEG data were recorded with 5000 Hz sampling frequency and a hardware band-pass filter of 0.1–1000 Hz using BrainVision Recorder (BrainVision LLC, Morrisville, North Carolina, United States) and a BrainAmp DC amplifier (BrainProducts, GmbH, Gilching, Germany). Electrodes were placed over PO3, PO4, Fz (ground), A1 and A2 (references, computed offline) (see Fig. 2). EEG electrodes were filled with conductive gel (OneStep Cleargel) and impedances were kept below 5 kΩ (ground and reference electrodes) or 10 kΩ (electrodes of interest).

2.5. Transcranial alternating current stimulation (tACS)

We used a tACS ring electrode montage (Datta et al., 2008) (inner/outer diameter 2.1/11 cm) to stimulate the left posterior parietal cortex (PPC) (Kemmerer et al., 2020; Schuhmann et al., 2019) (NeuroConn, Ilmenau, Germany). The inner ring was placed over position P3 of the international 10–20 system and the outer ring was centered on
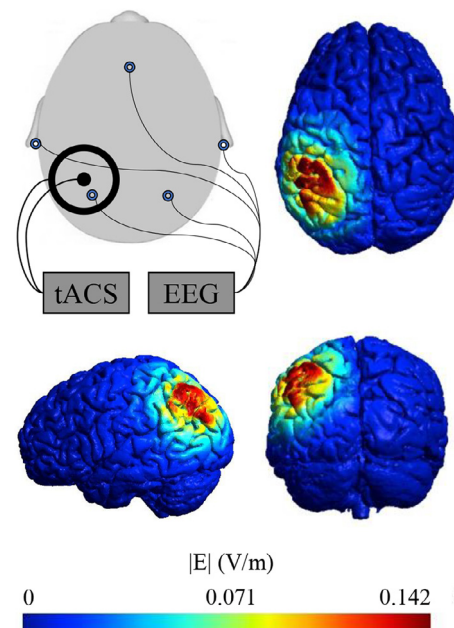

Fig. 2. EEG and tACS electrode montages and tACS current simulation results. A tACS ring electrode was centered position P3 of the international 10–20 system. EEG electrodes were positioned on PO3, PO4, Fz (ground) and both mastoids (references). tACS current simulations as created in SimNIBS show the norm of the electric field in V/m on an example brain, from three different viewpoints.

the inner ring. TACS current flow was simulated in the software program SimNIBS (see Fig. 2) (Heise et al., 2019; Saturnino et al., 2019, 2018). Conductive gel (Ten20, Weaver and Company, Aurora, CO, USA) was applied below both ring electrodes and the impedance was kept below 10 kΩ. Stimulation was controlled externally by using DataStreamer software, a digital-to-analog converter (National Instruments Corp., Austin, Texas, United States), and a Remote DC-Stimulator Plus (NeuroConn GmbH, Ilmenau, Germany) (for an in-depth description of the experimental set-up, see ten Oever et al., 2016).

Four tACS protocols were created in MATLAB using FieldTrip Toolbox (Oostenveld et al., 2011). For each participant, tACS protocols were individualized based on the 3-min eyes closed resting state EEG data recorded at the beginning of their first session, from electrode PO3 (left hemisphere) (see Figs. 2 and 3). The "*individual alpha frequency*" (IAF) protocol was created by cutting 5 s epochs, performing a fast Fourier transform with Hanning tapers, and creating a continuous sinusoid at the frequency with the highest power between 7 and 13 Hz (using a frequency resolution of 0.1 Hz). The "*broadband-alpha*" protocol contained a wider range of alpha frequencies, since it was created by band-pass filtering the EEG data using second-order Butterworth filters, first at 1 – 49 Hz and then at IAF ± 2 Hz. The "*alpha-removed*" protocol included frequencies outside of the alpha range and was created by first band-pass filtering the data using a second-order Butterworth filter at 1 – 49 Hz and then band-stop filtering the data at IAF ± 2 Hz.

