Externally induced frontoparietal synchronization modulates network dynamics and enhances working memory performance

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Figure 1. Stimulation parameters, behavioral tasks and RTs in Experiment 1. (A) Participants performed the Choice Reaction Task (CRT) and 1-back and 2-back versions of the N-back task. In the CRT task, participants were shown left or right pointing arrows and were asked to press a button as quickly and accurately as possible to indicate the direction of the arrow. In the 1-back and 2-back tasks, participants were shown a single digit number (0–9) sequentially and were required to report a repetition of the digit occurring one or two trials before, respectively. (B) tACS electrode set-up. Electrodes were positioned at frontoparietal locations F4 (middle frontal gyrus) and P4 (inferior parietal lobule) with a common return at T8 (middle temporal gyrus). TACS was applied at 6 Hz frequency with 0° relative phase between F4 and P4 in the synchronous condition and with 180° relative phase in the desynchronous condition. Stimulation was applied for the duration of the task except for the sham condition where tACS was applied for 30 s in the synchronous condition at the beginning of the task. (C) Reaction times for the CRT, 1-back and 2-back tasks for each of the stimulation conditions (n = 10). Synchronous tACS improved reaction times (RTs) for the more demanding 2-back condition compared both to desynchronous tACS and sham. Error bars represent SEM; *p<0.05, ***p<0.001.

DOI: 10.7554/eLife.22001.003

The following source data is available for figure 1:

Source data 1. This table contains the mean reaction time of each participant for each condition in Figure 1C.
DOI: 10.7554/eLife.22001.004
Figure 1—figure supplement 1. Simulation of the electric field distributions for each tACS condition. The electric field distributions on the cortex resulting from the two tACS conditions were calculated using a realistic finite element model as implemented in SimNibs 2.0. In the case of the tACS 0°, the electric field distributions are shown for each subject. The tACS 180° simulation shows similar patterns.
synchronous tACS condition three electrodes were included in the model: two anodes (F4 and P4) and one cathode (T8). The desynchronous tACS condition was modeled with an anode and a cathode (P4 and F4), to reflect the cancelling of currents in T8 by the opposing flow of currents in the anodes. The localization of each electrode was defined by transforming the electrode center coordinates in MNI space to the space of the individual meshes (native FreeSurfer (http://surfer.nmr.mgh.harvard.edu/) RAS space). The electric field distributions were very similar across participants and are represented for a cohort (n = 12) of the participants in Experiment 2 (n = 24).

DOI: 10.7554/eLife.22001.005
Figure 2. FMRI-tACS setup and stimulation protocol for Experiment 2. (A) The two stimulators were controlled and monitored through a digital to analog converter (DAQ). The stimulators were placed outside the MR shielded room and the current was delivered into the scanner room after being filtered from RF noise by two filter boxes. (B) In Experiment 2, tACS was applied in a pseudo-randomized order during Task blocks (30 s) and fixation (Fix) blocks (20 s). The figure shows tACS applied at the synchronous condition (6 Hz, 0° relative phase between electrodes F4 and P4). The application of short trains of tACS was chosen to investigate the neurophysiological correlates of tACS manipulations on BOLD activity and connectivity. Each participant performed one fMRI run of each task (CRT and 2-back) and tACS condition (synchronous and desynchronous). The order of the four runs was counterbalanced across participants. In each run participants performed 24 blocks (that is, six blocks/condition: ‘task’ + ‘tACS ON’, ‘task’ + ‘tACS OFF’, ‘fixation’ + ‘tACS ON’, ‘fixation’ + ‘tACS OFF’).

DOI: 10.7554/eLife.22001.006
Task-related and tACS ROIs BOLD activity. (A) Activation patterns elicited by the 2-back (n = 21) and CRT (n = 20) tasks for tACS OFF, synchronous (tACS 0°) and desynchronous (tACS 180°) conditions. Warm colors represent increased BOLD signal relative to baseline (task > fixation tACS OFF) and cold colors a decrease in activity (fixation tACS OFF > task). (B) Increased activity in the IPL-electrode region is correlated with faster reaction times (RT) in the 2-back task condition (r = −0.39, p=0.039, one-tailed, n = 21). Y axis corresponds to the contrast estimates for the tACS 0° condition (extracted from the voxels showing increased brain activity for tACS 0° > tACS OFF, (A)) and the X axis corresponds to RTs during the synchronous tACS 0° condition. (C) During the CRT task, BOLD signal was increased in the MFG-electrode region for the synchronous tACS condition compared to task periods without tACS (n = 20). White regions indicate the tACS electrodes masks (tACS ROIs). Images are in the Montreal Neurological Institute (MNI) space coordinates and in radiological space. R=right hemisphere. Threshold Z > 2.3 with a corrected cluster significance level of p<0.05.