The alpha-removed protocol was the spectral inverse of the broadband-alpha protocol. As a consequence, the alpha-removed tACS protocol contained more frequencies than the broadband-alpha tACS protocol. If left unchanged, any differences in the effects of broadband-alpha tACS and alpha-removed tACS might be explained by differences in the overall power present in these two tACS protocols. To eliminate this confound, we matched power between the broadband-alpha and alpha-removed protocols as follows. First, we ensured that both protocols had a maximum absolute value of 1 in the time domain (corresponding to 1 mA) by convoluting the power spectra by 1/maximum value across both conditions. As convoluting in the frequency domain is the same as multiplication in the time domain, this ensured that the
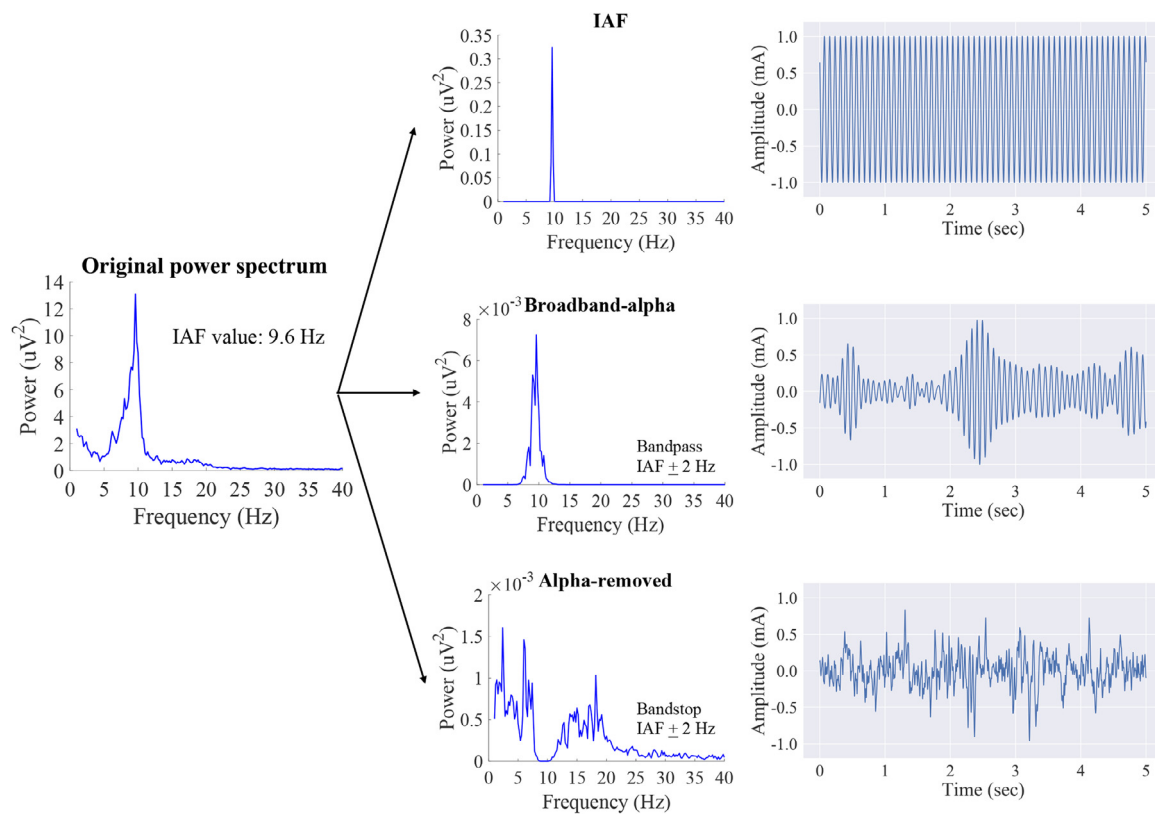
Fig. 3. Creation of individualized tACS protocols. Data are shown for one representative participant. The leftmost panel shows the original power spectrum resulting from the 3-min eyes closed resting state measurement at the beginning of the first session. Different brain stimulation protocols (middle panels) were created by filtering the original power spectrum (left panel) and calculating the inverse Fourier transform to go back to a time-domain signal (rightmost panels). The individual alpha frequency (IAF) protocol was created by selecting the frequency between 7 and 13 Hz with maximum power. The broadband-alpha protocol was created by bandpass filtering the power spectrum at IAF $\pm$ 2 Hz. The alpha-removed protocol was created by band-stop filtering the power spectrum at IAF $\pm$ 2 Hz. An additional processing step (see section 2.5) ensured that the broadband-alpha and alpha-removed protocols were matched in power. Rightmost panels show 5-s example segments of the resulting tACS protocols.

maximum value in the time domain value was 1. Then, we equalized the sum of the powers across both protocols as follows: we took the protocol (power spectrum) with the minimum (i.e., smallest) summed (i.e., total) power, and scaled the *other* protocol to this one by dividing each power value by the relative summed power across both protocols. Then we put back the original phase estimates and inverted the FFT to get the normalized time courses. As recorded (pre-measurement resting state) EEG data were only 3 min long (see Fig. 1a), we appended the data so that each protocol would cover the full intended stimulation duration (5 min). Though the power matching between the broadband-alpha and alpha-removed protocols was performed on the 3-min data, this should only lead to negligible differences in the 5-min protocols. In Supplementary Table 1, we report the minimum amplitude, maximum amplitude, and the standard deviation of the amplitude for the created broadband-alpha and alpha-removed tACS protocols for each participant, to provide some insight in the parameters of tACS protocols in the time domain after these various processing steps.

The "*sham*" protocol included a 15 s ramp up and a 15 s ramp down at IAF. All stimulation protocols included a 15 s ramp up at the start of each stimulation block, but only the sham protocol included a ramp down. All protocols had a (maximum) intensity of 2 mA peak-to-peak (as in Kasten et al., 2020). Note that for the broadband-alpha and alpha-removed protocols, the stimulation did not constantly reach this intensity due to the nature of signals with multiple frequencies (see Fig. 3). There were six stimulation blocks of 5 min each (see Fig. 1a), leading to a total stimulation duration of 30 min.

Though we did not formally record tACS side-effects, participants generally perceived all tACS protocols as tolerable. Most of our partici-

pants were tACS novices, and therefore did not know in advance what "real" tACS feels like. Based on informal conversations, it seems that our participants did not know in which session they received sham (ineffective) tACS, and that IAF-tACS was typically perceived to be the most uncomfortable/noticeable stimulation protocol.

2.6. Analyses

Data were analyzed using MATLAB version 2019a, FieldTrip Toolbox (Oostenveld et al., 2011), Python 3 and JASP version 0.12.2.

2.6.1. Behavioral analyses

The dependent variable for the two-alternative forced-choice (2AFC) task was reaction time (RT) in ms. Trials in which participants responded incorrectly or too quickly (< 200 ms) were excluded. Trials with blinks and/or saccades (defined as eye movements > 2 degrees visual angle (DVA)) during the cue-to-target interval were removed. On average 109 out of 1200 trials were excluded per session (63 due to blinks/saccades, 45 due to incorrect responses, and 1 due to a fast response). Median RTs were calculated for all participants for each condition cell and values more than 3 standard deviations away from the mean across participants were removed. One participant was excluded due to technical problems in the lab (i.e., tACS equipment failure). Two planned analyses were performed on the RT data from the main measurement. The first analysis involved two separate three-way repeated-measures ANOVAs, one for trials with distractors and one for trials without distractors, including the factors "brain stimulation" (IAF, broadband-alpha, alpha-removed, sham), "hemifield" (left versus right), and "cue validity" (valid, neutral,

and invalid). In the second analysis, we first calculated RT benefits (by subtracting scores in valid cue trials from those in neutral cue trials) and costs (by subtracting scores in neutral cue trials from those in invalid cue trials) (Duecker and Sack, 2015; Mangun and Buck, 1998). We then performed a three-way repeated-measures ANOVA on these attention benefits and costs, including the factors "brain stimulation", "hemifield", and "distractors" (present versus absent). As a post-hoc exploratory analysis, we then also performed the same three-way repeated-measures ANOVA for the dependent variable 'cueing effect' (which was calculated by subtracting RTs in invalid cue trials from RTs in valid cue trials). Significant interaction effects were followed by simple effects analyses. To assess the consistency of tACS effects, single subject effects were visualized using 'raincloud plots' (Allen et al., 2019).

2.6.2. EEG analyses

EEG files were cut into 5 s epochs. Signal variance was calculated for each epoch and the six tACS offsets were pinpointed by detecting sudden drops in EEG variance between epochs. The insufficient dynamic range of our EEG system and the limited number of electrodes prevented the analysis of EEG data during tACS (Kasten and Herrmann, 2019). We therefore selected artifact-free EEG data (see Fig. 1a), after which epochs were sorted into task and rest epochs. Epochs with a high signal variance were excluded based on the inter-quartile range (> Q3 + 1.5 x IQR criterion) (as in de Graaf et al., 2017). Power at frequencies 1 – 49 Hz was determined by calculating FFTs using Hanning tapers, separately for each cognitive state (task versus rest) and hemisphere (left versus right). Epochs were zero-padded to 10 s to reach a frequency resolution of 0.1 Hz and power values were log-transformed (Smulders et al., 2018). Alpha power was calculated by taking the sum of the power values from the frequencies within the range IAF ± 2 Hz. Next, we removed the 1/f trend from the power spectrum and fitted a Gaussian curve to the power spectrum. Alpha peak width was determined as the standard deviation of the fitted Gaussian (Dickinson et al., 2018; Haegens et al., 2014; van Albada and Robinson, 2013). Alpha peak width was calculated to allow assessment of tACS effects on the shape/width of the alpha-range power spectrum in EEG, given the different 'alpha-widths' in the current experiment between the broadband-alpha-tACS, IAF tACS, and alpha-removed tACS protocols. We previously reported that alpha peak width can be reliably estimated using this method (Janssens et al., 2021). For each of the four sessions, alpha power and alpha peak width values in the main-measurement and post-measurement were normalized to the pre-measurement. This was done by calculating the average alpha power/width in the pre-measurement, across cognitive states and hemispheres, and subtracting that value from the main- and post-measurement values. Our predefined analysis plan was to first investigate whether any brain stimulation effects were present in the main measurement (immediate tACS aftereffects). If this were to be the case, we would then proceed to analyze the post-measurement to investigate whether the brain stimulation effects persisted after the tACS had stopped entirely (longer tACS aftereffects). Two participants were excluded from the analyses due to technical problems in the lab (one due to a corrupted EEG file, the other due to tACS equipment failure). Two more participants were excluded due to the presence of multiple outlier values (defined as values > 3 SD away from the mean across participants). We then performed two repeated-measures ANOVAs with the factors "brain stimulation" (IAF, broadband-alpha, alpha-removed, and sham), "cognitive state" (task versus rest) and "hemisphere" (left/electrode PO3 versus right/electrode PO4), one for each dependent variable (alpha power and alpha peak width). Including the factor "hemisphere" allowed us to assess whether tACS affected alpha power and/or alpha peak width specifically in the left (stimulated) hemisphere, or perhaps also influenced the contralateral hemisphere.

We originally hypothesized that the alpha-removed tACS protocol would either have no effects on alpha power, or, if anything, might decrease alpha power ('de-entrainment') through a process of alpha desyn-

chronization – for instance by the enhancement of neighboring frequencies. From this perspective, in an explicitly exploratory analysis, we also assessed whether alpha-removed tACS increased theta (3 – 6 Hz), beta (15 – 25 Hz), or gamma (30 – 40 Hz) power compared to sham tACS. Note that these frequency bands were non-overlapping with the individually created alpha bands (IAF ± 2 Hz), since the minimum IAF was 8.2 Hz and the maximum IAF was 12.2 Hz in our participant sample. We performed three repeated-measures ANOVAs with the factors "brain stimulation" (alpha-removed versus sham), "cognitive state" (task versus rest), and "hemisphere" (left/electrode PO3 versus right/electrode PO4), one for each dependent variable (theta, beta, and gamma power).

It is possible that tACS effects were limited to particular experimental blocks in our cumulative tACS session, since early versus late tACS effects may be driven by different mechanisms (e.g., entrainment versus neuroplasticity) (Antal and Herrmann, 2016; Herrmann et al., 2013). We performed post-hoc analyses to explore this idea. More specifically, we repeated the abovementioned EEG analyses while including the factor "experimental block" (with three levels: blocks 1 & 2, blocks 3 & 4, and blocks 5 & 6). We furthermore performed the same EEG analyses specifically for block 1 and for block 6.