DOI: 10.7554/eLife.22001.007

The following source data is available for figure 3:

Source data 1. This folder contains the MRI contrast maps in Figure 3A, both thresholded (that is, corrected for multiple comparison using cluster correction) and non-thresholded.
DOI: 10.7554/eLife.22001.008

Source data 2. This folder contains the MRI contrast maps in Figure 3B, both thresholded (that is, corrected for multiple comparison using cluster correction) and non-thresholded and the IPL-electrode and MFG-electrode masks.
DOI: 10.7554/eLife.22001.009

Source data 3. This table contains the mean reaction time and BOLD parameter estimates used for the correlation in Figure 3B.
DOI: 10.7554/eLife.22001.010
Figure 4. Whole-brain patterns elicited by synchronous and desynchronous tACS conditions. (A) Synchronous tACS during the 2-back task increased BOLD signal in brain regions underneath the parietal, IPL-electrode (inferior parietal lobule), and frontal, MFG-electrode (medial frontal gyrus), electrodes \( n = 21 \). (B) During the 2-back task synchronous tACS showed significantly greater activity than tACS OFF in the right frontoparietal network and regions normally activated by task performance. Desynchronous tACS resulted in decreased activation compared to tACS OFF in default mode network regions. TACS applied during the CRT task resulted in greater activity in occipito-temporal regions for both synchronous and desynchronous tACS conditions. (C) Increased BOLD signal for synchronous compared to desynchronous tACS conditions, for tACS stimulation relative to no tACS stimulation, was observed in the left hemisphere in the inferior parietal lobule (IPL), superior frontal gyrus (SFG) and orbitofrontal cortex (OFC). This difference in brain activity is explained by decreased activity during desynchronous compared to synchronous tACS, right plot. Images are in the Montreal Neurological Institute (MNI) space coordinates and in radiological space. \( R = \) right hemisphere. All images have been thresholded with FSL clusterwise correction \( Z > 2.3, p<0.05 \).

*Figure 4 continued on next page*
The following source data is available for figure 4:

**Source data 1.** This folder contains the MRI contrast maps in *Figure 4*, both thresholded (that is, corrected for multiple comparison using cluster correction) and non-thresholded.
DOI: 10.7554/eLife.22001.012

**Source data 2.** This folder contains the MRI contrast maps in *Figure 4—figure supplement 1*, both thresholded (that is, corrected for multiple comparison using cluster correction) and non-thresholded.
DOI: 10.7554/eLife.22001.013

**Source data 3.** This table contains the parameter estimates for each subject in the bar plot in *Figure 4B*.
DOI: 10.7554/eLife.22001.014
Figure 4—figure supplement 1. Whole-brain BOLD signal elicited by synchronous and desynchronous tACS conditions during Fixation. Warm colors represent increased BOLD signal related to baseline using standardized fMRI subtraction analysis (fixation tACS ON > fixation tACS OFF) and cold colors a decrease in activity (fixation tACS OFF > fixation tACS ON). Only decreases in activity were observed. Fixation periods with tACS stimulation during CRT (n = 20) runs showed decreased BOLD signal in occipital, temporal, parietal and motor cortices extending to the middle and superior frontal gyri. During desynchronous stimulation of the fixation blocks for the 2-back run (n = 21) a decrease in BOLD signal was present in the frontal poles and superior frontal gyrus, while no modulation of BOLD signal was observed for the synchronous tACS condition. Comparisons of synchronous and desynchronous tACS conditions did not show significant differences either for the CRT or the 2-back runs. Images are in the Montreal Neurological Institute (MNI) space coordinates and in radiological space. All images have been thresholded with FSL clusterwise correction Z > 2.3, p<0.05.
DOI: 10.7554/eLife.22001.015
Figure 5. Functional connectivity in the 2-back task during synchronous and desynchronous tACS. Differential connectivity for synchronous versus desynchronous tACS during the 2-back task (n = 21). Synchronous tACS resulted in increased functional connectivity in comparison to tACS OFF between the parietal electrode region, IPL-electrode, and the dorsolateral prefrontal cortex during task performance. The desynchronous tACS condition increased functional connectivity between the parietal and frontal stimulated regions (IPL-electrode and MFG-electrode, respectively) and occipito-temporal regions. Images are in the Montreal Neurological Institute (MNI) space coordinates and in radiological space. All images have been thresholded with FSL clusterwise correction Z > 2.3, p<0.05.
DOI: 10.7554/eLife.22001.016

The following source data is available for figure 5:

Source data 1. This folder contains the MRI contrast maps in Figure 5, both thresholded (that is, corrected for multiple comparison using cluster correction) and non-thresholded.
 DOI: 10.7554/eLife.22001.017