3. Results

In a counterbalanced, fully within-subject design, we stimulated left posterior parietal cortex (PPC) in 24 participants using individually calibrated broadband-alpha-tACS, power-matched alpha-removed-tACS, IAF-tACS, and sham-tACS. All tACS conditions were well-tolerated by participants, including the new biologically inspired protocols. Below, we first evaluate the effects of tACS on attention task performance with and without distractors. We then assess whether tACS led to aftereffects in EEG alpha activity.
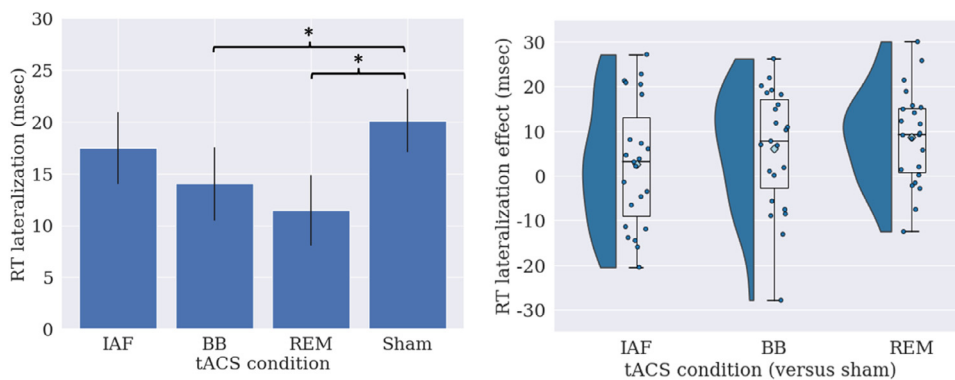
3.1. Behavioral results

3.1.1. Analysis 1

The first planned analysis included two repeated-measures ANOVAs with the factors "brain stimulation" (IAF, broadband-alpha, alpha-removed, sham), "hemifield" (left, right) and "cue validity" (valid, neutral, invalid) on median RTs in ms – one for trials with distractors, the other for trials without distractors.

In trials *with* distractors, there was a significant main effect of "hemifield" ($F(1,22) = 24.05$, $p < 0.001$). RTs were slower in the left hemifield as compared to the right hemifield (respectively $M = 522.49$ and $M = 496.29$ $SE = 10.60$). As expected, there was a significant main effect of "cue validity" ($F(2,44) = 32.47$, $p < 0.001$) (Chica et al., 2014; Duecker and Sack, 2015; Mangun and Buck, 1998). There were significant attention benefits, as evidenced by significantly lower RTs for valid cue trials as compared to neutral cue trials ($t(23) = 1.78$, $p = 0.04$ one-tailed, uncorrected, mean difference = -3.16, $SE = 1.77$). Attention costs also turned out significant, since RTs were slower in invalid cue trials as compared to neutral cue trials ($t(23) = 5.91$, $p < 0.001$, mean difference = 10.48, $SE = 1.77$). The fact that we replicated these well-documented effects validates our modified Posner task with distractors, indicating that it can be used to study endogenous visuospatial attention. Interestingly, tACS did not seem to modulate attention task performance in trials with distractors, since the factor "brain stimulation" did not show any significant effects (p's > 0.10).

In trials *without* distractors, the main effects of "hemifield" and "cue validity" were significant as well (respectively $F(1,22) = 29.18$, $p < 0.001$ and $F(2,44) = 37.39$, $p < 0.001$). Again, RTs were slower in the left as compared to the right hemifield (mean difference = 15.77, $SE = 2.92$). Both attention benefits and costs turned out significant (mean difference = 6.99 versus -6.84, respectively, $SE = 1.60$, p's < 0.001). There was a significant "brain stimulation" x "hemifield" interaction ($F(3,66) = 3.83$, $p = 0.014$). Raw RT data in trials without

Fig. 4. The effects of brain stimulation on attention bias. Left panel: average reaction time (RT) lateralization scores are shown for all tACS conditions (IAF = individual alpha frequency, BB = broadband-alpha, REM = alpha-removed). Error bars indicate standard error of the mean (SEM). Asterisks indicate statistically significant differences ($p < 0.05$). Right panel: single subject RT lateralization effects for each of the three planned comparisons (x-axis). RT lateralization effect (y-axis) was calculated by subtracting RT lateralization scores for 'active' (IAF, BB, or REM) tACS from sham tACS (i.e., RT lateralization sham-tACS minus RT lateralization active-tACS). A larger effect thus indicates a *larger reduction* in RT lateralization after 'active' tACS compared to sham-tACS. Dots indicate single subject effects, diamonds indicate mean effects, and data distributions are visualized using boxplots and probability distributions. Note that 17 out of 23 (~74%) subjects showed an effect in the expected direction (i.e., a reduction in the rightward attention bias, compared to sham tACS, as shown by dots > 0) in the broadband-alpha condition, but only 13 out of 23 (~57%) in the IAF condition.

distractors are shown in Supplementary Figure 1. The significant interaction was difficult to interpret, since follow-up simple effects analyses yielded no significant effect of "brain stimulation" for either hemifield in isolation (p's > 0.10), and the effect of "hemifield" was significant for all brain stimulation sessions (IAF: $F_{(1,22)} = 25.04$, $p < 0.001$; broadband-alpha: $F_{(1,22)} = 15.64$, $p < 0.001$; alpha-removed: $F_{(1,22)} = 11.54$, $p < 0.003$; sham: $F_{(1,22)} = 44.12$, $p < 0.001$).

Therefore, to further explore the pattern of results underlying the brain stimulation x hemifield interaction, and to replicate the analyses from two previous studies with positive results (Kemmerer et al., 2020; Schuhmann et al., 2019), we calculated RT lateralization scores (RTs to left hemifield targets minus RTs to right hemifield targets). Positive values indicate a rightward bias and negative values indicate a leftward bias. We conducted three planned follow-up paired t-tests, to compare the three 'active' tACS conditions with the sham condition (see Fig. 4). In contrast to previous reports (Kemmerer et al., 2020; Schuhmann et al., 2019), we did not find a significant difference in RT lateralization scores between IAF and sham stimulation ($t(23) = 0.97$, $p = 1.00$, Bonferroni-corrected). We did find a significant difference between broadband-alpha and sham stimulation in the expected direction ($t(23) = 2.23$, $p = 0.04$ one-tailed, Bonferroni-corrected), with a smaller rightward bias for the broadband-alpha condition ($M = 14.02$ versus $M = 20.12$, $SE = 2.74$). The direction of this effect is in line with the positive results from previous studies using 10 Hz tACS (Schuhmann et al., 2019) and tACS at IAF (Kemmerer et al., 2020). Though a direct comparison between the effects of broadband-alpha and IAF tACS was not statistically significant ($F_{(1,22)} = 1.31$, $p = 0.26$), in this experiment, broadband-alpha-tACS was able to reveal a hypothesized result that single-frequency (IAF) tACS could not successfully replicate. On the other hand, we also found a significant difference between alpha-removed and sham stimulation ($t(23) = 3.15$, $p = 0.01$ two-sided, Bonferroni-corrected), in the same direction as for broadband-alpha-tACS, which was contrary to our expectations ($M = 11.49$ versus $M = 20.12$, $SE = 2.74$). Note that the seemingly deviating observation in Fig. 4 (broadband-alpha versus sham tACS, lowermost dot) was not an outlier statistically, and conclusions did not change after excluding that observation/participant.

3.1.2. Analysis 2

In the second planned analysis, we performed two repeated-measures ANOVAs to investigate whether attention benefits (decrease in RT after valid cues, from neutral cues) and costs (increase in RT after invalid cues, from neutral cues) were influenced by our experimental factors "brain stimulation" (IAF, broadband-alpha, alpha-removed, sham), "hemifield" (left, right), and "distractors" (present, absent). For the analysis on attention costs, the only significant effect was a main effect of "distractors" ($F_{(1,22)} = 7.08$, $p = 0.014$), where attention costs

were higher in trials with distractors compared to trials without distractors ($M = 10.48$ versus $M = 6.84$, respectively, $SE = 1.37$).

There was also a significant main effect of "distractors" on attention benefits ($F_{(1,22)} = 5.39$, $p = 0.03$), with lower benefits in trials with distractors compared to trials without distractors ($M = 3.16$ versus $M = 6.99$, respectively, $SE = 1.65$). Importantly, there was also a strongly significant main effect of "brain stimulation" on attention benefits ($F_{(3,66)} = 4.77$, $p = 0.005$). Three planned follow-up tests, comparing the three 'active' brain stimulation conditions with the sham condition, showed that only the broadband-alpha condition differed significantly from the sham condition ($t(23) = 3.76$, $p = 0.003$ two-tailed, Bonferroni-corrected) (see Fig. 5). Attention benefits were smaller (in fact, nearly absent) in the broadband-alpha condition ($M = 0.82$ versus $M = 7.24$ in the sham condition, $SE = 1.71$), very consistently across participants (see Fig. 5, right panel). As in Analysis 1, broadband-alpha-tACS could reveal a significant effect (compared to sham tACS), while IAF-tACS could not, though the direct comparison between the effect of broadband-alpha (versus sham) tACS compared to IAF (versus sham) tACS was not significant ($F_{(1, 22)} = 1.88$, $p = 0.18$). Even though tACS was left-lateralized, we did not find a significant "brain stimulation" x "hemifield" interaction ($F_{(3, 66)} = 0.81$, $p = 0.49$). Raw RT data are shown in Supplementary Figure 1.

In a post-hoc exploratory analysis, we did not find any statistically significant main or interaction effects of "brain stimulation", "hemifield", or "distractors" on the attentional cueing effect (RT valid – RT invalid cue trials; all p's > 0.10).

3.2. Electroencephalography (EEG) results

We performed a repeated-measures ANOVA with the factors 'brain stimulation' (IAF, broadband-alpha, alpha-removed, sham), 'cognitive state' (rest, task) and 'hemisphere' (left/electrode PO3, right/electrode PO4) on the dependent variable 'alpha power'. There was a significant main effect of 'cognitive state' ($F_{(1,19)} = 45.09$, $p < 0.001$). In line with previous results, alpha power was higher during eyes closed resting state as compared to during task performance (mean difference = 31.05, $SE = 4.63$) (Barry et al., 2007; Barry and De Blasio, 2017; Başar et al., 1999; Osaka, 1984; Yamagishi et al., 2008). Moreover, there was a significant main effect of 'hemisphere' ($F_{(1,19)} = 12.75$, $p = 0.002$), with alpha power being higher in the left hemisphere as compared to the right hemisphere (mean difference = 8.97, $SE = 2.51$). This finding is the opposite of two previous reports (Çiçek et al., 2003; Gallotto et al., 2020), but note that Gallotto et al., 2020 looked at alpha power at a specific, short time window during an attention task. There were no significant main or interaction effects including the factor 'brain stimulation' (p's > 0.10). When specifically comparing the IAF and sham conditions, these conclusions did not change.
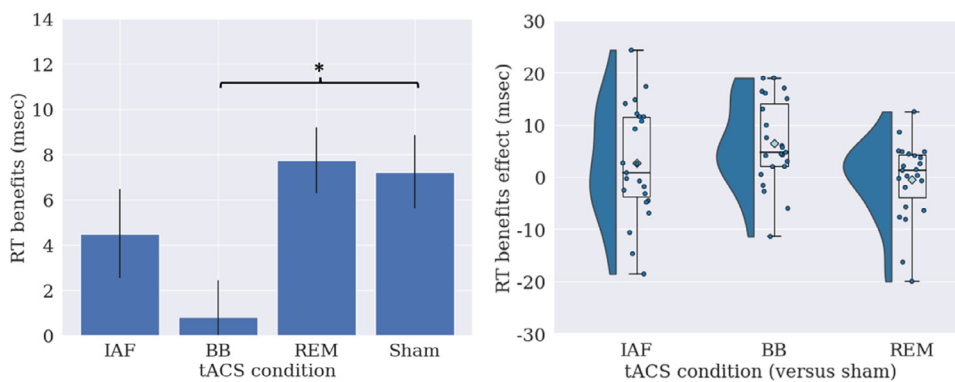
Fig. 5. The effects of brain stimulation on attention benefits. Left panel: average reaction time (RT) benefits are shown for all tACS conditions (IAF = individual alpha frequency, BB = broadband-alpha, REM = alpha-removed). Error bars indicate standard error of the mean (SEM). Asterisks indicate statistically significant differences ($p < 0.05$). Right panel: single subject effect for each of the three planned comparisons (x-axis). RT benefits effect (y-axis) was calculated by subtracting RT benefits for 'active' (IAF, BB, or REM) tACS from sham tACS (i.e., RT benefits sham-tACS minus RT benefits active-tACS). A larger effect thus indicates a *larger reduction* in RT benefits after 'active' tACS compared to sham-tACS. Dots indicate single subject effects, diamonds indicate mean effects, and data distributions are visualized using boxplots and probability distributions. In the broadband-alpha condition, 19 out of 23 (~83%) participants showed an effect in the expected direction (i.e., a reduction in attention benefits compared to sham tACS, as shown by dots > 0), but only 11 out of 23 (~48%) in the IAF condition.

We then performed a repeated-measures ANOVA with the same factors on the dependent variable 'alpha peak width'. There was a significant main effect of 'hemisphere' ($F(1,18) = 9.31$, $p = 0.007$), with alpha peak width being larger in the left hemisphere as compared to the right hemisphere (mean difference 0.23, $SE = 0.076$). There were no significant main or interaction effects including the factor 'brain stimulation' (all p's > 0.10).

Since the alpha-removed protocol essentially stimulated frequencies outside the alpha range, we performed exploratory repeated-measures ANOVAs on power in the theta, beta, and gamma bands (see section 2.6.2 'EEG analyses') focusing on factors 'brain stimulation' (alpha-removed versus sham), 'cognitive state' (rest, task), and 'hemisphere' (left/electrode PO3 versus right/electrode PO4). But there were no statistically significant effects for any of these ANOVAs/frequency bands (all p's > 0.10), also not when including the two statistical 'outlier participants'. Note that post-hoc analyses including the factor 'experimental block' (see section 2.6.2 'EEG analyses') did not reveal any new results (all p's > 0.10).

4. Discussion

We here introduced a new 'broadband-alpha' tACS protocol, as well as its spectral inverse ('alpha removed') protocol, stimulating participants with electrical waveforms directly based on their own (filtered and scaled) EEG activity recorded from the same left posterior target site. We asked whether broadband alpha-frequency tACS, including frequencies ± 2 Hz around individual alpha frequency (IAF), could amplify alpha power and/or modulate attention, perhaps more consistently or strongly than single-frequency IAF-tACS. After all, while IAF-tACS is tailored to individual M/EEG power spectra, it only marginally represents the complexity and distribution of alpha-band activity actually observed in neuronal oscillations. More complex, biologically informed tACS protocols targeting multiple frequencies could be superior, for instance if they impact a larger range of functionally relevant circuits with slightly different preferred frequencies.

A recent proof-of-principle study provided encouraging evidence that biologically inspired (EEG-based) electrical stimulation affords new, powerful neuromodulation approaches. Those authors extracted hand motor activity from primary motor cortex EEG based on functional source separation informed by coherence with EMG activity measured in the relevant contralateral hand muscles (Cottone et al., 2018). 'Individual neurodynamics stimulation', meaning electrical stimulation with a waveform based on such EEG/EMG-based endogenous hand motor activity, affected cortical excitability while conventional 20 Hz tACS did not. The current study took a similar approach, 'replaying' individual cortical activity measured with EEG, but with the different goal of enhancing oscillatory power across a functionally relevant (alpha) fre-

quency band, as opposed to general cortical excitability, to affect corresponding cognitive function. Our aims were to 1) develop this approach, 2) assess the effects of broadband-alpha-tACS and a spectral inverse ('alpha-removed') control tACS protocol on attention task performance and/or post-stimulation alpha power, 3) assess whether the effects of broadband-alpha-tACS are more consistent compared to conventional (single-frequency) tACS.

We first investigated whether broadband-alpha-tACS had any effects on EEG alpha activity and/or attention task performance. Broadband-alpha-tACS did not cause any significant aftereffects on EEG alpha power (in fact, none of the tACS protocols did, see below). Broadband-alpha-tACS reduced the rightward attention bias in attention task trials without distractors. This effect was statistically significant and observable in the majority of participants. The direction of this effect is consistent with previous studies, since it has been shown that the rightward spatial attention bias that is typically present in healthy volunteers (i.e., "pseudoneglect") (Jewell and McCourt, 2000) can be reduced by alpha tACS to left PPC (Kemmerer et al., 2020; Schuhmann et al., 2019). However, we found an unexpected similar result for alpha-removed tACS. The purpose of this protocol was more explorative, serving as an interesting control condition but without clear expectations based on prior research. If anything, we a priori speculated that by enhancing frequencies outside of the alpha band, we might get a (relative) reduction of alpha power (alpha desynchronization, by 'de-entrainment') and consequently opposite behavioral effects compared to the broadband-alpha and IAF tACS protocols. One possibility to consider is whether our unexpected behavioral finding in the alpha-removed tACS condition was directly caused by increased beta power (Battaglini et al., 2020a; Samaha et al., 2017), theta power, or gamma power. Exploratory analyses did not reveal enhanced beta, theta, or gamma power in the post-tACS EEG. Unfortunately, we cannot determine what exactly alpha-removed stimulation did to oscillatory power online, since we could not reliably analyze the EEG data recorded during tACS. These results thus do not offer an explanation regarding the underlying neuronal effects of tACS. It is difficult to explain why we found equivalent behavioral results for the broadband-alpha and alpha-removed tACS protocols in this analysis.

An effect that was specific to the broadband-alpha-tACS condition was a reduction in attention benefits (neutral – valid trial RTs) after broadband-alpha compared to sham tACS. There were no statistically significant effects of tACS on attention costs (invalid – neutral trial RTs) or on the 'cueing effect' (valid – invalid trial RTs). Attention allocation involves alpha desynchronization (Gould et al., 2011), and broadband-alpha-tACS was hypothesized to synchronize alpha oscillators across the individual alpha band (IAF ± 2 Hz). That synchronization might counteract the desynchronization that is required for attention benefits (e.g., de Graaf and Duecker, 2021; de Graaf et al., 2013). Since we stimu-

lated the left hemisphere, we might have expected any effects of brain stimulation to differ between hemifields based on hemispheric lateralization (Duecker et al., 2013). However, in our data, the effect of broadband-alpha stimulation on attention benefits did not significantly interact with the factor 'hemifield'. We thus found a generic, hemifield-independent improvement in cued attentional orienting. Is tACS perhaps not focal enough, does it relate to interhemispheric interactions, are there more complicated mechanisms at play, or does broadband-alpha-tACS not work the way we hypothesized? At this time, we cannot disentangle this further. The effects of broadband-alpha-tACS might not be explicable by indirect tACS effects such as somatosensory stimulation (Asamoah et al., 2019; Matsumoto and Ugawa, 2017; Raco et al., 2014; Vieira et al., 2020), since the effects did not occur in the IAF tACS condition which was typically perceived as involving stronger somatosensory stimulation. However, it is important to mention that this is based on informal observations and should therefore be further investigated. We cannot currently rule out the possibility that somatosensory side effects influenced our results, since we did not systematically record tACS side effects. Taken together, these consistent effects of broadband-alpha-tACS are promising, and exciting to pursue in future studies. At the same time, for the reasons outlined above, not all results are immediately clear or easily interpreted, and the full pattern of findings across our complex experimental design does warrant caution.

After establishing that broadband-alpha-tACS modulated attention task performance, we could assess whether it might do so more consistently than IAF tACS. As also recently reported by Coldea et al. (2021), we could not replicate previous reports of IAF tACS effects on attention task performance in similar paradigms (Kasten et al., 2020; Kemmerer et al., 2020; Schuhmann et al., 2019), although our paradigm differed in potentially crucial design aspects (e.g., the shorter 'blocks' of tACS). This underlines that IAF tACS effects can be unreliable, or sensitive to precise conditions/parameters, and actually highlights the importance of developing more robust stimulation protocols. Perhaps, lower amplitude (e.g., 1 or 1.5 mA peak-to-peak) IAF-tACS might have led to detectable changes in attention task performance because of a tACS strength-focality tradeoff (Tan et al., 2020), as in previous studies that used the same tACS electrode montage (Kemmerer et al., 2020; Schuhmann et al., 2019). It should also be mentioned that it is not possible to model the exact electric field induced by a tACS ring electrode montage, because the impedance can only be measured for the ring electrode as a whole (rather than for different subsections of the large ring). Future studies could opt for a tACS montage with a small center electrode surrounded with four (or more) small electrodes. After broadband-alpha-tACS, the majority of participants showed behavioral effects in the expected direction. Though the direct comparison between broadband-alpha-tACS and IAF tACS was not statistically significant, these first findings are promising. Future studies are needed to establish whether these broadband-alpha tACS effects are reliable, and whether broadband-alpha is superior to IAF-tACS, for instance by also comparing it to lower amplitude IAF-tACS in a double-blind design.

None of our tACS protocols caused changes in posterior alpha power following tACS. Our intermittent tACS blocks (5-min blocks always separated by 3 min) might have been too short to cause measurable aftereffects (Strüber et al., 2015). Previous studies reporting tACS aftereffects mostly stimulated continuously for longer durations (20–35 min), but with a lower intensity (Kasten et al., 2016; Kasten and Herrmann, 2017; Kemmerer et al., 2020; Neuling et al., 2013; Schuhmann et al., 2019). At the same time, tACS aftereffects have been found after only 10 min of continuous stimulation (Stecher et al., 2017; Zaehle et al., 2010) and after intermittent stimulation of 8 s for 11–15 min (Vossen et al., 2015). At this point, it is thus unclear under what circumstances tACS to PPC can induce EEG aftereffects. In any case, online tACS effects might rely on different mechanisms than tACS aftereffects. Our lack of tACS aftereffects on EEG signals is perhaps interesting in light of some previous reports, but does not invalidate any potential online tACS effects on behavior. In order to more directly investigate the effects of tACS,

analysis of M/EEG data during stimulation will be required, and artifact removal techniques will have to be improved (Helfrich et al., 2014; Holzmann et al., 2021; Neuling et al., 2015; Vosskuhl et al., 2020; Witkowski et al., 2016).

It is important to mention that our broadband-alpha tACS and alpha-removed tACS protocols were based on the individual EEG time series as measured during eyes closed resting state. We recently established that the IAF during cognitive (attention) task performance could be most accurately estimated using resting-state EEG data (rather than task EEG data) (Janssens et al., 2021). However, it is currently unknown to what extent the oscillatory power dynamics present within the broader EEG alpha band are consistent across cognitive states. Future studies could compare the effects of 'replaying' the individual alpha-filtered time series as measured during rest (as done in our study) and as measured during task. For our research questions, the actual time series was not as important as the distribution of frequency content within the alpha-band. One consequence of our approach of 'replaying' the individual oscillatory alpha dynamics is that we currently cannot distinguish whether the 'replay' of the individual time series, or the spectral distribution within the alpha-band, were crucial for inducing the observed broadband-alpha tACS effects.

The broadband-alpha and alpha-removed tACS protocols that we introduced here both include a (small) *range* of frequencies rather than a single frequency (as in the traditional IAF-tACS protocol). This brings to mind an existing form of transcranial electric stimulation (TES) that also includes multiple frequencies, namely, transcranial random noise stimulation (tRNS). Especially when it comes to the apparently similar effects of broadband-alpha and alpha-removed tACS on attention bias, one might wonder whether mechanisms underlying tRNS effects could explain some of our findings. Compared to our protocols, the frequency range in tRNS is much higher and broader (i.e., from ~0.1 to ~100 Hz for 'low-frequency' tRNS and, more conventionally, ~100 to ~700 Hz for ' high-frequency' tRNS) (Antal and Herrmann, 2016; Moret et al., 2019; Paulus, 2011). Our broadband-alpha protocol contained frequencies between the range IAF +/- 2 Hz, and the alpha-removed protocol contained frequencies between 1 and 49 Hz. Besides this, tRNS amplitude/frequency varies randomly, while for our protocols the amplitude/frequency was based on individual EEG data. High-frequency tRNS can increase cortical excitability (Terney et al., 2008), even after only 5 min of stimulation (Chaieb et al., 2011), but a broad range of high frequencies (i.e., much higher/broader than used here) seems to be necessary to achieve this (Moret et al., 2019). Interestingly, tRNS to parietal cortex has recently been shown to affect attention task performance (Contò et al., 2021). This could possibly result from stochastic resonance, where tRNS introduces noise that can modulate the neuronal signal-to-noise ratio in a beneficial way – if delivered at the appropriate intensity (Pavan et al., 2019; van der Groen and Wenderoth, 2016). While we cannot control or account for tRNS-related mechanisms affecting our current results, our protocols seem quite different from conventional tRNS. And such an explanation could only be part of the story, since we found similar effects of broadband-alpha and alpha-removed tACS on attention bias, but effects specific to broadband-alpha tACS on attention benefits. Nevertheless, future studies should explore this connection further, for instance by directly comparing the effects of broadband-alpha and alpha-removed tACS to the effects of established tRNS protocols.

From a clinical perspective also, it could be worth pursuing these broadband tACS protocols in the future. TACS is increasingly being explored as a potential treatment strategy for several brain-based disorders (Elyamany et al., 2020). For instance, alpha tACS has successfully been applied to patients with depression (Alexander et al., 2019; Riddle et al., 2020) and substance use disorder (Daughters et al., 2020). For such clinical applications, a more robust or powerful tACS protocol would be highly meaningful. Even if broadband-alpha tACS were non-inferior (rather than superior) to IAF-tACS in terms of its neural/behavioral effects, it could still be the preferred protocol if its so-

matosensory side-effects are less uncomfortable. Based on informal conversations, it seems that the IAF-tACS protocol was perceived to be the most 'painful' stimulation type, though this needs to be systematically addressed in the future. Furthermore, though speculative, any tACS protocol that could successfully reduce (desynchronize, 'de-entrain'), rather than enhance oscillations within a specific frequency band in a specific brain region, would enable interesting new applications. For instance, the strong rightward attention bias in hemineglect is associated with enhanced alpha power in the damaged right hemisphere (Lasaponara et al., 2019; Pirondini et al., 2020), and depression has been associated with increased gamma activity in frontal and temporal areas (Strelets et al., 2007). As a future outlook, tACS protocols that can reduce oscillatory power seem worthy of pursuit for the potential clinical applications alone. Unfortunately we could here not produce convincing evidence that our alpha-removed tACS protocol had any suppressive effects on local alpha oscillations.

5. Conclusions

Our new, biologically informed broadband-alpha-tACS protocol was well-tolerated by participants, reduced the rightward attention bias in trials without distractors, and reduced attention benefits. These effects were consistent across individuals. IAF-tACS, however, did not modulate attention, further highlighting that its effects can be inconsistent, and that more robust tACS protocols are needed. Still, not all findings were as expected: alpha-removed tACS *also* reduced the rightward attention bias, the reduction in attention benefits after broadband-alpha-tACS was not specific to one hemifield, and attention task performance did not significantly differ in a direct comparison between IAF-tACS and broadband-alpha tACS. These novel developments and findings are thus promising, but in need of further exploration and validation.

Data and code availability statement

All data and code are available on request (without conditions) via the following link: https://doi.org/10.34894/3LYMZF.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Credit authorship contribution statement

Shanice E.W. Janssens: Conceptualization, Investigation, Project administration, Formal analysis, Funding acquisition, Visualization, Writing – original draft, Writing – review & editing. **Sanne Ten Oever:** Conceptualization, Methodology, Software, Supervision, Writing – review & editing. **Alexander T. Sack:** Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing. **Tom A. de Graaf:** Conceptualization, Methodology, Software, Funding acquisition, Supervision, Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2022.119109.

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